Temporal Logic-based Fuzzy Decision Support System for Diagnosis of Rheumatic Fever and Rheumatic Heart Disease

Sanjib Raj Pandey

Department of Computing and Information Systems

Faculty of Architecture, Computing and Humanities

University of Greenwich

London, UK.

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DECLARATION

"I certify that this work has not been accepted in substance for any degree and is not concurrently being submitted for any degree other than that of Doctor of Philosophy being studies at the University of Greenwich. I also declare that this work is the result of my own investigations except where otherwise identified by references and that I have not plagiarized from the work of others"

Sanjib Raj Pandey	Date
Dr. Jixin Ma (1st Supervisor)	Date
Prof. Choi-Hong Lai (2nd Supervisor)	Date

DEDICATION

In loving memory of my grandfather Padma Dhoj Pandey, grandmother Tikka Kumari Pandey, grandmother Oaj Kumari Pandey and brother Suraj Raj Pandey; all of them would have been very proud of this achievement.

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ABSTRACT

This is a collaboration project between the Nepal Heart Foundation (NHF) and the University of Greenwich (UoG), United Kingdom (UK). Our mutual aim, agreed at the outset, has been to analyse, design and develop a cost effective Clinical Decision Support System (CDSS) for diagnosis and recognition of Acute Rheumatic Fever (ARF) and Rheumatic Heart Disease (RHD) at an early stage by developing/adopting UK's and NHF's treatment practices and procedures that would be appropriate for the Nepalese environment and lifestyle. The Application we developed was designed for use by community health workers and doctors in the rural areas of Nepal where laboratory facilities, expert services and technology are often deficient.

The research undertaken investigated three problems that previously had not been addressed in the Artificial Intelligence (AI) community. These are: 1) ARF in Nepal has created a lot of confusion in diagnosis and treatment, due to the lack of standard procedures; 2) the adoption of foreign guidelines is often not effective and does not suit the Nepali environment and lifestyle and 3) the value of combining (our proposed) Hybrid Approach (Knowledge-based System (KBS), Temporal Theory (TT) and Fuzzy Logic (FL)) to design and develop an application to diagnose ARF cases at an early stage in English and Nepali.

This research presents, validates and evaluates a proposed Hybrid Approach to diagnose ARF at three different stages: 1) Detected; 2) Suspected and 3) Not-detected and also to identify the severity level of detected ARF in the forms of Severe Case, Moderate Case or Mild Case. The Hybrid Approach is a combination of the KBS/Boolean Rule Model, Temporal Model and Fuzzy Model. The KBS/Boolean Rule Model has four components for design and implementation of KBS. These are: identifying the ARF stage in a case; Rule Pattern Matching; New Rule Formation and Rule Selection Mechanism. The Temporal Model has four components namely: Descriptive Explanation of ARF symptoms; Temporal Lookup-Table/Rules and Temporal Reasoning which produce a Temporal Template for demonstrating the relationship between the signs and ARF. The Fuzzification, Fuzzy Inferences and Defuzzification components are applied to design and implement a Fuzzy Model. The research undertaken divided the overall ARF diagnosis problem, in effect its requirements, into several sub-problems and each model of the Hybrid Approach

addressed particular sub-problems for example, *Identify the stage of the ARF* component of the KBS/Boolean Rule Model used to solve the question of identifying the stage of ARF based on the symptoms presented. Each problem was therefore handled using a particular model's components. This significantly helped to improve maintainability, reliability and the overall quality of our final ARF Diagnosis Application.

The developed ARF Diagnosis Application was experimentally tested and evaluated by NHF's experts and users through applying NHF's data sets consisting of 676 real patients' records. The ARF Diagnosis Application was found to match 99% of the cases derived from NHF's datasets. The overall ARF diagnostics performance and accuracy was 99.36%. Therefore, the experiments and evaluations of our ARF Diagnosis Application proved that it was logically and technically feasible to employ the Hybrid Approach for developing a new and practical ARF Diagnosis Application. The Application was ultimately developed and succeeded in embracing NHF's requirements and guidelines thereby matching the Nepalese setting and making it suitable for use in Nepal having fully by met the exigencies of the Nepalese environment and lifestyle. Application of a new ARF diagnosis system (ours) proved that the Hybrid Approach, applied methods of diagnosis of ARF, medication and treatment plan, including help and supporting information which were identified and defined, were shown to be appropriate to support effectively community health workers and doctors who actively care for ARF and RHD cases in rural Nepal.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

AHP	:	Analytical Hierarchy Process
AI	:	Artificial Intelligence
AIRS	:	Artificial Immune Recognition System
ANN	:	Artificial Neural Network
ARF	:	Acute Rheumatic Fever
ASOT	:	Antistreptococcal antibody Titres
BPG	:	Benzathine Penicillin G
CDSS	:	Clinical Decision Support System
CRP	:	C-reactive protein (blood test)
DBMS	:	Database Management System
DSS	:	Decision Support System
DWT	:	Discrete Wavelet Transforms
ECG	:	Electrocardiogram
ECHO	:	Echocardiography
ECS	:	Ensemble Classifiers Strategy
EM	:	Erythema Marginatum
EMR	:	Electronic Medical Record
ESR	:	Erythrocyte Sedimentation Rate (blood test)
FCM	:	Fuzzy Cognitive Maps
FL	:	Fuzzy Logic
FM	:	Fuzzy Model
FMMC	:	Fuzzy Max–Min Composition
FSVM	:	Fuzzy Support Vector Machines
GA	:	Genetic Algorithm
GABHS	:	Group A Beta-Haemolytic Streptococcus (GABHS)
GAS	:	Group A Streptococci
GDSS	:	Group Decision Support System
ICM	:	Intelligent Computing Method
ICU	:	Intensive Care Unit
KBS	:	Knowledge-based System
MBR	:	Model-based Reasoning
MediKES	:	Medical Knowledge Elicitation System

MICU	:	Medical Intensive Care Unit
MILMF	:	Monotonically Increasing Linear Membership Function
MLM	:	Medical Logic Modules
NHC	:	National Health Centre
NHF	:	Nepal Heart Foundation
NLP	:	Natural Language Processing
NN	:	Neural Networks
NRF	:	New Rule Formation
OLAP	:	Online Analytical Processing
RBS	:	Rule-based System
RHD	:	Rheumatic Heart Disease
RPM	:	Rule Pattern Matching
RSM	:	Rule Selection Mechanism
SMS	:	Search and Match Stage
SN	:	Subcutaneous Nodules
TL	:	Temporal Logic
TM	:	Temporal Model
UMLS	:	Unified Medical Language System
WHF	:	World Heart Federation
WHO	:	World Health Organization

Chapter 1: Introduction

"Everyone is a genius. But if you judge a fish by its ability to climb a tree it will live its whole life believing that it is stupid." Albert Einstein

1.1. Introduction

This is a collaboration project between the Nepal Heart Foundation (NHF) and the University of Greenwich (UoG), United Kingdom (UK). Our mutual aim is to analyse, design and develop a cost effective Clinical Decision Support System (CDSS) for diagnosis and recognition of Acute Rheumatic Fever (ARF) and Rheumatic Heart Disease (RHD) at an early stage by developing/adopting the UK, Australia, World Health Organization's and NHF's treatment practices and procedures that will be appropriate for the Nepalese environment and lifestyle. It was acknowledged from the outset that the model should be especially applicable for use by community health workers and doctors in rural areas where laboratory facilities, expert services and technology are often deficient.

ARF and RHD is a challenging and life-threatening disease among children aged between 5-15 years, particularly in the rural areas of Nepal. Untreated streptococcal throat infection, which is common among Nepalese children, is the primary cause of ARF and this is considered to be one of the biggest health risks in comparison with other heart diseases. Early diagnosis of ARF/RHD will cost the patient NRs. 25.00 (relative to GB Pound = £0.25) but the late diagnosis or in the event of neglecting the symptoms, the delay can cost around NRs. 2,00,000 to 3,00,000 or more (equivalent to GB Pound £1,225 – £1,837) for treatment and paradoxically can be sometimes the cause of death.

The ARF and RHD control program exists in Nepal and it is funded by the Nepalese Ministry of Health (MoH) and facilitated by NHF. NHF is a group of cardiac specialists and other medical professionals established in 1988 as a non-government organization with a view to promoting awareness and other programs regarding heart diseases throughout 63 districts out of a total of 75 districts. Details are provided in Chapter 4, Research Methodology

1.2. Country Background

Nepal is a mountainous and landlocked country in South Asia, covering an area of 147,181 Km^2. Its neighbouring countries are China to the North and India to the East,

West and South. The country is divided into three regions Himalayan/Mountain (all the northern part), Hilly (Middle Part) and Terai (Southern Part), with agriculture as the main occupation. Although, the majority of people are Hindu, Nepal has adopted the policy of embracing other religious through secularism. Nepal is recognised as one of the world's developing countries with a population of 30.49 million, with 80% of the population living in rural areas (UN: World Statistics Pocketbook, 2013). Kathmandu is the capital with nearly one million inhabitants. Nepali is the native language, but most of the urban population can speak English. According to a World Health Organization (WHO) report, 35.58% of the population are under 15 years and life expectancy for both sexes (Male and Female) is 68 (WHO: Nepal Statistics Summary, 2014). The total expenditure on health was 5.4% of GDP in 2011 and the density of physicians was 0.21 per 1000 people in 2004 (WHO: Country Cooperative Strategy at a Glance, 2014). The general government expenditure on health is 9.6% of total government expenditure and private expenditure on health was estimated at 60.7% of total expenditure on health in 2011 (WHO: Country Cooperative Strategy at a Glance, 2014). The country's human development index was ranked 157 out of 186 countries in 2012 (WHO: Country Cooperative Strategy at a Glance, 2014).

The majority of the country's health resources, infrastructure, and manpower are focussed in the urban areas (Shrestha and Bhandari, 2012). The country has recently overcome big political unrest due to a Maoists insurgency, which claimed several thousand lives. The country had a monarchical system, now it is the Federal Democratic Republic of Nepal. After restoration of democracy, Nepal remains a much under-developed country. Twenty-five per cent of the population live below the poverty line with the majority residing in rural areas. They are deprived from a basic health care system and do not have good knowledge of health literacy either (Shrestha M. K., 2014). Most of the rural inhabitants still believe in traditional treatment procedures, which include consultant priests and astrologers for the cure of diseases. A Nepali has a very low per capita income so that modern hospitals found in big cities are only affordable by a few. Due to treacherous geographical conditions, lack of modern facilities and low-income potential, medical and other experts tend not want to live and work in rural areas to provide their services. Thus, the majority of rural people are suffering from a deficient basic health care system. As a result, computer-based clinical information systems could provide alternative solutions where expert services are unavailable or very expensive.

1.3. Problem Justification

ARF and RHD is a very a serious problem in Nepal. As many as 1,000 children die each year due to ARF and RHD. The disease can be cured at the initial stage if firstly we are able to recognize and treat the Group A Streptococcal (GAS) infection in the throat and secondly if there is correct diagnosis of the ARF and RHD's signs and symptoms followed by application of proper treatment procedures. Thus, if we develop and implement an effective ARF diagnosis system, we can not only save children's lives but also save cost and time. We therefore postulated that the use of a practical CDSS in the diagnosis of ARF would be of great help to inexperienced doctors, community rural health workers and other medical practitioners.

During my first field visit to Nepal, the aim was to establish a collaborative link with NHF and to carry out a fact finding exercise that would allow me to devise suitable data collection methods, study the existing ARF and RHD situation, recognize the country's technology, and understand the local procedures currently being used to diagnose ARF and RHD. My initial assessment revealed that although the country's district hospitals have Information and Communication Technologies (ICT) infrastructure, such technologies are limited to basic office work and not being applied to clinical tasks e.g. diagnosis processes, medication therapy planning, laboratory processes, interpretation of results, scheduling for patient check-up and so forth. In regard to the diagnosis of ARF and RHD, I found that doctors make their decisions based on laboratory results when they are available, and usually use their own judgement based on experience to diagnose eventually a case. In some cases, where experts are not present, some inexperienced doctors may employ trial and error methods to make a diagnosis. This crude approach can be dangerous and harmful for patients. In summary, the following problems were identified regarding diagnosis and management of ARF and RHD in Nepal:

- In most rural areas, lack of awareness and ignorance of the initial signs and symptoms of ARF are key causes of serious damage to the heart (RHD).

- Also in rural areas, people continue to believe in folk treatment practices. Patients consult the local priests or astrologers and follow their instruction for the treatment of ills e.g. visit the numerous deities and worship or sacrifice hens, goats, buffalo, duck etc. Eventually when the patient's situation gets worse only then they decide to visit the nearest hospital for treatment, which in many cases, is too late and culminates in death.

- The diagnosis of ARF and RHD is complicated and often missed by health professionals including doctors and community rural health workers leading inevitably to damage of the heart (RHD).

- It is difficult for inexperienced doctors and community rural health workers to assess accurately the severity of ARF and RHD when multiple symptoms and associated multiple risk factors are present.

- According to NHF, patients often complain about penicillin injections because of pain. As a result, about 5% of patients on secondary prophylaxis are known to stop taking prescribed Benzathine Penicillin G (BPG).

- It is a problem for community rural health workers to treat and manage ARF and RHD after diagnosis having to take into account all aspects such as injection or oral treatment, appropriate length of treatment period, dosage of injections or whether to use oral medication or not. Safe injecting methods clearly can reduce the pain and ensure effective treatment.

- At the National seminar on ARF/RHD Prevention and Control in Nepal, 2011, it was stated clearly that "*The lack of guidelines on ARF/RHD in Nepal has created a lot of confusion in diagnosis and treatment, even among qualified doctors. It was found that adoption of foreign guidelines was not effective as they do not match the Nepali environment and lifestyle.*

- At present Nepal does not have standard procedures and practices to diagnose and manage ARF/RHD. Diagnosis and treatment is exclusively based on the judgement and decisions of individual doctors and community rural health workers. There is therefore a high chance of misdiagnosis and mistreatment of ARF/RHD.

- Due to high poverty levels in Nepal, most rural dwellers can hardly access good medical care as fully equipped hospitals with experienced specialists for treating ARF/RHD can only be found and afforded in urban areas. Efforts are being made to explore the use of CDSS to help inexperienced doctors in the diagnosis of ARF/RHD. CDSS along the lines used currently in various sectors of medical sciences in developed countries. Unfortunately, for under-developed countries such as Nepal, these technologies are still not available. Although Nepal has invested in ICTs the use of CDSS in medical diagnosis has yet to be undertaken. To date there is no

information system designed to support medical diagnostics, consequently, our proposed research aimed at exploring the use of CDSS in the diagnosis of ARF.

1.4. Research Overall Goal

This research was designed to investigate the three problems which had previously not been addressed in the AI community, which are: 1) ARF in Nepal has created a lot of confusion in the diagnosis and treatment, due to the lack of standard procedures; 2) the adoption of foreign guidelines is not effective and does not suit the Nepali environment and lifestyle, 3) using (our proposed) Hybrid Approach (Knowledge-based System, Temporal Theory and Fuzzy Logic) together in order to design and develop a system for diagnosis of ARF cases at an early stage in English and Nepali.

The overall goal of this research was to design, develop and experiment symptoms and guidelines to be based on a CDSS for diagnosis of ARF in Nepal. The developed system would need to accord with the demands of the Nepalese environment and lifestyle and must be suitable for use by both qualified doctors and community rural health workers engaged in diagnosis and management of ARF cases.

1.5. Research Questions

The research was aimed at answering the following questions:

1.5.1. Is it feasible to apply Hybrid Approach (Knowledge-based System, Temporal Theory and Fuzzy Logic) to design and develop a cost effective and practical CDSS model for the diagnosis of ARF that is suitable for the Nepalese environment and lifestyle?

The above research question is more general, more specific questions are:

1.5.1.1. Is it appropriate for the diagnosis of ARF disease in the form of either Detected ARF (severity level: Severe Case, Moderate Case and Mild Case) or Suspected ARF (laboratory test) or Not-detected ARF (other diseases) in Nepal.

1.5.1.2. Is it valid to develop a New Rule Formation process for the rule-based system for diagnosis of ARF?

1.5.1.3. Is it appropriate to produce the temporal constraints to show the relation between symptoms and ARF?

1.5.1.4. Is it applicable to feed the Fuzzy value into pre-satisfied rules; justifying it to make a final decision in an ARF case?

1.5.1.5. Is it possible to develop the CDSS for diagnosis of ARF in Nepal based on the country's available ICT resources?

1.5.1.6. What type of user interface should be provided to a user, suitable for doctors and community rural health workers and those who are not familiar with using a clinical decision support system at all?

1.5.1.7. Is it practical to apply and implement an automated ARF Diagnosis Application in the rural areas of Nepal?

1.6. Research Objectives

The objectives of the research is outlined below:

- To examine existing clinical practice and procedures of doctors and community rural health workers in diagnosis and management of ARF in Nepal.
- To investigate existing ARF diagnosis processes from the World Health Organization, Jones criteria, World Heart Federation, Australia, New Zealand, National Health Service (NHS Choice, UK) and NHF's expert guidelines.
- To acquire the required ARF knowledge (clinical dataset, diagnosis process and practice) from the Nepalese environment and lifestyle and use the research findings to support development of English and Nepalese versions.
- To investigate the feasibility of employing the ARF Diagnosis Application in a Hybrid Approach using C#.NET, MS Access, Windows O/S etc.
- To develop techniques in Knowledge-based Systems, Temporal Theory and Fuzzy Logic for use in a new ARF diagnosis model.
- To develop a suitable, easy to use and affordable CDSS application for diagnosis of ARF in Nepal.
- To evaluate and verify the application using NHF's real dataset.

1.7. Research Significance

The research investigates the ARF diagnosis process and practice from other countries Australia, New Zealand, NHS Choice (UK), WHO, Jones criteria, WHF and NHF. However, it was appreciated that due to the geographical location and environment, ARF treatment practice and procedure might differ from one country to another. WHF's guideline indicated that for diagnosis and management of ARF, local guidelines are very important in making a decision in a local ARF case. Therefore, in this research we focussed on how to organize the treatment practice according to NHF experts' guidelines in order to design and develop a unique procedure for diagnosis of ARF by integrating those with the WHO's and other countries' guidelines. This is discussed in more detail in the Research Methodology, Chapter 4.

The research investigates the use of knowledge-based, reasoning, temporal theory and fuzzy logic together appropriately and develops a clinical decision support system for

The research investigates the use of Knowledge-based, reasoning, Temporal and Fuzzy Logic combined appropriately and develop a CDSS for diagnosis of ARF in Nepal. The research explores the concept of New Rule Formation algorithm based on the knowledge base and explains how such types of algorithm can help to produce rules without expertise support. In addition, how easily community health workers or doctors can use this rule to diagnose ARF without expert support. The research shows how the Rule Selection Mechanism supports the selection of the best-matched rule and avoids superfluous rules. The research also investigates how Temporal Logic, especially Point-based Temporal Theory, can be applied to analyse the relation between the symptoms and diseases.

The guidelines for the diagnosis of ARF have changed frequently (in 1944, 1956, 1965, 1988, 1992 and 2003 (Appendix 2.1). The ARF symptoms also vary slightly from country to country due to the geographical location, environment, social conditions and country's treatment procedure and practice. Consequently, an ARF diagnosis system needs to be updated according to changing requirements. Thus, a symptom and guideline based decision support system is appropriate for the diagnosis of ARF. Knowledge about ARF will inevitably expand and change in future and it is unlikely that the rural health worker will know about these changes without support. Our developed ARF Diagnosis Application will inform/alert such changes to the users.

1.8. Road Map of this Thesis

This thesis comprises seven chapters, which are set out below:

Chapter 1: Introduction

This chapter provides an introduction with background information on Nepal, problem justification, research questions, research objectives, research significance and thesis structure.

Chapter 2 : Literature Review

This chapter provides a survey of literature relevant to the research particularly ARF and RHD signs and symptoms and the current situation of ARF and RHD in Nepal. The diagnosis process from different sources specially WHO, WHF, NHS Choice (UK), New Zealand, Australia. CDSS, Temporal Theory and Fuzzy Logic, Hybrid methodology and approach are also discussed. Although there are many publications with useful information on medical system the review was limited to research publications relevant specifically to our work with the intention of demonstrating that the research questions are of relevance and value to the CDSS community.

Chapter 3 : Acute Rheumatic Fever and Conceptual Framework

This chapter describes the ARF and RHD prevention and control plan. It also explains the signs and symptoms of ARF with illustrations, diagnosis processes, required laboratory tests and a treatment plan for ARF in Nepal. The chapter describes details of the conceptual framework of Diagnosis of ARF in the Nepalese setting.

Chapter 4 : Research Methodology

This chapter describes country specific procedures to diagnose ARF disease; related important signs and symptoms and a proposed Hybrid Approach for diagnosis of ARF. It also describes each of the models of our employed for a Hybrid process: Knowledge-Based/Boolean Rule Model, Temporal Model and Fuzzy Model.

Chapter 5 : Research Analysis, Design and Development.

The aim of this chapter is to prove the validity of our proposed Hybrid Approach and whether or not it can be applied to the diagnosis of ARF in the Nepalese setting. The chapter describes the analysis, design and development process of a prototype. The design architecture, algorithm of all processes, domain knowledge modelling, prototyping, inference engine, user interface, databases, and the use of a three-layer architecture of ARF Diagnosis Application are discussed.

Chapter 6 : Experiments and Evaluation

This chapter describes ARF Diagnosis Application by experiment and evaluation. It also describes the overall performance of ARF Diagnosis Application where the focus is on the evaluation of a Hybrid Approach, experimentation and evaluation of all applied techniques and algorithm.

Chapter 7: Conclusion and Future work

This chapter summarises the whole research study, recapitulates the main findings, of the research, its contributions and future improvement. It finally discusses the potential for future research.

Chapter 2: Literature Review

"Imagination is more important than knowledge", Albert Einstein

2.1. Introduction

This chapter describes ARF and RHD signs and symptoms, diagnosis criteria of ARF, the current situation of ARF and RHD in Nepal and NHF's program for the prevention of ARF. It also investigates information and guideline on ARF disease from other countries. Similarly described are the DSS/CDSS, its history and CDSS methods and techniques. In addition, the Knowledge-based System, a non-knowledge-based system, Temporal Theory, Fuzzy Logic and Hybrid methodology, which are being used in different medical domains, are also expressly described. The uncertainties of CDSS and the fundamental problem of technology transfer from developed countries to Nepal are discussed. The conclusion underlines and presents our (NHF and University of Greenwich) Hybrid Approach for the diagnosis of ARF with full justification for the Hybrid Approach provided in the final summary.

2.2. Acute Rheumatic Fever and Rheumatic Heart Disease

ARF is a type of sickness caused by reaction to bacterial infection and is usually a precursor to RHD. ARF is a non-supportive complication of Group A Beta Haemolytic Streptococcal (GABHS) sore throat. It affects joints, skin, subcutaneous tissue, brain and the heart (English PC, 1999). An untreated Group A streptococcal infection can lead to ARF and untreated ARF can lead to RHD. Similarly, repeated GAS infection or recurrent ARF can lead to damage heart valves that may necessitate expensive surgery. ARF can be diagnosed in people up to 20 years old. ARF is less common after the age of 35 years and is rare under 4 years and over 40 years of age. However, it should be accepted that ARF could occur in all age groups within any high-risk population (World Heart Federation, 2007).

It has been noted that ARF is particularly common amongst school-aged children in developing countries. Even in developed countries, it was found to be a major cause of death in children until 1960. ARF is caused by "*Lancefield group A beta-haemolytic streptococci (GPA BHS) of which those with the M antigen are most likely to cause the disease (M types 3, 5, 18, 19, 24). However ARF and RHD have been discovered in communities where other responsible serotypes have been found*" (Cilliers AM, 2006).

The incidence of ARF in developing countries remains high. Even the indigenous populations of technically advanced Australia and New Zealand have some of the highest incidences recorded in recent years, with 374 per 100,000 per year in those aged 5 to 14 years. Around 60% of these patients develop RHD. Sub-Saharan Africa also has the highest estimated regional prevalence of RHD (5.7 per 1,000) (Cilliers AM, 2006).

The WHO's technical report of 2001 on Rheumatic Fever (RF) and RHD states "*RF and RHD are nonsuppurative complications of Group A streptococcal pharyngitis due to a delayed immune response. Although RF and RHD are rare in developed countries, they are still major public health problems among children and young adults in developing countries (1–6)"* (WHO, 2001). There is no exact figure to identify the global burden of GAS. However, there are at least 517,000 deaths each year due to ARF, RHD, Post-Streptococcal glomerulonephritis and invasive infections (Carapetis *et al*., 2005). According to WHO, approximately 18.1 million people are currently suffering from serious Group A Streptococcal Disease (GAS), whilst 1.78 million new cases occur each year with 0.5 million deaths recorded each year. The same report states that a minimum of 15.6 million people worldwide have RHD, with 282,000 new cases each year and 233,000 cases resulting in deaths each year (WHO, 2005). According to Carapetis (2005), invasive GAS diseases are very high suggesting a minimum of 663,000 new cases and 163,000 deaths each year.

ARF affects the joints, skin, heart and nervous system. ARF is an autoimmune disorder with a high inheritability. The disease is dependent upon the immune response of the individual and only 3-6% of people have the requisite genetic configuration. The discovery of all genetic susceptibility loci through whole genome scanning may provide a clinically useful genetic risk prediction tool for ARF and its sequel, RHD (Engel M.E., *et al*., 2011). The use of echocardiography in developing countries helps to recognize the prevalence of RHD (Marijon E. *et al*., 2007). *RHD presents itself as damage to the heart valves as the result of repeated attacks of ARF. The valves become stretched and scarred and do not move normally. The valves may not close properly which can allow blood to leak backwards, and/or the valves may not open properly which can cause blood flow to be blocked. If RHD is not diagnosed and managed early, it may result in heart failure and premature death* (WHF, 2008).

The percentage of ARF major and minor criteria in WHO regions are provided in Table 2.1, adapted from Michael D. S., (2011).

Table 2.1: Percentage of Major and Minor ARF Criteria by WHO

WHO region	Males	Recurrences	Major criteria					Minor criteria				
			Carditis	Arthritis	EM	Chorea	Nodules	Arthralgia	Fever	↑PR	ESR	ASO
The Americas	54.7%	22.0%	52.8%	64.4%	7.8%	15.3%	3.8%	40.9%	63.9%	23.3%	84.2%	79.4%
Europe	54.7%	7.9%	62.0%	65.7%	5.5%	12.3%	8.0%	43.1%	68.9%	26.3%	81.5%	78.3%
Africa	50.1%	17.9%	63.3%	48.9%	1.7%	8.8%	4.8%	55.5%	35.4%	22.7%	52.9%	48.7%
Eastern Mediterranean	54.4%	27.9%	60.3%	63.5%	2.8%	8.0%	1.6%	34.5%	74.8%	20.3%	90.5%	86.9%
Western Pacific	48.2%	22.6%	67.5%	54.3%	11.0%	11.7%	1.5%	35.1%	68.4%	24.7%	91.0%	72.3%
Southeast Asia	57.4%	33.9%	66.0%	46.0%	0.8%	15.4%	4.4%	45.5%	71.3%	28.9%	71.9%	60.9%
All	53.7%	21.9%	59.5%	59.3%	5.9%	12.9%	3.7%	40.7%	65.6%	24.1%	81.4%	75.3%

Note: Proportions are restricted to acute rheumatic fever patients.
Abbreviations: EM, erythema marginatum; ↑PR, prolonged PR interval on ECG; ESR, increased erythrocyte sedimentation rate; ASO, elevated antistreptolysin O titer.

The following Figure 2.1 shows the worldwide incidence of ARF 1970 to the present, based on (Michael D. S., 2011).

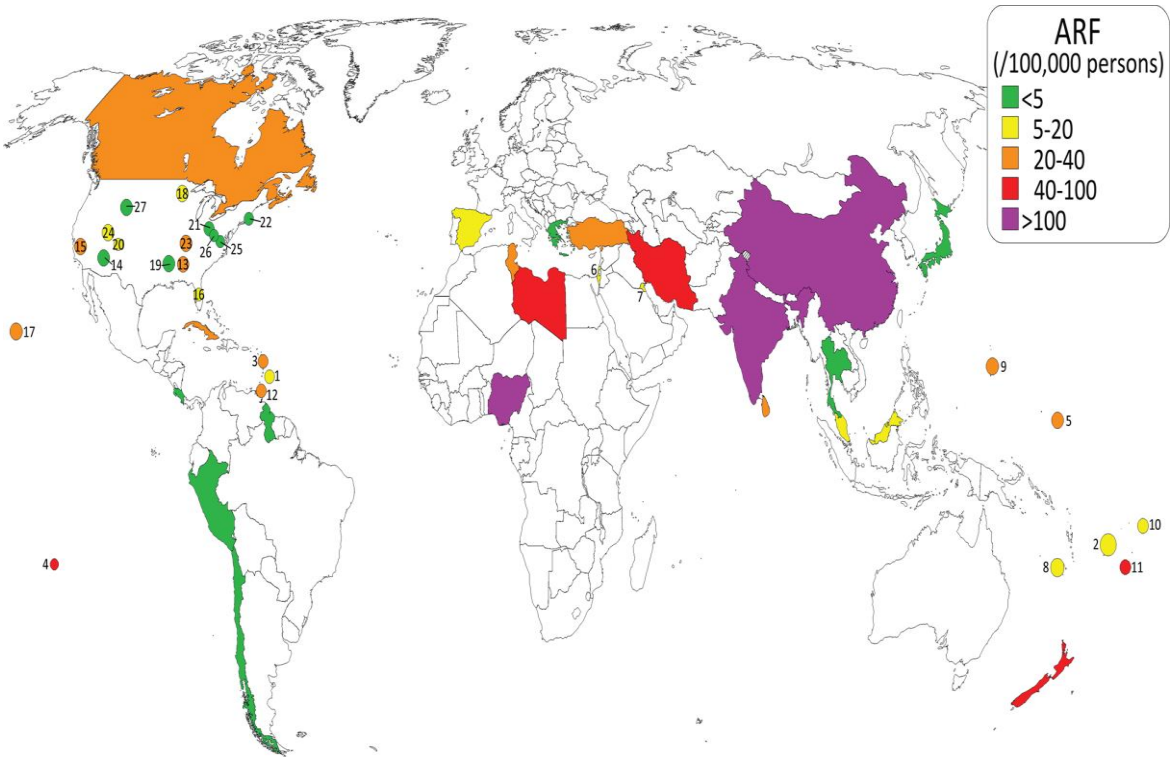


Figure 2.1: Worldwide Incidence of ARF from 1970 to 1990

Figure 2.2 illustrates the worldwide incidence of ARF from 1991 to the present, based upon Michael D. S., (2011).

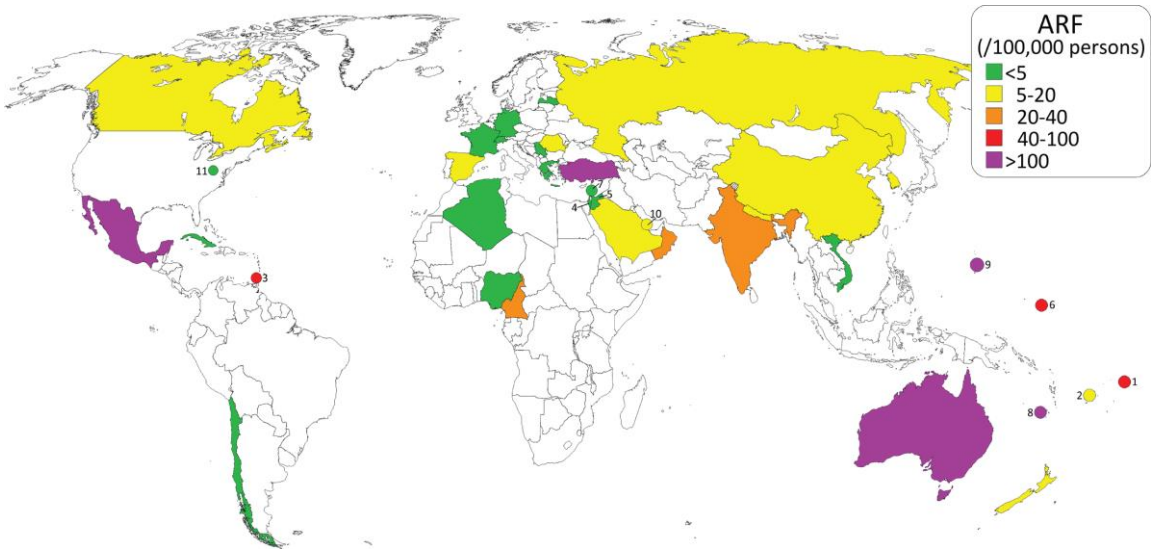


Figure 2.2 : Worldwide Incidence of ARF From 1991 tro the present.

2.3. Consequences of ARF

ARF evidently affects children's heart, joints and central nervous system. "*ARF is its ability to cause fibrosis of heart valves, leading to crippling valvular heart disease, heart failure and death"* (WHF, 2012).

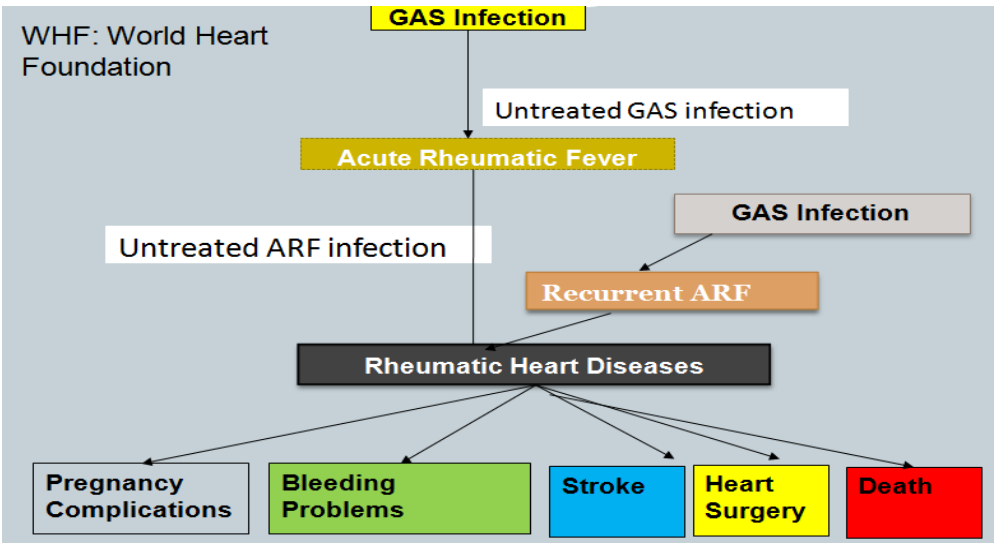


Figure 2.3: Progression of Heart Disease

2.4. Causes of ARF

Poor housing, poor economic conditions, poor sanitation, over-crowding, lack of balanced diet, lack of proper awareness about diseases, lack of access to basic healthcare, living in a tropical climate (WHF, 2007), are the causes of ARF in developing countries (Mendis S. *et al*., 2011). Although it is clear that socio-economic and environmental factors play

an indirect role among the causes of ARF, the most important prevailing reason is poor quality health-care delivery systems, notably shortage of basic health-care resources, inadequate expertise of health-care providers and fundamentally poor awareness of the ARF disease itself. Details are summarised in Table 2.2 adapted from WHF (2007).

Table 2.2: Direct and Indirect Results of Environmental and Health-System Determinants on ARF/RHD

Determinants	Effects	Impact on ARF & RHD burden
Socioeconomic & environmental factors 1. Poverty 2. Poor nutrition 3. Overcrowding 4. Poor standard of housing.	1. Rapid spread of Group A streptococcal strains 2. Difficulties accessing health care	1. Higher incidence of acute strep pharyngitis and complications 2. Higher incidence of ARF and recurrent ARF.
Health system related factors: 1. Shortages of resources for health care 2. Low level of knowledge of disease among health-care providers 3. Low-level of awareness of the disease in the community.	1. Inadequate diagnosis and treatment of strep pharyngitis 2. Misdiagnosis or late diagnosis of ARF 3. Inadequate secondary prophylaxis delivery.	1. Higher incidence of ARF and recurrent ARF 2. Missed first ARF episode. 3. Inadequate secondary prophylaxis delivery 4. Higher rates of recurrent ARF with more frequent and severe heart valve involvement. 5. Higher rates of repeated hospital admissions and expensive heart valve surgery.

2.5. Symptoms of ARF and RHD

Our research included review of journals, conference papers and WHO, and WHF,, reports relating mainly to Australia and New Zealand; NHF; NHS Choice Website (UK) and MedScape Website, focussing largely on the signs and symptoms of ARF. Similarly, ARF's diagnosis process, practice and medication technique were studied based upon their country-specific guidelines. ARF signs and symptoms are inevitably different from one country to another and the impact of signs and symptoms can also differ due to their geographical, environmental, cultural, social and economic situations. Accordingly, the international standard guidelines for the diagnosis of ARF are prepared by WHO based mainly on the revised Jones criteria. It was noted however, that some countries develop their own guidelines by modifying the WHO guidelines, adding the variations that are associated with ARF types occurring locally. It is clear that locally derived guidelines are important for diagnosis and treatment of ARF in each specific country. The WHF (2007) report supports the principle of following local guidelines and treatment of ARF's disease by reflecting the fact that each country has its own country-specific guidelines and treatment procedures. For example, some countries include the following for consideration of ARF diagnosis criteria: (WHF, 2007):

- the involvement of only one joint (mono-arthritis);
- poly-arthralgia in children who are at high risk of ARF (instead of poly-arthritis);
- Subclinical Carditis (evidence of rheumatic valve disease on echocardiogram).

Consequently, in this research we put most emphasis on designing and developing an ARF diagnosis model for Nepal by applying the NHF guidelines and procedures.

2.5.1. World Health Organization

It is recognised that the WHO guidelines set the international standard (WHF, 2007) for the diagnosis of ARF. The WHO / WHF, clinical presentation of ARF is given below (WHF, 2007 and WHO, 2004). The clinical feature of RF is divided into major and minor categories, based on the prevalence and specificity of manifestations (see Table 2.2). The major manifestations, minor manifestations and evidence of GAS infection are considered in diagnosis of ARF. The appearance of ARF varies among individuals and between populations. Occasionally, a sore throat may have resolved 1-2 weeks before other symptoms. People with ARF may present with the following:

Major Manifestations:

Arthritis: (the most common symptom, in up to 75% of first episodes).

- Pain, redness and swelling in the joints (commonly the ankles, knees, wrists, elbows).
- Less commonly the small joints of the hands, feet and neck; often the first complaint.
- Usually 'migratory'- disappearing in one joint as it begins in another.
- Inflamed joints are characteristically warm, red and swollen.
- Polyarthritis and Sydenham's chorea virtually never occur simultaneously.

Carditis (inflammation of the heart)

- Commonly presents as a heart murmur.
- Chest pain and/or difficulty breathing may be present in more severe cases.

Sydenham's chorea

- Chorea occurs primarily in children and is rare after the age of 20 years.
- Extrapyramidal disorder.
- Muscular Hypo tonus and emotional liability.
- First sign: difficulty walking, talking, writing.
- Usually a late manifestation: months after infection.
- Often the only manifestations of ARF are twitchy, jerking movements and muscle weakness (most obvious in the face, hands and feet).

- May occur on either sides or only one side of body.
- May be associated with irritability and or depression.
- The onset may often be difficult to determine, as initially the child may become fretful, irritable, inattentive to schoolwork, fidgety, or even severely disturbed.
- May begin up to 3-4 months after the streptococcal infection, and may occur alone ("pure" chorea), or in association with other manifestations of ARF.
- Maybe polyarthritis and Sydenham's chorea do not occur together.
- Usually resolves within 6 weeks (rarely lasts 6 months or more).
- May recur in females during pregnancy.
- The prevalence of Chorea in ARF patients varied from 5 –36% in different reports.

Subcutaneous nodules

- Painless lumps on the outside surfaces of elbows, wrists, knees, ankles in groups of 3-4 (up to 12).
- The skin is not red or inflamed.
- Subcutaneous nodules are round, firm, freely movable, painless lesions varying in size from 0.5 – 2.0 cm.
- Last 1-2 weeks (rarely more than one month).
- Nodules are more common when carditis is also present and usually appearing several weeks after the onset of cardiac findings.

Erythema marginatum

- Erythema marginatum occurs in up to 15% of ARF patients.
- Painless, flat pink patches on the skin that spread outward in a circular pattern.
- Usually occurs early, may last months, and rarely lasts years.
- Usually on the back or front of body, almost never on the face.
- Hard to see in dark-skinned people.
- Is associated with carditis but, unlike subcutaneous nodules, not necessarily with severe carditis. Nodules and erythema marginatum tend to occur together.

Minor manifestations:

- Cough and Abdominal pain.
- Arthralgia.
- Prolonged P-R interval on ECG.
- Raised ESR or CRP.
- Fever: usually ranging from 101°F to 104°F (38.4^0C – 40.0°C).

Evidence of a GAS infection is required to confirm a case of ARF with the above signs and symptoms.

- GAS on throat swab (culture).
- Raised Anti-streptolysin O titre (ASOT).
- Raised Anti-deoxyribonuclease B (Anti-DNase B).

2.5.2. National Health Service: NHS Choice

According to (NHS Choice, 2014), the symptoms of Rheumatic Fever are given below:

Arthritis: It is a very common symptom affecting 3 out of 4 people. The large joints knees, ankles, elbows and wrists pain and swelling. Symptoms of arthritis should pass within four weeks without causing any permanent damage.

Inflammation of the heart (Carditis): Carditis can be present in about 30-60% people and can persist for several months. Shortness of breath, persistent cough, rapid heartbeat (tachycardia), and feeling tired all the time, chest pain.

Sydenham's chorea:

- Uncontrollable jerking and twitching of the body – most often, the hands and feet.
- Difficulties for hand movement e.g. writing and difficulties with balance.
- Unusual emotional outbursts such as crying or laughing for no apparent reason.

Skin Rash: it is known as erythema marginatum. Rash is painless and not itchy and spreads slowly over the child's body. It will normally come and go over a few weeks or months.

Less Common Symptoms

- Subcutaneous skin nodules-small painless lumps under the skin, usually found on the wrists, elbow and knees.
- A very high temperature (fever) of 39^0C (102^0F) or above.
- Abdominal pain.
- Nosebleeds.

- Causes of ARF: throat infection with Group A streptococcus bacteria.

2.5.3. Medscape

According to (Thomas K. C. and Lawrence K. J. (Medscape), 2014), the signs and symptoms of ARF are:

Major diagnostic criteria: Carditis, Polyarthritis, Chorea, Subcutaneous nodules, Erythema marginatum.

Minor diagnostic criteria: Fever, Arthralgia, Prolonged PR interval on electrocardiography, Elevated acute-phase reactants (APRs), which are erythrocyte sedimentation rate and C-reactive protein. Three notable exceptions to strict adherence of the Jones criteria are:

- Chorea: It may occur late and be the only manifestation of rheumatic fever.
- Indolent carditis: Patients presenting late to medical attention months after the onset of rheumatic fever may have insufficient support to fulfill the criteria.
- Newly ill patients with a history of rheumatic fever, especially rheumatic heart disease (RHD), who have supporting evidence of a recent GAS infection and who manifest either a single major or several minor criteria: distinguishing recurrent carditis from preexisting significant RHD may be impossible.

Evidence of previous GAS pharyngitis (One of the following must be present):

- Positive throat culture or rapid streptococcal antigen test.
- Elevated or rising streptococcal antibody titer.

Other clinical manifestations: Abdominal pain, Arthralgia, Epistaxis, Fever, Rheumatic pneumonia.

2.5.4. Australia

According to (Jonathan *et al*., 2006), the ARF signs and symptoms are as below:

- Major Manifestations: Arthritis, Sydenham's chorea, Carditis, Subcutaneous Nodules, Erythema Marginatum.
- Minor Manifestations: Arthralgia, Fever, Elevated acute-phase reactants, Electrocardiogram.
- Evidence of Group A streptococci (GAS).

2.5.5. New Zealand

According to (Diana L. *et al*., 2006), the signs and symptoms of ARF are as below:

- Major Manifestations: Arthritis, Sydenham's chorea, Carditis, Subcutaneous nodules, Erythema marginatum.
- Minor Manifestations: Arthralgia, Fever, Elevated acute-phase reactants, Electrocardiogram.
- Evidence of Group A Streptococcus (GAS).

The New Zealand guidelines slightly modify the Jones criteria of 1992 and add echocardiographic evidence of carditis as a major manifestation and more emphasis is given on mono-arthritis that may be present, if there is a history of non-steroidal anti-inflammatory drugs (Diana L. *et al*., 2006).

2.6. Diagnosis of ARF

2.6.1. WHO and Duckett Jones criteria for diagnosis of ARF

Firstly, Duckett Jones introduced diagnostic criteria for ARF in 1944 as a set of clinical guidelines (Jones T. D., 1944). These guidelines were divided into Major and Minor Jones' criteria for the diagnosis of acute rheumatic fever and are shown in Table 2.3 (Michael D. S. and Tracey R. H. 2011). The diagnosis can be made based on the presence of either two Major or one Major and two Minor criteria and evidence of recent streptococcal infection (Committee, 1992). In 1956, 1965, 1984, 1988, 1992 and 2003 some modifications were made for the diagnosis of ARF (WHO, 2004), which are shown in Appendix 2.1. The WHO criteria published in 2002-2003 (based on the revised Jones' criteria) for diagnosing RF (WHO, pp.31, 2004) are presented.

Table 2.3: Jones' Criteria for the Diagnosis of ARF

Major Criteria	Minor Criteria
Migratory polyarthritis	Arthralgia
Carditis	Fever
Erythema marginatum	First degree heart block
Sydenham chorea	Elevated inflammatory markers (ESR, CRP)
Subcutaneous nodules	

Note: CRP: C-reactive protein; ESR – erythrocyte sedimentation rate.

2.6.2. Australia's Guidelines

The Australian guidelines for the diagnosis of ARF are divided into high-risk groups and other groups (Jonathan *et al*., pp. 19, 2006), which are given below:

Initial episode of ARF: 2 major or 1 major and 2 minor manifestations plus evidence of a preceding GAS infection.

Recurrent attack of ARF in a patient with known past ARF or RHD: 2 major or 1 major and 2 minor or 3 minor manifestations plus evidence of GAS infection.

2.6.3. New Zealand's Guidelines

The New Zealand guidelines for the diagnosis of ARF are given below (Diana L. *et al*., 2006).

Initial episode of ARF: 2 major or 1 major and 2 minor manifestations plus evidence of a preceding GAS infection - **Definite ARF Category.**

Initial episode of ARF: 1 major and 2 minor with inclusion of evidence of a preceding GAS infection as a minor manifestation - **Probable ARF Category.**

Recurrent attack of ARF in a case with known past ARF or RHD: 2 major or 1 major and 2 minor or several minor plus evidence of GAS infection – **Possible ARF Category**.

2.7. The Status of ARF and RHD in Nepal

ARF and RHD are Nepal's the most important problems in comparison with other heart diseases. According to Shahid Gangalal National Heart Centre (SGNHC) report of 2007, RHD had the second highest incidence rate with 430 cases (SGNHC, 2007). Around 591 patients were admitted in the Medical Intensive Care Unit (MICU) where RHD was the leading cause of admission. RHD cases involved 58 males and 87 females. From these figures, the mortality rate recorded showed 14 males and 11 females (SGNHC, 2007). According to the NHF's report, "ARF caused 25-40% of all cardio-vascular disease in developing countries. Death by RHD is mainly caused by recurrent attacks of ARF." According to the National Heart Centre (NHC), 0.34% of admitted cases were related to ARF. Recently, this figure increased to 1.3%. All admitted cases of cardiovascular disease were for patients under the age of 18. (SGNHC, 2007). The June 2007 – Oct 2011 (Regmi P. R. *et al*., 2012) register of National ARF / RHD Prevention and Control Programme from 32 Hospitals in Nepal, revealed that 6028 ARF / RHD cases had been

registered for secondary prevention. These patients were suffering from ARF and were receiving three weekly Benzathine Penicillin G (BPG) injections or oral antibiotics for secondary prevention of ARF (Regmi P. R., *et al*., 2012). Furthermore, based on the NHF's ARF/RHD registers, during the period of June 2007 to February 2010, from 35 hospitals, 4,712 patients were receiving three weekly injections of BPG, where 2.540 (53.9%) and 2,172 (46.1%) were female and male patients respectively. Positive diagnosis of ARF cases numbered 665 (14.1%) and for RHD there were 4,047 (58.95%). These figures indicate that all the 4,712 patients suffering from ARF who were unable to obtain treatment for ARF resulted in succumbing to RHD eventually. The 36.7% of patients were below 18 years and 63.3% were older than 18. In a continuous treatment process, 286 (6.0%) of the total patients had missed more than two doses of BPG injection. The reasons for dropout from the BPG injection were phobia of injection pain (4.95%), prohibitive distance (0.8%), unaffordable cost (0.2%) and other (0.3%) (NHF, unpublished data, 2012).

It was established that in Nepal, ARF/RHD is one of the main reasons for mortality in young people. Treatment is a key issue with treatment of RHD being potentially for long periods, sometimes requiring surgical treatment and with successful treatment not always guaranteed. Records indicate that in Nepal, 800 children per year die from ARF/RHD (NHF Seminar, 2011). According to WHO data for developing countries, in general 10 per 1000 children suffer from ARF/RHD and 1 per 1000 children die. It became evident that ARF/RHD can be cured at the initial stage, if we are able to make a proper diagnosis. This would not only save children's lives, but also save time and expense. In Nepal, especially in rural areas, lack of awareness and most importantly ignorance of people towards initial symptoms, is causing the damage. In the world, Nepal is in the list of highest frequency rates of ARF/RHD. NHF estimates the incidence of ARF cases is approaching 15,000 per year and that RHD is prevalent at a rate of 2/1000 children (Regmi, P. R., and Wyber, R, 2013). The very high occurrence rate of RHD in rural areas underlines the challenges caused by a general lack of adequate health-care services.

A national seminar on ARF/RHD Prevention and Control in Nepal in 2011, (NHF Seminar, 2011), revealed that "*The lack of guidelines on RF/RHD in Nepal has created a lot of confusion in the diagnosis and treatment even among doctors. The adoption of foreign guidelines is not effective as it does not match the Nepali environment and lifestyle.*" Therefore, this collaboration research was initiated with one key objective being to design and develop a suitable and affordable Decision Support System that

would fit into the Nepalese environment and lifestyle specifically. It is estimated that early diagnosis of ARF/RHD will cost the patient NRs. 25.00 (relative to GB Pound = £0.25) but late diagnosis or neglect of symptoms can cost around NRs. 2, 00,000 to 3, 00,000 or more (equivalent to GB Pound £1225 – £1837), (NHF Seminar, 2011). In the context of the Nepalese economy, these costs are high and usually cannot be afforded in the rural economy.

The proposed diagnosis model will not only offer assistance to rural health workers or doctors but also assist with diagnosis of ARF at an early stage. It will also save costs and reduce the financial burden on the government. In addition, the proper implementation and use of the model, particularly in rural areas, will support government in tracking down cases of ARF throughout Nepal. Although Nepal follows the WHO guidelines in the diagnosis of ARF, other local guidelines may be included during ARF diagnosis. It is recognised that the diagnosis process of ARF can be delayed due firstly to a combination of ARF symptoms required with evidence of GAS infection and secondly that ARF's signs and symptoms could be similar to other diseases. As a result the community rural health worker may have difficulty recognising the symptoms of ARF (NHF, 2007), without additional diagnostic support. Professional guidelines therefore, for methodical and careful patient observation, recognition and analysis of symptoms, are essential for the proper diagnosis of ARF. We therefore have proposed a better method by adding ARF symptoms and diagnosis criteria to facilitate in identification of ARF. Detailed discussions of this topic are provided in the Research Methodology, Chapter 4.

2.8. Decision Support System

Decision Support Systems (DSS) have evolved over the past three decades from simple model-oriented applications to advanced multi-function entities. During the 1960s, most DSS were designed and developed based on powerful and expensive mainframe computers. Such types of DSS only provided periodic reports to managers. During that time, DSS was more concerned with building a model-driven DSS system. The first conference for DSS was held in Atlanta, Georgia in 1981, (Power D.J., 2007). By the mid-1980s, spread sheet-based DSS and Group DSS were in use, especially for financial planning. Between 1980 and 1990 data warehouses, executive information systems and business intelligence systems proliferated (Power D. J., 2007). Much of the Group Decision Support System and Organizational Decision Support System evolved in the mid-1980s.

Raymond (1966), Turban (1967) and Urban (1967) systematically researched computerized models to support the decision making process and planning. During the 1990s, DSS were applied on more complex systems in many areas of business by incorporating advanced database technology and client/server techniques. By mid-1990, Knowledge-driven DSS and Web-based DSS systems had been developed and started to be introduced in various sectors of business (Power D. J., 2007). The rapid expansion of the internet provided additional opportunities and scope for DSS so that many new innovative systems such as Online Analytical Processing (OLAP) and other web-driven systems were soon developed.

Different authors have diverse definitions of DSS; there are no precise definitions of DSS. Descriptions of DSS have been based entirely on individual author's opinions. (Druzczel and Flynn, 1999). According to Keen and Scott Morton (1978) definition, "It is a computer-based support system for management decision-makers who deal with semi-structured problems". On the other hand, Sprague and Carlson (1982), explained that DSSs are "interactive computer based systems that help decision makers utilize data and models to solve unstructured problems." According to Power (1997), "the term DSS remains a useful and inclusive term for many types of information system that support decision making". In 1994 DSS was defined as "a computer-based system that aids the process of decision making". Turban (1995), defined DSS as *"an interactive, flexible, and adaptable computer-based information system, especially developed for supporting the solution of a non-structured management problem for improved decision making. It utilizes data, provides an easy-to-use interface, and allows for the decision maker's own insights"*. Later, in 1998 Cleves referred to "DSS as an integrated collection of tools used in decision support as a "toolbox."

To date there is no universally accepted definition. For our purposes we have defined DSS as a 'decision-making system for solving a specific problem by integrating precise procedures, technologies and databases'. Our emphasis is that DSS intelligence helps the decision-maker to choose the design, implementation and monitoring, underpinned by a suitable explanation. In our view, DSS fundamentally also supports strategic, tactical and operational level staff to help them make decisions in particular cases.

Today DSS has become an integral part of multidisciplinary studies especially medical research, database research, AI applications, human/computer interactions, telecommunication and engineering research, chemical research, plant scheduling and a

multitude of circumstances where data storage, retrieval for research and decision-making are paramount functions and for consequential decision-making

2.8.1. Types and Components of DSS

The different types of DSS have been classified at conceptual and technical levels. In the conceptual level DSS are Communication-driven DSS, Data-driven DSS, Document-driven DSS, Knowledge-driven DSS (Power D. J., 2002). In the technical level, the versions of DSS are Enterprise wide, Desktop DSS, Model Driven DSS (Power D. J. 1997).

Different authors have defined the components of DSS in different ways. Sprague and Carlson (1982), have defined the components of DSS as: a) database management system (DBMS), b) model-base management system (MBMS) and d) dialog generation and management system (DGMS) (Sprague and Carlson, 1982). Power D.J. defined four components; 1) user interface, 2) database, 3) model and analytical tools and 4) DSS architecture and network (Power D. J, 2002). Maraks proposed five components of DSS, 1) data management system 2) model management system, 3) knowledge-engine, 4) user interface and 5) user. Our considered view is that the database, model/techniques and user interface should be considered as the three most important components of DSS systems and that these three components should be interrelated always in the design and development phase.

2.9. Clinical Decision Support System

The CDSS has been used for almost 50 years. During this period various theoretically and practically significant researches has taken place on the subject. It is well-known that the effective use of CDSSs in various sectors of medical domains has increased the life expectancy in developed countries. However, providing sufficient and effective health-care service to everyone has proved to be a big challenge to all governments, even in developed countries. We postulated that an efficient CDSS system and effective implementation plan would certainly be a big step forward and would certainly help the Nepal government to provide a better health-care service all rounds. The various CDSS systems have all been developed to assist health-care professionals to make a speedy decision by providing the related information and analytical tools. Currently CDSSs has been recognized as an outstandingly useful and important tool, which improves the quality of care and provides better treatment and medication for patients. The benefits of

CDSS can be divided into three parts (Enrico Coiera, 2003): *"(a) improved patient safety for example through reduce the medication error, improved medication and test ordering (b) improved quality of care for example by increasing clinician's available time for direct patient care, and (c) improved efficiency in health care delivery e.g. by reducing cost through faster order processing, reduction in test duplication, drug prescribing."* Doctors always apply their theoretical knowledge in making a decision over a particular problem and also concentrate on providing a better care for patients' safety. During the decision-making process, physicians have to remember a huge amount of information which is often difficult for health-care professionals working under trying circumstances. CDSSs are therefore developed to help them store and retrieve data quickly and conveniently for effective decision-making, medication, laboratory testing and therapy planning.

There are several obstacles to be overcome relating to uncertainties in clinical environments which need to be addressed by introducing ways of modifying methodology or enhancing prevailing methods or by finding opportunities for combining one or more methods and techniques. Details on this topic are discussed in the Research Methodology, Chapter 4.

2.9.1. Definition of CDSS

Our literature review identified various definitions for CDSSs, usually based on an individual researcher's point of view. Some of these are summarized below:

According to Shortliffe (1987), "CDS is a medical decision-support system is any computer programme designed to help health professionals make clinical decisions" (Shortliffe E.H., 1987).

Other definitions include: Medical decision-making is an "active knowledge system in which to use two or more items of patient data to generate case-specific advice." (Wyatt J, Spiegelhalter D., 1991).

Ida Sim *et al*., (2001), defined "CDSS to be software that designed to be a direct aid to clinical decision-making, in which the characteristics of an individual patient are matched to a computerized clinical knowledge base and patient-specific assessments or recommendations are then presented to the clinician or the patient for a decision".

"CDSSs are computer systems designed to impact clinical decision making about individual patients at the point of time that these decisions are made" (Berner and Lande, 2007.)

From these it is seen that CDSSs can be a computer-based program which is designed with a view to providing additional assistances to health-care professionals to facilitate making clinical decisions. CDSS supports skilled medical practitioners to help them store, maintain and retrieve medical knowledge whenever and wherever needed. These systems improve significantly all round quality of care by providing readily accessible and time oriented data on which they can rely. A modern CDSS system is therefore based on these principles, whether a diagnosis system, bed management system, therapy planning system, appointment system, laboratory processing system, medication system, dosage calculation or allergic warning system and is an immensely important tool for providing better health-care.

2.9.2. History of CDSS

In the past, computer scientists were interested in designing and creating an "electronic brain" which has the same human reasoning capacity to solve problems. They developed a machine (computer) with an electronic brain that can provide solutions to specific problems automatically emulating the way a human expert might respond. Later, scientists designed and created a technique called "Artificial Intelligence", the AI already mentioned, that has reasoning capabilities for solving a wide range of problems. Clinical information systems today are able to use AI effectively and efficiently.

Ancient physicians made their medical diagnoses based on what they observed and perceived using their eyes and ears (Darlene, B., 1998-2000). With the passage of time, new methods and techniques evolved and were used in various sectors of medical science. The first medical informatics article was published in 1959 by Ledley and Lusted, who proposed a mathematical model for diagnosis: "Reasoning foundations of medical diagnosis; symbolic logic; probability and value theory aid our understanding of how physicians' reason". In 1961 Homer Warner developed a mathematical model for the diagnosis of congenital heart diseases. Morris Collen of Kaiser developed a system for automated multiphasic diagnosis in 1964. In 1969 Howard Bleich developed a system to suggest therapy for the acid-base disorders. F.T.de Dombal in 1972 built a probabilistic model to diagnose abdominal complaints. In 1975 Ted Shortliffe of Stanford University developed a MYCIN, an expert system for antibiotic dosing. In 1976 Pauker and Gorry

developed the 'present illness program' system and in the same year Clem McDonald published "Protocol-based computer reminders, the quality of care and the non-perfectibility of man" (Timeline of the Development of Clinical DSS - Clinfowiki, 2015).

Nowadays CDSSs system and tools provide wide-ranging assistance for health-care professionals helping them to prescribe medication, record drug reactions, make dosage calculation as well as therapy planning, diagnosis processes, Intensive Care Unit (ICU) patient monitoring, telemedicine, hospital management systems, pharmacy data management, laboratory tasks and so forth. In addition, CDSSs aims to reduce health-care costs provide fast and reliable service, and above all quick diagnosis whilst avoiding human error (Adams A. *et al*., 1986).

CDSS can be developed in different ways with focus upon Passive systems or Active systems. The Active system approach is used to interact with clinical data sets and provide conclusions whereas the Passive system relates and reconciles information for particular cases and is only used when necessary (Haji S off, 1998). Passive CDSSs does not have the capability of producing options they only have the capacity to organize data in meaningful order. A Passive CDSS system can be used to seek acquired case-related information when necessary. By contrast, the Active system expressly offers automatic assistance and optional guidelines for users. In the Active system, automatic assistance and guidelines are designed within pre-defined sets of conditions. In the Passive system, the user has full control to accept or reject the advice. Most users analyse the advice and its sources and then make a decision. These systems are designed in standalone machines and are used for particular internal medicine management for example DXplain system, analysis of ECG, analysis of pain etc. Active systems on the other hand process the data, analyses knowledge, consider applicable rules and display solution options automatically. This means, an Active system automatically invokes a decision when the pre-defined conditions have been satisfied. These systems are especially useful for monitoring ICU patients and drug allergies, and are able to send 'alert and reminder' messages to doctors, laboratory warning signals, medical device controls etc. Examples of their usage include Knowledge-based hospital information system such as HELP, which provides alert/reminders, data interpretation, patient diagnosis, patient management, suggestions and reminders plus therapy advice; (HELP) and CARE, for reminders. Examples of the guideline-based decision support systems are: Arden Syntax (Clayton P.D. *et al*., 1989), Guideline Interchange Format (Lohono-M *et al*., 1998), and PROForma (Fox J. *et al*., 1998). The Active system automatically adjusts if the set programmed condition has been

changed. The Active system provides advice and options that users can analyse and either accept or reject.

2.9.3. CDSS Types and Methodology

Various case studies and research papers (conferences and journals) accessed through UoG's library, e-Library online resources (databases, journals, books), different search engine (digital library, IEEE, Springer link, Google scholar etc.) have been referred to for my project.

There is a variety of techniques and methodologies being used to design and develop CDSSs. Some of these are based on Case-based reasoning, Probabilistic-based system, Rule-based reasoning, Module-based reasoning and Fuzzy rule-based reasoning, Evidence-based, Guideline-based and Intelligent Computing Method (e.g. machine learning, inductive tree method, artificial neural network, Fuzzy logic, Genetic algorithm, Temporal theory etc.) and Expert system – Knowledge-based method (Ali S *et al*., 1999). The statistical and hybrid methods or combination of two or more methodologies (Hu Y., Pchia *et al*., 1999; Kloper H. and Anderson H. *et al*., 2006; Demmer-Fushman D. and Lin J. 2007; Houeland, T. G., & Aamodt, A., 2009), offer two modern trends being applied in CDSS. Statistical methods are used for data collection, data analysis and production of various reports in the form of charts or graphs. Data can be collected by interview, questionnaire, survey report etc. A Hybrid methodology is combination of two or more methodologies applied together as a single method to solve a particular problem. In the Hybrid system, the selection of methodology depends upon the nature of the problem and individual user preference. Fundamentally, however, the most important criteria for selection of methods are suitability and practicality for solving specific problems smoothly and effectively.

CDSSs can be divided conveniently into two broad categories:

1) Knowledge-based CDSSs (Production Rule-based, Evidence-based, Guidelines-based, Case-based Reasoning, Fuzzy Rule-based Reasoning etc.)
2) Non-knowledge CDSS (Neural Network, Genetic Algorithm, Machine Learning, Decision Tree Learning etc.)

2.9.4. Knowledge-based CDSS

Data, information, theoretical knowledge, practical experience, training etc. are considered as Knowledge and as such it is a very important factor to improve the quality and accuracy in medical diagnosis. An expert is somebody who has deep theoretical knowledge, understanding of particular subject and has enough experience on specific subject matter. Doctors or physician use their knowledge to make a judgment or decision on a case-by-case basis. It is self-evident therefore that means for knowledge capturing, managing and sharing is a particularly important aspect of work within the medical domain.

The Knowledge-based System (KBS) has reasoning capabilities to enable use of explicit knowledge to solve a particular problem. KBS uses AI techniques or methods for solving a problem, which will support users for decision-making in order to take appropriate remedial action. Experts are capable of expressing their understanding in the form of rules to solve the problem. Consequently, rules could represent the knowledge expressed in a precise way for solving a problem. KBS is, in effect, a specialized database for capturing, sorting, refining and retrieving knowledge to solve a particular problem. The expert knowledge in the decision making process can be presented in different ways such as the Rule-based format defined by Brownston L. *et al*., (1986). According to Guilankong *et al*., (2008), medical knowledge is dividable into two parts, 1) "*Declarative knowledge includes propositions and sentences. Propositions are statements about the world that are either "true" or "false". These statements may be connected by Boolean operators such as "and", "or", and "and not" to form sentences and 2) Procedural knowledge provides more explicit information about what action can be taken or what conclusion can be drawn from declarative knowledge".* Declarative knowledge is description of notation, facts and the rules of a particular domain, it is non-procedural and it is independent and used for problem solving. Procedure knowledge is used to describe the procedures to solve the problem. Knowledge and action are thus organized in sequence.

Knowledge also can be categorized by Explicit and Tacit knowledge. Explicit knowledge is information that is in easy format and easy to capture, organize, distribute and share with others. Examples of these are rheumatic fever symptoms, rheumatic fever management policies and remedial procedures etc. Tacit knowledge includes skills, theoretical information of subject matter, practical experiences on particular domain that a person can acquire and apply to solve the problems. Consequently Tacit knowledge is

difficult to capture, organize and sometimes difficult to transfer to other individuals (Awad E. M., 2010). According to Polanyi (1966), tacit knowledge is concerned with an individual's skills and experiences in a particular domain and it is comparatively difficult to transfer into a computer in readable format. Tim Thornton (2006) discussed the "*role that tacit knowledge plays in what might seem to be an area of knowledge that can be made fully explicit or codified and which forms a central element of Evidence Based Medicine*."

The KBS (Rule-based reasoning (RBR), Case-based reasoning (CRR) and Model-based reasoning (MBR), intelligent computing method (Genetic algorithm (GA), Artificial neural network (ANN), Fuzzy Logic (FL) or combination of them (CBR-RBR, CBR-MBR, RBR-CBR-MBR, ANN-GA, Fuzzy-ANN, CBR-ANN, Fuzzy-RBR, Fuzzy-CBR, Fuzzy-CBR-ANN) in diagnosis, treatment and planning are reviewed for the period mid-1970s to 2008 (Pandey and Mishra, 2009). Their conclusion was that most of the methods are used in diagnosis rather than in planning. Methods used are mainly algorithms, CBR and RBR. Genetic algorithms, genetic programming, evolutionary strategies, evolutionary programming, classifiers and the Hybrid system with six types of evolutionary algorithms have been discussed to provide an overview of evolutionary computation that are applied in medicine especially in diagnosis, prognosis, imaging, signal processing, planning and scheduling (Pena-Reyes and Sipper, 2000).

2.9.5. Knowledge Acquisition, Representation and Management

According to Buchanan *et al*., (1983), knowledge acquisition, representation and management are: "The transfer and transformation of potential problem-solving expertise from some knowledge source to a program". The important part of knowledge acquisition is knowledge elicitation, which means obtaining knowledge from a human expert and then being able to structure the knowledge. In the knowledge elicitation process, the main focus is on collecting sufficient knowledge about a particular domain in detail with the knowledge acquisition process focussing on refining or structuring the resulting knowledge. During the design and development of the expert system, knowledge elicitation is one of the critical tasks (Shadbolt and Burton, 1995; Gebus and Leiviska, 2009). In CDSS, knowledge is gathered from experts who have long experiences in the particular sector of the medical domain. Their knowledge could be in the form of tacit data, which are difficult to extract (Ford and Sterman, 1998). Acquiring, organizing, formulation, implementation and testing knowledge are the most important components

of knowledge acquisition. In summary, data acquisition is the process of extracting knowledge from experts and transcribing it into a computer-useable form (Garbay C., 2000).

The basic methods for acquiring knowledge are: manual, semi-automated, and automated (Brownston L R. *et al*., 1986). Data mining, machine learning (inductive learning, analogical reasoning and explanation-based learning) and discovery knowledge (Garbay C., 2000) are being used today in various sectors of the medical domain. Similarly, a data-driven approach is also being used for knowledge extraction, which enables system operators to create and update Knowledge (Garbay C, 2000). Interview techniques include those defined by TEIRESIAS (Davis and Lenat, 1982) and ETS (Boose, 1985). The knowledge acquisition environment such as AQUINAS (Boose and Bradshaw, 1987) and MORE (Kahn *et al*., 1985) are examples of methods for knowledge acquisition tools (Garbay C. 2000). Knowledge elicitation approaches have been addressed in various other sectors for example business management, education, cognitive science, philosophy, knowledge engineering and linguistics (Cooke, 1994), but these are rare in the medical domain (Agorastos *et al*., 2009). A Medical Knowledge Elicitation System (MediKES) has been developed which uses the automatic knowledge elicitation method aiming to capture and embed medical knowledge in an Electronic Medical Record (Ting S.L *et al*., 2011). The MediKES method provides health-care professionals with an effective solution for visualizing medical knowledge, improving elicitation and sharing tacit knowledge that is acquired by physicians (Ting S.L *et al*., 2011).

The main aim of Knowledge presentation is to provide intelligent systems with information within a domain about a particular case in a form that can be accessed and processed efficiently (Carter J.H., 1999). Knowledge acquisition and representation are vital for designing and developing a knowledge-based system. Kris *et al*., (2007), have discussed key points for representing knowledge; some of them are summarized below:

1. Knowledge must be represented in a humanly understandable but computer-interpretable manner.
2. CDSS architecture must be able to support different types of knowledge and be able to manage, administer and support them.
3. The clinical knowledge models must offer expressive power to allow the definition of all kinds of knowledge in an unambiguous way to overcome complexity.

4. Clinical knowledge should be shareable effectively between different user departments and organizations.

Knowledge representation methods are usually divided into logic, procedural, graphs/network and structured (Carter J. H., 1999). Various other methods are available to represent the Knowledge for example symbolic methods (declarative language - logic, Fuzzy Logic, description logics, propositional logic, first order logic, imperative language – C, C++, Java, C#, hybrid language, production rule, frames, semantic networks, natural language, Boolean rule, Bayesian networks etc.) and non-symbolic methods (neural networks, genetic algorithms). Some other are: frame representation and object-oriented language for example HIV-pneumonias (Fiore *et al*., 1993). A Unified Medical Language System (UMLS) are based on knowledge acquisition tools used for development of the blood transfusion rule-based decision support system. In this system, the domain ontology design was based on the UMLS and represented in the knowledge-based system (Achour SL *et. al*., 2001). The use of fuzzy evidential reasoning and dynamic adaptive fuzzy petri nets has been discussed for knowledge acquisition and representation (Hu-Chen Liu *et al*., 2013). The Database Management System (DBMS) can also be applied for Knowledge representation, which provides a structured format for relational and object-oriented DBMS in which two types of database are often used in CDSS (Carter, 2007).

A variety of research has been conducted in relation to the clinical knowledge model Six, Asbru, EON, GLIF, GUIDE, PRODIGY, and PRO*forma*, computer-interpretable guideline-modelling methodologies have been compared to understand their commonalities and differences (Peleg *et al*., 2002). As a result, Asbru is a task-specific and intention-based plan representation language used to embody clinical guidelines and protocols as time-oriented skeletal plans developed by Vienna University of Technology and Stanford Medical Informatics (Open Clinic:Absru, 1998). EON was developed at Stanford University, which contains an extendable modelling framework as follows: 1) a patient-data information model; 2) a medical concept model and 3) a guideline model (Peleg *et al*., 2002). GLIF is a computer-interpretable language for modelling and executing clinical practice guidelines developed by Stanford Medical Informatics, Harvard University, McGill University and Columbia University (Open Clinic: GLIF, 2000). GUIDE is a component-based multi-level architecture designed system to integrate a formalized model of medical knowledge contained in clinical guidelines and protocols

with both workflow management systems and electronic patient record technologies developed by Laboratory for Medical Informatics, Department of Computer and System Science, University of Pavia, Italy (Open Clinic : GUIDE, 1998). PRODIGY guideline model for support of chronic disease management developed by Sowerby Centre for Health Informatics at Newcastle (SCHIN) (Open Clinic: Prodigy, 1998). Protégé is a free open source ontology editor platform that provides users with a suite of tools to construct domain models and knowledge-based applications (Protégé, 2015). The advanced Computation Laboratory of Cancer Research, UK, developed PROforma, which has a method for specifying clinical guidelines to represent a set of tasks and protocols in a form that can be executed by a computer system (Fox J. *et al*., 1996). Similarly, Arden Syntax was developed by a group at the Arden Homestead in Harriman, New York State, USA. It is a rule-based procedural system for encoding medical knowledge in a knowledge-based form as individual Medical Logic Modules (MLMs) (Open Clinic: Arden Syntax, 1990). Case-based reasoning is another well-used technique being applied in the medical diagnosis process (David and Leak B., 1996).

The development of KBS requires at least three basic components. They are: 1) the Knowledge base; 2) inference engine and 3) communication mechanism. The Knowledge base contains information to solve the problem or resolve the facts and contains the rules (knowledge representation) in the form of *IF-THEN*. For example to determine drug interactions, the rule might be: *IF drug X is taken AND drug Y is taken THEN ALERT user*. The user could access, revise the Knowledge base and thus maintain and keep the information up-to-date. The inference engine is a reasoning process, a problem solving method, which combines the rules from the Knowledge base with specific domain data. The communication mechanism will allow the system to display the result to the concerned individuals, the medical practitioners.

2.9.6. Non-Knowledge-Based CDSS

CDSS that do not use a Knowledge base uses a form of AI called machine learning, which allows computers to learn from past experiences and/or find patterns in clinical data. The two types of Non-knowledge-based systems are: 1) Artificial Neural Networks (ANN) and 2) Genetic algorithms.

2.9.6.1. Artificial Neural Networks (ANNs)

ANNs are inspired by biological neural networks (the central nervous system section of the brain) and applied to approximate functions which depend upon inputs. ANNs learn by example and are being used in pattern recognition, medical diagnosis, financial application, sequence recognition, data processing, robotics etc. ANNs use nodes and weighted connections between them to analyze the patterns found in target patient data to derive the associations between the symptoms and a diagnosis. This eliminates the necessity for writing rules and for expert input. However, the system cannot explain the reason it uses the data in the way it does, so that most clinicians tend avoid them on account of concerns over reliability and accountability.

2.9.6.2. Genetic Algorithms

Genetic Algorithm main features:

- Genetic Algorithms are based on simplified evolutionary processes using directed selection to achieve optimal CDSS results. The selection algorithms evaluate components of random sets of solutions to a problem.
- The solutions that come out on top are then recombined and run through the process again. This repeats until the proper solution is achieved.
- They are the same as neural networks in that they derive their knowledge from patient data.
- Non-knowledge-based networks often focus on a narrow list of symptoms such as those relating to a single disease as opposed to the Knowledge-based approach which has the capability of covering diagnosis for many different diseases.

In the medical diagnosis process, doctors will observe a patient's symptoms and study his/her medical history this is followed by methodical analyses of possible relationships between available data and diseases; determines any requisite laboratory test; analyses the laboratory result and eventually determines the diagnosis. In this way a well structure and efficient CDSS greatly assists in the ability to analyse the relationship between symptoms and diseases, determine requisite laboratory tests and make a valid diagnosis and choice of suitable medication supported by a tenable justification.

Our collaboration research investigated and discussed the range of methodologies for the development of CDSS. Final selection of a particular methodology proved to be difficult

because it is entirely dependent upon the nature of the problems and other parameters. Examples of these are: domain, ranges of solutions, availability of data and technology, researcher knowledge and options available. Information acquired and a researcher's own experiences always help when choosing an appropriate methodology. A major hurdle is that there is no guarantee of success that any one methodology is suitable for solving all problems.

2.9.7. Functions of CDSS

CDSS has specific functions that will help health-care professionals to carry out any particular task effectively and efficiently; such as prescribing, identifying the relationship between symptoms and diseases, interpretation of laboratory tests, therapy planning and review, indications of drug reaction etc. Systems of this kind are referred to as 'Expert systems' (Stuart M.T., 2008). An Expert system can be applied in clinical information methodologies for better treatment and overall care of the patients; some of them are discussed below, based upon Corea E., (2003).

2.9.7.1. Alerts and Reminders

Alerts and reminders are very useful functions for laboratory test monitoring and patient health monitoring systems. For example a reminder system might alert the doctor by showing a pop-up message on the monitor or by sending an email to alert a particular patient's therapy due date. It can also provide support for monitoring a patient's status, examples being ICU patient's ECG or blood pressure device monitors which are able to inform the doctor about a patient's real-time condition. It can also observe and monitor rules for laboratory results and forward pop-up alert message on the screen or send an email to a clinician. Other functions include being able to display lists of patients who are eligible for vaccination, due dates etc. Whilst an alert and reminder system can incorporate many useful routine functions a most important benefit is that they are able to alert a doctor to any serious data changes or if a patient is in potential risk of some kind.

2.9.7.2. Diagnostic Assistance

The diagnostic assistant system is particularly useful in complex cases or in unrelated cases where the doctor has limited knowledge about the particular disease to enable him/her makes a reliable diagnosis. This is clearly beneficial for a doctor who is not conversant with or confident about a patient's condition and his/her knowledge is not

sufficient to make a decision on procedure. Basically, diagnosis systems will accomplish the decision-making task based on a patient's data, laboratory results and information regarding the diseases which would have been stored in its Knowledge base. Systems of this kind are convenient and immensely effective when introduced in under-developed countries such as Nepal where expert support is rare and invariably expensive.

2.9.7.3. Therapy Critiquing and Planning

In the treatment plan of a particular patient, a critiquing system will examine errors, inconsistencies or omissions. Critiquing systems do not provide specific options for any particular treatment plan. These are provided by the planning system which would be based upon requisite Knowledge that can be introduced to formulate treatment protocols and proper guidelines which would facilitate making an appropriate treatment plan.

2.9.7.4. Image Matching and Interpretation System

Clinical images such as X-rays, CT scans, MRI scans etc. can be matched automatically and interpreted via an Expert system. Systems of this kind are especially useful for detecting any tiny changes in an image and flag any abnormality.

2.9.7.5. Prescribing Decision Support System

In medical treatment, prescribing the medication is a common clinical task. Therefore use of a specialized Expert system or a "prescribing decision support system" becomes invaluable in prescribing medication principally by checking drug-to-drug reaction, drug errors, calculation of drug dosages and drug contraindications such as drug allergies. These systems also enable automated script generation and sometimes may be organized to permit electronic transmission of the script to the pharmacy.

2.9.7.6. Information Retrieval

Intelligent information retrieval systems can help retrieve accurate and suitable information relating to defined clinical questions. It also assists with identifying the location of relevant data and appropriate guidelines that can be used for diagnosis or treatment planning. It also supports the web engine or complex software to search most appropriate information quickly by offering search filters or query facilities. Most complex software would have a sophisticated clinical knowledge base that can address questions and retrieve digital responses efficiently and effectively.

2.10. Temporal Theory

Time is a vital part of all data management and plays a fundamental and significant role in the Intelligence system domain, which deals with representation and reasoning in relation to time. This function is vital in modelling systems where human activities take place using natural language descriptions. Such disciplines are an integral part of the clinical information system, knowledge-representation and reasoning, diagnosis and explanation, cognitive science, historical data, prediction and planning, linguistic etc. where Time is a fundamental factor.

There are long debates in the literature on this topic with emphasis on the kind of objects, which should be taken as the time primitive; it is invariably an argument embracing contradictory theories (James F. A and Patrick J. H, 1987). One side argues that points are needed for both theoretical and practical modelling of temporal phenomena for example "Patient record was updated at 0:00 midnight" with instantaneous points rather than duration intervals; on the other hand, intervals are also necessary for representing temporal phenomena which concern Time having a recorded duration for example, "Martin ran 2 hours yesterday morning". There are two approaches to representing time interval and points (Yuval S., 1998). James Allen (1983) presented a Temporal Logic based on intervals and their qualitative relationship in time. Allen's interval logic that uses time intervals as primitives, which correspond to events rather than points that correspond to instants (Yuval S., 1998, and Allen, J. F., 1983). McDermott proposed point-based theories, which provide a precedence temporal operator on time points (Yuval S., 1998). McDermott's temporal primitive are points whereas Allen's are intervals. In particular, the following objectives can be taken as the time primitive but which one is suitable for modelling depends upon the nature of the problem:

- Points: for example instant of time with no duration.
- Intervals: for example periods of time with positive duration.
- Both points and intervals.

2.10.1. Point-based Theory

Bruce (Bruce B.C., 1972) first proposed point-based time structure. In the point-based time theory, a typical time structure represented was based on points only as a primitive ordered set of points $(P, \preceq)$. Where, P is set of points and $\leq$ represent a relation that totally or partially orders P. In the point-based theory, the intervals represented as a derived

temporal object or sets of points (Das G. *et al*., 1997; McDermott, 1982), or as an ordered pair of points (Bruce B.C., 1972; Galton A., 1990). Point-based time theory provides an efficient indexing method for temporal systems; however some researchers have argued the so-called Dividing Instant Problem (Ma J. and Knight B., 2003; Allen J. F. and Hayes P.J., 1989; Bruce B.C. 1972) when defining intervals as objects derived from points; for example Benthem J.V., 1983; Allen J.F. and Hayes P.J., 1989, explain the problem in an expressive way:

"A fire that had been burning was later burnt out."

Based on the above statement, we can assume two states, 1) "The fire was burning" and 2) "the fire was not burning". This holds true through two successive point intervals which can be defined based on the point-based approach as $< p_1, p >$ and $< p, p_2 >$ respectively. So, what is the answer to "Was the fire burning or not burning at point *p?"* If this is in terms of the *open/closed* nature of the point-based intervals, then which of the two successive intervals in $< p_1, p >$ and $< p, p_2 >$ is *open/closed* at the dividing point *p*. Ma J., (2007), expresses the possible cases in this situation, which might be as follows:

1. The fire was burning rather than not burning at *p.*
2. The fire was not burning rather than burning at *p*;
3. The fire was both burning and not burning at *p*;
4. The fire was neither burning nor was it not burning at *p* ;

Based on these, point 3 and 4 violate the *Law of Contradiction* and *Law of Excluded Third* mentioned by (Benthem J.V., 1983), and points 1 and 2 must be arbitrary which do not provide enough reasoning to answer the question. As a result, there is no better reason for saying that the fire was burning than for saying that it was not burning at the dividing-instant. An arbitrary approach of this kind has been criticized as unjustifiable and unsatisfactory (Benthem J.V, 1983; Allen J., 1984; Ma J. and Knight B., 1994).

2.10.2. Interval-based Theory

A time interval approach is proposed as an alternative to the point-based structure. Allen's temporal theory (Allen J., 1984; Allen J.F. and Hayes P.J., 1989) is an example of the interval-based approach where points are a set of intervals as the primitive temporal entities. Allen (1989), presented thirteen temporal relations to define the relationship among them. The Allen's relationship definitions are: "Equal", "Before", "After", "Meets", "Met-by", "Overlaps", "Overlapped-by", "Starts", "Starts-by", "During", "Contains", "Finishes" and "Finished-by". Allen (1984), discusses these by introducing

the interval-based approach to manage or overcome the difficulties of the *dividing instant problem.* In the interval-based approach, there is no need to classify points or nothing can be true at a point, as these are not entities where things happen or are true for a point. It seems that Allen's theory is inadequate and is inappropriate to systems that need to reason properly about continuous change (Galton A., 1990). In the real world, some instantaneous phenomena do exist and points need to be dealt with in the temporal modelling concept; for instance, Ma J. and Knight B., (2003) explain the limitation of the interval based theory in the following scenario:

"*A ball was thrown into the air from the east to the west*"

Based on the above statement; the state of that ball was in the east and below its apex. Then ball movement was immediately followed by the statement that the ball was in the west and below the apex. Hence, the point where the ball was at its apex was neither east nor west of the apex and should be represented as a point with zero duration, rather than any interval (Allen J.F. and Hayes P.J., 1989). In fact, in the particular moment where motion of the ball was proceeding, the ball's velocity became zero when the ball was as its apex. Clearly, Allen's proposed interval – based theory lacks clarity in semantics and completeness (Galton A, 1990).

2.10.3. Point and Interval-based Theory

The time theory is proposed where both point-based and interval-based are addressed as the temporal primitives on an equal basis (Ma J. and Knight B., 1994) where points are not defined as limits of intervals and intervals do not consist of points.

In the general time theory, the basic set of axioms concerns the triad (*T, Meets, Dur)*. Time theory reduces the 13 relations that were defined by Allen and Hayes (1989), and presented as one. This is the *Meets* relationship. The time theory's axiom triad, which takes both points and intervals as primitive and consists of sequence of triads, which are given below (Ma J. and Knight B., 1994):

- In the general time theory, *T* takes a non-empty primitive time elements.
- Primitive order relation *Meets* among *T* and other elements becomes a binary order relation.
- A function *Dur* means a duration that represents a non-negative real number;

So that the triad (*T,Meets,Dur*) is :

$$\text{<A1>}\ \forall t_1,t_2,t_3,t_4\,(Meets(t_1, t_2) \wedge Meets(t_1, t_3) \wedge Meets(t_4, t_2) \Rightarrow Meets(t_4, t_3))$$

In <A1>, time element *t* is interval only if *Dur(t)* > 0; else *t* is a point. If a time element meets two other time elements then any time element that meets one of these two must also meet the other. Actually, this axiom is based on intuition that the *'place'* where two time elements meet is unique and closely associated with the time elements.

$$\text{<A2> } \forall t \exists t_1,t_2(\text{Meets}(t_1, t) \wedge \text{Meets}(t, t_2))$$

In <A2> it shows that each time element has at least one immediate predecessor, as well as at least one immediate successor.

$$\text{<A3> } \forall t_1,t_2,t_3,t_4(\text{Meets}(t_1, t_2) \wedge \text{Meets}(t_3, t_4) \Rightarrow$$

$$\text{Meets}(t_1, t_4) \nabla \exists t'(\text{Meets}(t_1, t') \wedge \text{Meets}(t', t_4)) \nabla \exists t''(\text{Meets}(t_3, t'') \wedge \text{Meets}(t'', t_2)))$$

In <A3> indicate that any two meeting places are either identical or there is at least a time element standing between the two meeting places if they are not identical.

$$\text{<A4> } \forall t_1,t_2,t_3,t_4(\text{Meets}(t_3, t_1) \wedge \text{Meets}(t_1, t_4) \wedge \text{Meets}(t_3, t_2) \wedge \text{Meets}(t_2, t_4)) \Rightarrow t_1 = t_2)$$

In <A4> it shows that the time element between any two meeting places is unique.

$$\text{<A5> } \forall \underline{t_1,t_2}(\text{Meets}(t_1, t_2) \Rightarrow \text{Dur}(t_1) > 0 \vee \text{Dur}(t_2) > 0)$$

In <A5> indicates that the time elements with zero duration cannot meet each other.

$$\text{<A6> } \forall t_1,t_2(\text{Meets}(t_1, t_2) \Rightarrow \text{Dur}(t_1 \oplus t_2) = \text{Dur}(t_1) + \text{Dur}(t_2))$$

In <A6> it shows that the "ordered union" operation over time elements is consistent with the conventional "addition" operation over the duration assignment function, i.e., *Dur*.

In the general time theory *T is* represented above the two adaptations have been taken from a real number theory given below:

Adaption 1: The set of real numbers is totally ordered by the less than or equal to relation '≤', where '>' is the "bigger than" relation, that is, not '≤'.

Adaption 2: *'+'* is the conventional addition operator over *(non-negative*) real numbers.

In terms of the *Meets* relation, Allen (1989), defined 13 temporal relations that are reduced in to one – *Meets* relation. The relation statements and reduction are listed below:

1. $\textit{Equal}(t_1, t_2) \Leftrightarrow \exists t',t''(\text{Meets}(t', t_1) \wedge \text{Meets}(t', t_2) \wedge \text{Meets}(t_1, t'') \wedge \text{Meets}(t_2, t''))$
2. $\textit{Before}\ (t_1, t_2) \Leftrightarrow \exists t(\text{Meets}(t_1, t) \wedge \text{Meets}(t, t_2))$
3. $\textit{Overlaps}\ (t_1, t_2) \Leftrightarrow \exists t,t_3,t_4(t_1 = t_3 \oplus t \wedge t_2 = t \oplus t_4)$

4. *Starts* $(t_1, t_2) \Leftrightarrow \exists t(t_2 = t_1 \oplus t)$
5. *During* $(t_1, t_2) \Leftrightarrow \exists t_3,t_4(t_2 = t_3 \oplus t_1 \oplus t_4)$
6. *Finishes* $(t_1, t_2) \Leftrightarrow \exists t(t_2 = t \oplus t_1)$
7. *After* $(t_1, t_2) \Leftrightarrow$ *Before*(t_2, t_1)
8. *Overlapped-by* $(t_1, t_2) \Leftrightarrow$ *Overlaps* (t_2, t_1)
9. *Started-by* $(t_1, t_2) \Leftrightarrow$ *Starts* (t_2, t_1)
10. *Contains* $(t_1, t_2) \Leftrightarrow$ *During* (t_2, t_1)
11. *Finished-by*$(t_1, t_2) \Leftrightarrow$ *Finishes* (t_2, t_1)
12. *Met-by* $(t_1, t_2) \Leftrightarrow$ *Meets* (t_2, t_1)

The completeness of the 13 possible exclusive order relations (the above 12 plus *Meets*) between any two time elements can be simply characterised by a single axiom as below:

$$\forall t_1,t_2\ (Equal(t_1, t_2) \vee Before(t_1, t_2) \vee After(t_1, t_2) \vee Meets(t_1, t_2) \vee Met\text{-}by(t_1, t_2) \vee Overlaps(t_1, t_2) \vee Overlapped\text{-}by(t_1, t_2) \vee Starts(t_1, t_2) \vee Started\text{-}by(t_1, t_2) \vee During(t_1, t_2) \vee Contains(t_1, t_2) \vee Finishes(t_1, t_2) \vee Finished\text{-}by(t_1, t_2))$$

The exclusiveness of these 13 order relations needs to be characterised by 78 axioms of the following form:

$$\forall t_1,t_2(\neg Relation1(t_1, t_2) \vee \neg Relation2(t_1, t_2))$$

Where, Relation1 and Relation2 are two distinct relations from the above 13 relations.

Ma J. and Knight B., (1994), proposed both point-based and interval-based time theory to be appropriate and efficient enough for temporal representation. However, they only focused on the specifications of temporal order and temporal relationship but neglected temporal gap.

The possible relations over intervals and points may be classified into the following four groups proposed by Ma J. and Knight B. (1994):

1. Point – Point:

{*EQUAL, BEFORE, AFTER*} – Which relates one point to other points;

2. Interval-Interval:

{*EQUAL, BEFORE, MEETS, OVERLAPS, STARTS, DURING, FINISHES, FINISHED-BY, CONTAINS, STARTED-BY, OVERLAPPED-BY, MET-BY, AFTER*} –which relate intervals to intervals;

3. Point-Interval:

{*BEFORE, MEETS, STARTS, DURING, FINISHES, MET-BY, AFTER*} – which relate points to intervals.

4. Interval-Point:

{BEFORE, MEETS, FINISHED-BY, CONTAINS, STARTED-BY, MET-BY, AFTER} – which relate intervals to points.

Based on the above classification, there are in total 30 possible temporal relations over time-elements that may be both intervals and points.

2.11. Temporal Logic in CDSS

Time is an essential part and plays a vital role in CDSS notably diagnosis of diseases, therapy planning, and prescription of medicine, observation of the patient's progress and maintenance of the data in the clinical database. In the medical diagnosis process, a physician needs to deal with the symptoms and their associated time order. For example how long has the particular symptom lasted?. Which symptom presented first and which one after that within the primitive time order?. This becomes the time-oriented information that makes an impact on the diagnosis process. Therefore, a proper CDS needs to deal with the representation and reasoning about the temporal order of symptoms properly to achieve a high accuracy of diagnosis.

Almost all clinical tasks such as diagnosis of disease, treatments, interpretation of laboratory results, medication planning, therapy planning, scheduling of check-ups, ordering, etc. need temporal reasoning either Explicit (e.g. last Friday) or Implicit for example: "*First, I have severe knee pain after that I have moderate headache with mild fever"*. In other situations, there might be some degree of uncertainty appearing: during the night, sometimes, a few days etc., knowledge of which may be required in order to deal with the medical diagnosis. Every clinical activity relating to the case symptoms' duration, ordering of medicine, laboratory process, drug prescription etc. holds some sort of time information. Therefore, it is evident that these time-stamped data are dependent

upon an effective time model and need appropriate theory to act on them appropriately in the medical domain.

In the temporal reasoning there are generally two categories generally taken into account: a) *reasoning about actions and b) changes* and *reasoning about temporal constraints* (Luca C. and Angelo M., 2000). Reasoning about action and changes focuses on the study of the changes of the world due to the occurrence of actions and events that are related to predicting the future effects of an event that may occur, including explanations of a given situation in terms of possible causes. In this category, the situation calculus (McCarthy J. and Hayes P., 1969), event calculus (Kowalski R. and Sergot M., 1986) and fluent calculus are used. The second category, reasoning about temporal constraints, is related to the management of relations among points and intervals such as therapy planning, appointment scheduling, explaining the symptoms then become natural language processing. Qualitative constraint, duration-based representation etc. are used on representing time in this category (Allen J.F., 1991). In the temporal medical reasoning process, "*mapping occurrences across temporal contexts, determining bounds for absolute occurrences (start and end point of occurrence), persistence derivation, inconsistency detection and clipping of uncertainty, deriving new occurrences from other occurrences, deriving temporal relations between occurrences, deriving the truth status of queried occurrences, deriving the state of the world at a particular time"* described by Elpida T. K. (1996), need to be considered appropriately for the development of a proper diagnosis system.

Temporal reasoning is therefore the ability to reason about Time and temporal relations, which are essential in the clinical diagnosis process to be able to make effective decisions. It has been applied in various sectors of the medical domain particularly in the fundamental diagnosis of diseases, monitoring patients' progress, planning treatment etc. (Chandrasekaran B. *et al*., 1986). In temporal reasoning, time activities are involved in the particular problem by analysis, which enhances the performance of the system. But in the medical diagnosis process, catching the Time and understanding the symptoms' sequential order are crucial. When a patient explains his/her problem with natural language, it is important to consider carefully the duration (symptom start time and end time) and time-related order of symptoms. To achieve this, Allen (1984), proposed interval-based temporal reasoning and his logic is based on the intervals discussed above. Allen defined three types of proposition to be held over an interval. They are: 1) **Properties** – holding over any subinterval of an interval; so **Holds (*p,T)*** where *p* holds

over interval *T*; for instance *Radha's knees were swelling throughout Friday;* 2) **Events –** hold only over a whole interval, not a sub-interval of an interval, **Occurs (*e,T)*** where, event *e* occurred at time *T;* for instance *Krishna has broken his nose at 2pm.* and 3) **Processes –** hold over *some* subintervals of the interval, **Occurring (*p,T)*** where the process *p* occurs during time *T;* for instance *Krisshna is waiting for a doctor.* Allen's interval-based temporal logic lacks the concept of branching time in the past or the future.

McDermott (1982), presented point-based temporal logic and his temporal primitives are based on the points that are used to model causality, planning and continuous change. Time is continuous and the set of the time line are numbers. McDermott defined two types of propositions, one is **Facts –** it is interpreted over point, the form of the Facts : (T *s p*) where, *p* is true in *s* where *s* is a state and *p* is a proposition and $s \in p$ and another one is **Events** *e*: (Occ s_1 s_2 *e*) where, event *e* occurred between the states s_1 and s_2 — that is, over the interval [s_1 s_2]—where [s_1 s_2] $\in$ *e*. McDermott's logic presented time as ordered and branching into the future but totally ordered for the past. States are instantaneous shots of the world with an order-preserving *date* function that maps them into time points (Yuval S., 1987).

Shoham (1987), presented a temporal logic in which the primitives of times are points and propositions are interpreted over time intervals. He went on to refine first order logic, for example TRUE (t_1, t_2, *p*), where, *p* (proposition) was true during the interval <t_1, t_2>. Ma. J and B. Knight (1994), presented interval and point based theories. There are different theories presented for the treatment of the two important issues of linearity and density of time elements and they explain that "*The question of the density of time elements depends on the type of primitives assumed for the system. For interval based systems, a dense system is taken to be one where every interval is (infinitely) decomposable. For point based systems, a dense system is one in which between any two points on the same time line, there is a third. Bruce's proposed system leaves the density question open, whereas McDermott's system is decidedly dense. Knight and Ma's system is decidedly not dense, being a discrete system: i.e., one where every time element has a unique predecessor and successor fundamental time element. Other systems, such as that of Allen and Hayes, permit a mixture of dense and discrete time elements."*

In the temporal clinical database system, it is obviously necessary to store, process, maintain and retrieve the time-oriented clinical data. Therefore, the issues of how to organize properly a time oriented medical data set in the clinical database and what sort of

temporal dimensions are needed are crucial considerations. Snodgrass R. and Ahn I. (1986), presented three different types of temporal dimensions: 1) transaction time; 2) valid time and 3) user defined time. Transaction time is the time at which records are stored in the database for instance when exactly a patient's ESR blood record is entered into the patient medical database. Valid time is the time at which the data were true for the model in the real world, for example the time when blood ESR was observed. User defined time is a Time that is defined by the user for example time recorded when a patient's blood CRP was positive.

Time intervals and time instants are the common choice for clinical data reasoning. The example of time intervals is found in drug therapy where time intervals are represented by start and end time. Time instant involves establishing the difference between times, which relate to instantaneous events such as myocardial infraction (Yuval S., 1998). In Yuval (1998), it is stated that "*another difference exists between the basic time primitives, usually instants (time points). In defining basic time entities time points are often adopted. Intervals are then represented by their and lower temporal bounds."* In defining basic time entities, there are various options: linear time, branching time, parallel time, circular time. The linear time is a set of time points and it must be ordered. Linear time is appropriate for a clinical database system. Branching time is also suitable and requires application within various sectors where diagnosis, projection and forecasting are involved. Circular time is necessary for recurrent events such as GAS infection recurring for rheumatic fever patients or managing of insulin for rheumatic fever patients. Figure 2.4 shows circular, parallel and branching time based on Ma J. and Knight B. (1994).

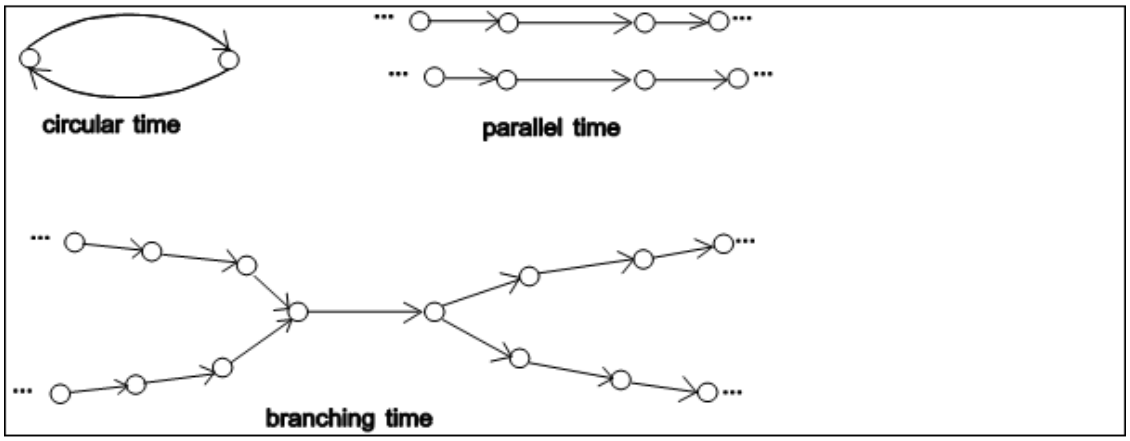


Figure 2.4: Circular, Parallel and Branching Time

In medical diagnosis processes, absolute time is used to indicate the exact position of an event. For example, a patient has a chest pain "*on July 21, 2014 at 4 pm – 4:30pm*" and

relative time expresses the position relatively: "*the day after patient has severe pain on his knees*". Basically absolute time is associated with a metric which reflects its position by specifying its start and finish points. An example of this is ECG *monitors 3pm to 3:30pm*, which defines unambiguously a start to finish time point. After defining the absolute time, then relative times can be given quantitatively for example "*four days after GAS infection on the throat*" or "*one day before the GAS infection*" and qualitatively for example "*chest pain after exercise.*"

In temporal logic, there are two commonly used methods to capture the temporal data (clinical data): 1) point-based (instant) and 2) interval-based duration. Point-based is associated with a single time-stamp whereas interval-based is represented by two time-stamps (start time and end time). Both point-based and interval-based methods have been applied in medical informatics to represent time (Carlo C. and Yuval S, 1997). Most medical informatics system applications were developed on the point-based approach. The point-based method is similar to McDermott's point concept in contrast with the time interval concept proposed by Allen (Carlo C and Yuval S, 1997). The most popular method used in medical diagnosis processes is point-based (Kahn M. G. and Marrs K. A., 1995).

Temporal logics are being used in various areas of the medical sector. Examples include HIV (DAS A.K. *et al*., 1992), Diabetes mellitus domain (Bellazzi R. *et al*., 2000), therapy management (Duftschmid G. *et.al*, 2002), diabetes therapy (Shahar Y. and Cheng C., 1999), heart disease diagnosis (Long W., 1996), intensive care units etc. (Charbonnier S., 2003). Various studies and researches have been done in time-oriented applications in the medical domain: psychiatry, cardiology, oncology, infectious diseases, anaesthesiology, paediatrics etc. particularly when modelling medical reasoning with the event calculus for intensive care (Chittaro L, *et al*., 1995). Multi-Service medical software packages have been constructed for cardiology patients (Pinciroli *et al*., 1992). Shengbing J and Kumar R., (2006), constructed a system based on temporal-logic for the diagnosis of repeated failures. Bellazzi R et al., (2000), presented a general multi-step methodology: temporal abstraction with the pre-processing, extraction and post and described intelligent analysis of clinical time series data in cases of chronic diabetes patient monitoring. Temporal representation formalism and two temporal reasoning algorithms were presented and showed how the algorithms can be exploited to deliver a clinical guidelines system with different types of temporal facilities. This approach enables one to present temporal constraints and check their consistency (Luca A. *et al.*, 2006). A temporal fuzzy min-max

neural network based classifier and particle swarm optimization algorithm-based rule extractor, temporal features, intelligent fuzzy rule for effective decision support in medical diagnosis have been proposed by (Ganapathy S. *et al.*, 2014). Silvana B. and Marco F., (2010), apply a fuzzy temporal constraints system that consists of temporal reasoning and fuzzy constraint to Severe Acute Respiratory Syndrome diseases. Three types of semantic heterogeneity in the integration of temporal data have been identified and Hongwei Zhu (2004), proposed a temporal extension to the COIN (context interchange) framework, which shows a capability for solving temporal context problems (Hongwei Z. *et al.*, 2004). The Idan (*Idan is the Hebrew word for era, or a long time period*) architecture fully implements the temporal-abstraction mediation approach and it integrates multiple time-oriented data sources, domain specific knowledge sources, computation services and a controller that integrates all services. It is a distributed temporal abstraction database mediator, which integrates patients', time oriented data and clinical knowledge to answer abstract, time oriented queries (David B. and Yuval S, 2003). David B and Yuval S, implemented full IDAN architecture in medical applications that show the potentiality for supporting the automation of various clinical tasks including diagnosis, monitoring, therapy and quality assessment (David B. and Yuval S., 2005).

Jose P *et al*., (2006), proposed a temporal behavioural model for capturing the temporal evolution of diseases. The temporal component is modelled by the Fuzzy Temporal Constraints Network for the representation of quantitative and qualitative imprecise temporal information in order to provide a theoretical framework and diagnostic process. Goralwalla (1997), presented a uniform behavioural temporal object model that consists of the histories and timeline feature, on the application of pharmacoeconomic (field of medical economics) medical trials which shows the costs and outcomes of alternative treatments and presents the appropriate treatment for a particular illness in a particular setting (Goralwalla *et al*., 1997). Joeng S. (2014), proposed a chronological clustering method for identifying a temporal variation of metabolic syndrome and investigated the temporal changes of disease status. A chronological distance variance model was developed which estimated and examined results of MS risk factors (Jeong S. *et al*., 2014).

A proposed framework that consists of time-dependent data by using ontology uses machine-learning techniques to identify automatically trends in time series data that shows the patient's particular pathology and adds the pathology classification to the ontology while expressing the uncertainty that is related to predication. The framework

was evaluated detecting sepsis; it is the number one cause of death in the ICU according to Ongenare *et al*., (2010). Klaus-Peter A., (2006), identifies four research areas 1) fuzzy logic, time and medicine; 2) temporal reasoning and data mining; 3) health information system, business processes and time and 4) temporal clinical databases that deserve investigation to develop software systems.

The use of time-related issues or temporal logic and its techniques have been growing rapidly in the various sectors for further research and development of a dynamic system (Bettini C. and Montanari A., 2001). Essentially, temporal logic techniques can be used for the representation and analysis of time-related data that support development of an effective diagnostic system.

2.12. Fuzzy logic

Lotfi Zadeh, a Professor at the University of California at Berkley, USA, introduced Fuzzy Logic in 1965. At that time, Fuzzy Logic was criticized hugely and it has not been well popularised and accepted at large. Later, in the 1980s, Fuzzy Logic and an automatic-drive fuzzy control system were successfully applied on a Sendai Subway Train in Sendai, Japan (Legind L., 2005). According to Zadeh (2008), "*Fuzzy logic is not fuzzy. Fuzzy logic is a precise logic of imprecision and approximate reasoning. More specifically, fuzzy logic may be viewed as an attempt at formalization/mechanization of two remarkable human capabilities".* Fundamentally, the aim of Fuzzy Logic is to formalize approximate reasoning. In the narrow sense Fuzzy Logic is a logical system, which has the sole purpose of the formalization of approximate reasoning; in the wide sense, Fuzzy Logic is coextensive with fuzzy set theory, s theory of classes with unsharp boundaries (Lotfi A. Z., 2004). The most significant of numerous contributions of Fuzzy Logic are : fuzzy logic generalization, such as fuzzy control, fuzzy linear programming, fuzzy probability theory, linguistic variables and fuzzy if-then rules, fuzzy logic modelling language, computing with perception, computation with imprecise probabilities, possibility theory etc. (Lotfi A. Z., 2004, 2008).

Fuzzy is logic where everything is dealing with fuzziness or the logic of fuzzy sets. Fuzzy Logic is the better alternative and has more alternatives in describing the vagueness of real world problems (Bart K. and Satoru I., 1993). In traditional Crisp Set theory, any statement is either true or false and there is nothing in between. The statements might have the imprecise, vagueness and uncertainty information, which is often hard to deal with using Crisp Set or Conventional Set theory. The important instinct in Fuzzy Logic is

that decision-making is not always a matter of 0 or 1, true or false, but instead it comprises some value in between 0 to 1 to make decisions in real world problems. In addition Fuzzy logic has a great potential to use linguistic variables, for example few, slow, fast, large, heavy, severe, mild, low, medium, high, short, average, tall etc. (Pandey S. *et al*., 2015). A Crisp set is two-valued logic, where each element has only two possible values of either true or false, or each statement must have either 0 or 1 in membership degree: if 0, the statement is completely false and outside the set, if 1, the statement is completely true and inside the set. In a Crisp set, completely true membership or completely false membership of element x in set A is described by the function $\mu_A(x)$, where $\mu_A(x) = 1$, if $x \in A$ (x is completely true in set A), $\mu_A(x) = 0$, if x is completely false in set A (Bai, Y *et al*., 2006). Fuzzy Logic is a suitable model for nonlinear by nature problems, which are difficult to model mathematically. Thus, in fuzzy set theory, every element of universal discourse maps with a membership function to a membership value between 0 and 1, which means that in a fuzzy set, any statement can partially belong to a set. In a fuzzy set and every statement is a matter of degree, which is characterized by a membership function and provides a membership value between 0 and 1. Thus in a fuzzy set, a statement might be very true, partially true or somewhat true with a degree of 0.9, 0.6 or 0.2 in numerical terms (Pandey S. *et al*., 2015).

As stated by Lotfi A. Z (1965): "*a* fuzzy set *A is usually expressed in terms of its membership function μA which maps domain elements (x) to their respective degrees of belonging in the interval [0,1]*. Figure 2.5 shows Crisp Vs. Fuzzy Sets.

Crisp Vs. Fuzzy

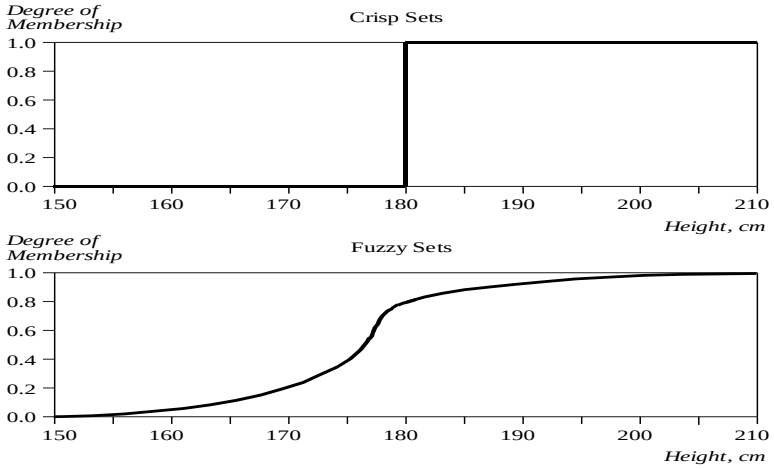


Figure 2.5: Crisp Vs. Fuzzy Sets

In the classical set, the mapping is straightforward with a sharp boundary without uncertainty or ambiguity. Fuzzy a set allows members to belong with a smooth boundary,

which means a fuzzy set allows a member to belong to a given set with some sort of partial degree.

2.12.1. Fuzzy Logic Operator, Operation and Property

The operation on fuzzy sets (Lotfi A. Z.) is Intersection, Union and Complement, which are described below:

Intersection: The logic operator corresponding to the intersection of sets is **AND.**

$$\mu_{(A \text{ AND } B)} = \text{MIN}(\mu_{(A)}, \mu_{(B)})$$

Union: The logic operator corresponding to the union of sets is **OR.**

$$\mu_{(A \text{ OR } B)} = \text{MAX}(\mu_{(A)}, \mu_{(B)})$$

Negation: The logic operator corresponding to the complement of a set is the negation.

$$\mu_{(\text{NOT } A)} = 1 - \mu_{(A)}$$

2.12.2. Operation of Fuzzy Set

The operations on fuzzy set are:

Complement: If A is the fuzzy set, its complement $\neg A$ then, $\mu_{\neg A}(x) = 1 - \mu_A(x)$

Intersection: The fuzzy intersection of two fuzzy sets A and B on the universe of discourse X can be expressed as: $\mu_{A \cap B}(x) = \min [\mu_A(x), \mu_B(x)] = \mu_A(x) \cap \mu_B(x)$, where $x \in X$

Union: The fuzzy union of two fuzzy sets A and B on the universe of discourse X can be expressed as: $\mu A \cup B(x) = \max [\mu A(x), \mu B(x)] = \mu A(x) \cup \mu B(x)$, where $x \in X$

2.12.3. Properties of Fuzzy Set

The properties of fuzzy sets are:

Equality of two fuzzy sets: Fuzzy set A is considered equal to a Fuzzy set B, IF AND ONLY IF: $\mu_A(x) = \mu_B(x), \forall x \in X$

Inclusion: Inclusion of one fuzzy set into another fuzzy set. Fuzzy set $A \subseteq X$ is included in (is a subset of) another fuzzy set, $B \subseteq X$: $\mu_A(x) \leq \mu_B(x), \forall x \in X$

Cardinality: Cardinality is expressed as a SUM of the values of the membership function of A, $\mu_A(x)$: $card_A = \mu_A(x_1) + \mu_A(x_2) + \ldots \mu_A(x_n) = \Sigma\mu_A(x_i)$, for i=1..n

Empty Fuzzy Set: A fuzzy set A is empty, IF AND ONLY IF: $\mu_A(x) = 0$, $\forall x \in X$

Alpha – cut : An α-cut or α-level set of a fuzzy set $A \subseteq X$ is an ORDINARY SET $A_\alpha \subseteq X$, such that: $A_\alpha = \{\mu_A(x) \geq \alpha, \forall x \in X\}$.

2.12.4. Membership Functions

The Membership Functions (MF) is the ways to fully define the fuzzy set or for it provide the degree of truth-value between 0 and 1. There are different shapes of membership functions some of them are; Triangular function, Trapezoidal function, Piece-wise linear function, Gaussian distribution function, Sigmoid curve, Quadratic and cubic polynomial curves, Singleton Membership Function, Bell-shaped, L function etc. (Fuzzy Tool Box). The features of membership function are given (Figure 2.6) below:

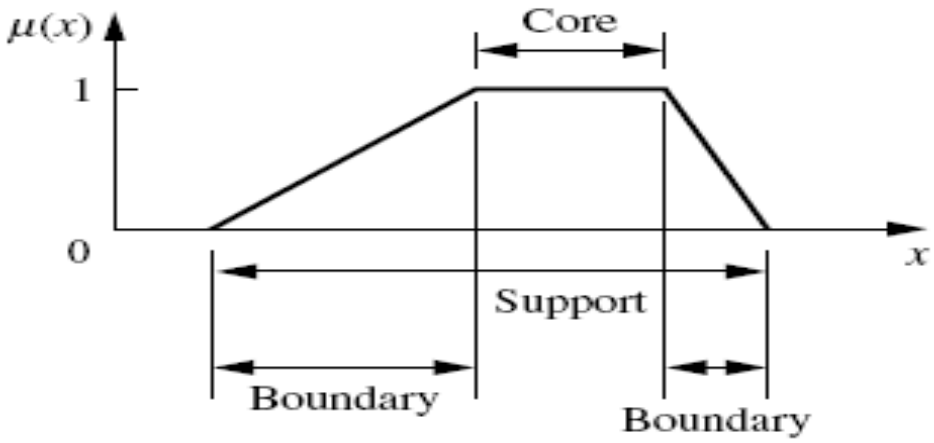


Figure 2.6: The feature of membership function

The meaning of **core** membership function is a complete and full membership in the set of A, μA*(x)* = 1. The **support** membership function is a nonzero membership in the set A, μ*A(x)* > 0. The **boundaries** of a membership function are containing elements that have a non-zero membership but not complete membership. There are different types of membership functions available and being applied in various areas.

2.12.5. Selection of Membership Function

Various discussions and approaches are appearing to determine the fuzzy membership function and input/output parameters for the clinical diagnosis processes. Nevertheless,

there are as yet no suitable guidelines or methods for choosing the membership functions and input/output parameters for the diagnosis of ARF. To determine the particular membership functions and input / output parameters for the diagnosis of ARF is difficult and a time consuming process especially in areas where relevant data sets are not available. To apply fuzzy logic to a clinical decision support system or medical diagnosis system, appropriate membership functions and suitable input/output parameters are required. Various membership functions are available: singleton, triangular (3 parameters), and trapezoidal (4 parameters), nonlinear e.g. Bell shaped (3 parameters), Gaussian (2 parameters) and Π-shaped, monotonically increasing linear membership function, decreasing linear membership function etc. which are being used in fuzzy controllers (Math Work, Fuzzy Logic Tool Box, http://uk.mathworks.com/products/fuzzy-logic/). The choice of membership functions and input/output parameters depends upon the application's domain and its functional areas. No guidelines, theory and methods have been shown to be fully suitable for selecting the specific membership functions that are suitable for exact application (Medasani S *et al*., 1998). Therefore, selection of membership functions is often dependent upon experience or randomly selected. Although the input/output parameters or membership function's variables certainly do have an impact on the overall performance of a fuzzy controller (Liu, 2000). Forward selection and backward selection methods were used for feature selection for pattern classification in the 1960s (Marill and Green, 1963). In the forward selection method, we are able to make models, which have a gradually increasing number of variables. And in backward selection method that consist of all input variables removing one variable at each stage by evaluating a collection of simpler models (Stephen L.Chiu., 1996). The selection of a membership function depends upon the nature of the problem and related data sets.

2.12.6. Implementation of Fuzzy Logic

The required steps are given below to implement a fuzzy logic technique for a real application.

- Fuzzification: fuzzification is the process of converting the Crisp values into Fuzzy values.
- Fuzzy Inference Process: Inference process applies to combine fuzzy value with fuzzy rules to get the fuzzy output, or it will combine the facts obtained from the fuzzification with the rule base and conducts the fuzzy reasoning process.

- Defuzzification: defuzzification is the process of converting the fuzzy value into a Crisp value.
- Knowledge base – KB contains a collection of fuzzy rules also known as the rule base, and database

Fuzzy Logic is a process of Crisp-Fuzzy-Crisp, which means converts Crisp value into fuzzy and fuzzy value into Crisp for a real system. The original input and the final output must be Crisp variables but in between is a fuzzy inference process. In the fuzzy system, the process of decision-making is performed by the inference engine using the collection of rules, which is contained in the rule-base. The rules will define the connection between input and output fuzzy values. For example,

If <condition > **then** <consequent>; **If** *x* is *A* **then** *Y* is *B*

The condition or antecedent is a fuzzy logic expression made by one or more simple fuzzy expressions that are connected with fuzzy operators and the consequent expression that assigns fuzzy values to the output variables. Then, the inference engine evaluates all the rules and combines the weighted values (consequents) for all fired rules into a single fuzzy set applying the aggregation operation.

Fuzzy Modelling is the process of identification of the parameters for a fuzzy inference system. The parameters of a fuzzy inference system are defined by class i.e. logical class (reasoning mechanism, fuzzy operators, membership functions types, defuzzification methods), structural class (relevant variables, number of membership functions, number of rules), connective class (antecedents of rules, consequents of rules, rule weights) (Pena-Reyes C.A. and Sipper M., 1999; Pena-Reyes C.A. and Sipper M., 2002). Logical parameters are usually predefined by the designer based on his/her experiences of a specific problem's characteristics. It can be also defined based on expert guidelines and support but experts must have sufficient experience and knowledge in a particular problem domain. The popular reasoning mechanisms are: Madami-type, Takagi-Sugeno-Kang (TKS)-type and Singleton-type (Yager R.R and Filev D.P., 1994). The common fuzzy operator views: min, max and product and common membership functions, which are triangular, trapezoidal, bell-shaped and S, function. Various methods are available for defuzzification. The most popular are Mean of Maxima and Centre of Area (Yager R.R and Filev D.P., 1994; Mendel J.M., 1995). Structural, Connective and Operational parameters might be predefined or obtained by various search methods.

2.13. Fuzzy Tools and Techniques in CDSS

In the 1960s, the first medical computer appeared based on bivalent logic, which could not map the medical vagueness needed in medical diagnosis. Lotfi Zadeh (1965), introduced a new theory of fuzzy sets and systems and proposed to apply it in the medical domain. Later, Mario Bunge published a systems-theory approach to medical philosophy named iatrophilosophy in the 1970s and following that the application of fuzzy systems in medicine began, (Rudolf S., 2006). Since then in the medical domain, various terms and notions have been created including health, illness, diseases, diagnosis etc. which cannot be sufficiently defined by the basic principles of classical logic (Julia L. and Rudolf S., 2007) yet in the case of consistent sectors classical logic might be an appropriate tool (Kazem S.Z, 2000). The fuzzified notation of fuzzy health (matter of degree), fuzzy illness (matter of degree) and fuzzy disease (matter of degree) are presented and discussed based on the fuzzy set theory by (Kazem S.Z, 2000). "*Health, illness, and disease are not the only subjects of medical and philosophical concern, but are also intriguing ontological objects"* as stated by Kazem, S.Z, (2000). Fuzzy logic has the capabilities to formalize medical uncertainties and vagueness in a clinical decision support system (Jim W. *et al*., 2000).

Fuzzy logic, artificial neural network, genetic algorithm and any combination of these has been studied and reviewed for important medicine applications from 2000 to 2008. The conclusion of these studies has revealed that Fuzzy Logic and neural networks are significantly used. Neural networks and genetic algorithms are also used in various medical domains (Yardimci, 2009). A multi-objective genetic algorithm has been applied to optimize the accuracy and transparency of fuzzy rule-based systems. In addition, the Ensemble Classifiers Strategy (ECS) method is proposed to improve the classification ability of the fuzzy rule-based system. As a result, applying this method has improved the ability for diagnosing coronary heart disease (Adel L., *et al*., 2012).

Application of fuzzy technology in the medical domain has been studied where the domain has been divided into main and subcategories. The nine main categories are: 1) conservative disciplines; 2) invasive medicine; 3) regionally defined medical disciplines; 4) neuro medicine; 5) image and signal processing laboratory; 6) basic science; 7) nursing; 8) healthcare and 9) oriental medicine. The main conclusions reached for our study were in: a) the consideration fields where fuzzy methods are applied: internal medicine, anaesthesia, radiology, electrophysiology, pharmacokinetics and aeromedicine;

b) no specific application is used in surgical disciplines, dental medicine, general practice and nursing and c) growing fields such as medical reasoning and decision support science (Abbod, M.F. *et al*., 2001).

The seven Fuzzy techniques: basic controller, rule based open loop, rule based closed loop, self-learning, model based and adaptive, hybrid systems, neural, genetic and wavelets', hierarchical system as well as three fuzzy algorithms are discussed: fuzzy clustering, fuzzy classifications and fuzzy modelling, specifically to address and find a solution to the control problem inherent to the medical domain (Mahfouf M. Abbod and Linkens D.A., 2001).

Fuzzy logic today is becoming more popular and is being applied in the different sectors of the medical domain the best examples being: automated diagnosis (Adlassing K-P, 1986), image processing (Lalande, A. *et al*., 1997), pattern recognition (Zahlmann G., Scherf M. and Wegner A., 1997), control systems (Mason D., Linkens, D. and Edwards N.,1997), laboratory processing, therapy planning etc.

Various fuzzy tools and techniques are applied in CDSS. Kosko (1986), introduced the Fuzzy Cognitive Maps (FCMS) theory / tools which is good for modelling and simulation of the dynamic system. It incorporates a graphical representation of human thinking or knowledge. It is a combination of cognitive mapping and Fuzzy Logic. It is used for casual knowledge acquisition and knowledge reasoning process. It was found that the combined model of discrete wavelet transforms (DWT) and fuzzy support vector machines (FSVM) modelling are better than other machine learning methods for the classification of electromyography (EMG) classification (Subasi A., 2012). It is particularly useful if we need to deal with images as an input since it gives better accuracy than neural-networks. FSVM is basically used in object detection and recognition, image retrieval, text recognition, speech recognition and biometrics. Rabelo *et al*., (1996) have proposed the Analytical Hierarchy Process (AHP) for building the "kernel" of a clinical decision support system. AHP is a multi-criteria decision analysis method that uses mathematical algorithms, which transform qualitative subjective judgments into quantitative data or "weights"; essentially a decision analysis technique (Hartwich and Janssen, 2000). AHP can be appropriate for use in particular cases where support is required from different people participating at a variety of levels within the organization. In these, often complicated circumstances, it is clearly helpful and appropriate for use during a group decision-making process (Steiguer *et al*., 2003).

Kavan S. *et al*., (2009), discussed the interpretable genetic fuzzy rule that highlights the feature's subset selection based on the Michigan Learning approach and Training Fuzzy Rule-based approaches for the construction of Breast Cancer Diagnostic. In the first phase, a number of independent fuzzy rule-based systems are trained using genetic operation and in the second phase, a fuzzy rule-based system is trained based on features selected from the previous phase (Kavan S. *et al*., 2009). PROAFTN is a new Fuzzy Multicriteria Classification Method, which belongs to the class of supervised learning algorithms and enables it to determine the fuzzy data in different relations by generalising the indices used in the ELECTRE III method. It has been applied and implemented in acute leukaemia, astrocytes and bladder tumours (Belacel N., 2000; Belacel N. and Boulassel M.R., 2001). Fuzzy Data Mining is also used in the medical domain. Fuzzy *k*-nearest neighbour algorithm, a fuzzy clustering-based modelling, and the adaptive network-based fuzzy inference system are used showing that selection is important in mining medical data (Sean N. G. and Thunshun W. L., 2008). The weighted fuzzy reasoning algorithm, the fuzzy set theory and fuzzy production rules are used to handle medical diagnostic problems (Shyi-Ming C., 1994). A cardiovascular disease predicting diagnosis system is built by combining the advantages of fuzzy logic, neural network and genetic algorithms (Vijaya *et al*., 2010). There are several applications: A fuzzy decision tree (Levashenko V. and Zaitseva E., 2012), ontology-based fuzzy decision support system (Esposito *et al*., 2011), AI techniques or Genetic Algorithms (GA), Rule-based System (RBS), Fuzzy Logic (FL), Neural Networks (NN), Case-based Reasoning (CBR) etc., are used for the development of different tools, especially diagnosis and predicting in the medical domain (Wan W. and Fadzilah, 2006). Fuzzy soft set theory, introduced by Molodtsov for dealing with uncertainties) and fuzzy arithmetic operation is applied for medical diagnosis (Celik *et al*., 2013). A Fuzzy-c-mean (FCM) clustering, semi-supervised method and region growing techniques are used for automated tumor image segmentation from patients with meningioma (Thomas M. H. *et al*., 2011). Knowledge-based, rough set theory, fuzzy rules weight are applied in the development of fuzzy decision support systems for the diagnosis of coronary artery disease (Noor A.S. *et al*., 2009). A five-layer fuzzy ontology is developed in the Fuzzy Expert system to describe knowledge with uncertainty plus a semantic fuzzy decision-making mechanism is developed for the diagnosis of diabetes (Chang-Shing L *et al*., 2011). A Fuzzy Max–Min Composition technique is proposed for medical diagnosis (Edward Samuel A. and Balamurugan M. 2012). A hierarchical model of the fuzzy inference has been proposed as

a solution to the difficulties in designing an inference system for the diagnosis of arthritis diseases.

The diagnostic process itself is divided into two levels: the first level reduces the scope of diagnosis to be processed by the second level. Fuzzy relational theory is used in both levels to improve accuracy (Lim C.K *et al*., 2002). Machine learning methods, especially rule induction and instance-based learning methodologies, are applied for the early diagnosis of rheumatic diseases. Over 200 different rheumatic diseases have been grouped into eight diagnostic classes and the numbers of patients belonging to each class are recorded. Some reasons have been given regarding the unreliability. An example of this is high level of noisiness of the data, which can occur when grouping about 200 different diagnoses into eight diagnostic classes. Problems such as this are discussed and can be found in (Dzeroski *et al*., 1996).

Artificial Neural Network (ANN) is inspired by the biological nervous system, the brain, and is appropriate in handling non-linear and noisy data. However, it does not have a good explanatory mechanism, which is always desirable within any clinical decision-making support system (Uzoka O. and Baker 2009). ANN is suitable for discovering regularities within a set of patterns, adaptive learning, real time operation etc. The Neuro-Fuzzy Inference System is based on self-learning intelligence capable of handling uncertainties in a diagnosis process (Jang *et al*., 1997). Applying a fuzzy method of supervised and unsupervised qualitative clustering techniques to build a patient monitoring system is discussed: the first level determines whether the state is normal or an alarm; the second level determines the degree of membership of sets of normal situations plus six groups of cardiovascular disease. The final level determines specific membership to a selected group of cardiovascular emergencies (Cesar *et al*., 2011). The Fuzzy Rule-based system is also applied in the diagnosis of myocardial infarction by use of fuzzy learning techniques (González A. *et al*., 1995), medical data analysis and the fuzzy-set based approach (Smidt, E. *et al*, 2003). Fuzzy logic is applied on some medical applications such as: Tuberculosis, Cancer, HIV, Pharmacy, Heart diseases, Asthma, image and signal processing, Diabetes, Aphasia, Malaria, Hypothyroidism, Meningioma and Arthritis (Prasath V. *et al*., 2013).

The main benefit of the fuzzy logic-based medical diagnosis system is that it is highly effective in handling both quantitative and qualitative information. In the case of quantitative inputs, for example fever, white cell in blood, blood pressure and so forth, the

process of fuzzification does not present any real difficulty. But qualitative information such as severe pain, redness on the hand, swelling, feeling very hot etc. are organized on a linear scale of 0 to 5. In these circumstances, doctors quantify observation on the scale of 0-5 based on his/her perception. Fuzzification, fuzzy inference mechanism, membership function, defuzzifications, linguistic variables, fuzzy rules, etc. are the components of fuzzy logic. Further details of this process are discussed in Research Methodology, Chapter 4. To summarize, fuzzy sets and Fuzzy Logic are appropriate tools to apply in any kind of problem where:

- A particular problem arising when objects are needed to be deal with imprecision, uncertainty or incompleteness of information,
- A particular problem where objects are needed to deal with linguistic variables and *IF-THAN* rules.
- A particular problem arising when the universal set is not a singleton.
- A particular problem where objects are needed to deal with partiality of truth and possibility.
- A particular problem when there is more than one local maximum of a membership function.
- A particular problem when the membership function takes a value other than 0 and 1.

2.14. Hybrid Methodology in CDSS

In the Hybrid Methodology, two or more methods are combined together and applied to solve a particular problem. Some analyses of the Hybrid system being used in the medical domain is given below:

- Investigate a computer-assisted colonoscopy image diagnosis system based on the artificial neural network plus differential evolution algorithm (Magoulas *et al*., 2004)

- A hybrid method that uses fuzzy weighted pre-processing and artificial immune recognition system (AIRS) for the diagnosis of heart disease (Kemal P. *et al*., 2006).

- A neuro-fuzzy-case base reasoning – hybrid (combined neural network, fuzzy logic and case base reasoning) is applied for the diagnosis of depression disorders (Victor E. E. *et al*., 2012).

- A neuro-fuzzy hybrid system is applied for the development of artificial ventilation modelling (Liu F. *et al*., 2006). Selected a fuzzy K-nearest neighbour and applied to diagnosis of the Parkinson's disease (Chen H.L *et al*., 2013).

- Fuzzy methods, genetic algorithm and support vector machine was used to develop the model for the diagnosis of Heart, Liver and Diabetes diseases (Jin, B. *et al*., 2007).

- Genetic Algorithms, Logistic Regression, and Chi-square tests have been applied to identify the risk factors of asymptomatic carotid stenosis (Bilge U. *et al*., 2013).

- Artificial neural network, multivariate adaptive regression used for the diagnostic system of breast cancer (Chou *et al*., 2004).

- Applied an evolutionary machine learning, decision tree, genetic algorithm for identifying the cardiovascular problems for young patients (Vili P. *et al*., 2005). The fuzzy rule base decision tree is applied to automatic diagnosis of coronary artery diseases by using a method of extracting a set of Crisp rules from the decision tree, convert the Crisp rules into a fuzzy model and then the system can provide an explanation for the decision made (Tsipuouras M.G. *et al*., 2008). Further examples of some developed CDSS systems are provided in Appendix 2.2.

2.15. Uncertainties of CDSS

The basic schema to represent human knowledge is influenced by a variety of factors. For example, involvement of the uncertainty, ambiguous, imprecise and incomplete information which needs to be carefully considered during representation of the knowledge process. In addition, to design and develop a clinical diagnosis system for uncertainty issues appears in most medical domains. It is therefore necessary to establish clear cut-off ideas or concepts to be able to bring them appropriately into the system otherwise the system cannot function. Some uncertainty issues that might arise in this research work are highlighted below:

1. A patient cannot explain or is not able to describe exactly what his/her problems are. This aspect of research is especially important for ARF diagnosis relating to children who might find it difficult to describe their problems or how they feel.
2. Laboratory results might not be 100% accurate.
3. This research frequently relates to under-developed countries like Nepal, especially in rural areas where laboratory facilities are scarce, for making patients' physical

observations which are nearly always essential for understanding the severity of symptoms.

4. Some doctors do not have sufficient knowledge and do not have any experience in particular a disease's symptoms or ARF symptoms.
5. Pharmacologists do not have proper knowledge of the effectiveness of particular drugs.
6. Generally inadequate knowledge.
7. Incomplete patient data.

In regard to these key issues, Lotfi A. Z. (1983) explained, "*Management of uncertainty is an intrinsically important issue in the design of expert systems because much of the information in the knowledge base of a typical expert system is imprecise, incomplete or not totally reliable. In the existing expert systems, uncertainty is dealt with through a combination of predicate logic and probability-based methods. A serious shortcoming of these methods is that they are not capable of coming to grips with the pervasive fuzziness of information in the knowledge base, and, as a result, are mostly ad hoc in nature. An alternative approach to the management of uncertainty which is suggested in this paper is based on the use of fuzzy logic, which is the logic underlying approximate or, equivalently, fuzzy reasoning."*

2.16. Problems of Technology Transfer

No computer-based decision support system and associated technology can be considered as a universally perfect and useable package. Systems being used in developed countries cannot be transferred directly to under-developed countries for many reasons. Firstly it is necessary to investigate whether the selected system and technology are appropriate or not; essentially whether they accord with a country's government policy, social and cultural values, information and communication technology, manpower, geographical structure and other resources. According to WHO primary health care is essential health-care that should meet three criteria: 1) technically valid; 2) economically feasible and 3) socially acceptable. If these criteria are not satisfied then probably the technology cannot be used.

Secondly, we realised that while considering transferring the DSS system in Nepal, the prevailing government policy, available technology and user needs must be taken into account. Similarly, other important points that need to be considered from inception are

the local guideline and treatment procedures of ARF and RHD since it is often not necessary for every country to use identical guideline and procedures.

Nepal does have the basic infrastructure of communication and information technology. Unfortunately, due to lack of government policy, proper national health policy and lack of trained manpower, information technology has not been applied effectively in the healthcare sector. The basic constraints in transferring the DSS system in Nepal are listed below:

- The country does not have any electronic patient record system.
- The system currently uses paper-based methods, which are far from perfect; data are not entered accurately, duplication is commonplace, information is sometimes omitted, all reflecting the shortcomings that may be caused by human error.
- The country has limited budget and limited professional human and technical resources.
- The country's treatment and medication procedures, those relating to treatment, might be different from those used in more technically advanced western countries.
- Doctors must be willing to use computerized DSS systems and undertake training, to keep themselves up to date on technology.
- The user interface must be appropriate and suitable by employing a system that should be easy to update.
- High-speed data / information communication infrastructure are rare and internet facilities are limited.
- Climate must be taken into account, especially the monsoon season, which is often detrimental to transportation, and communications.
- Data utilization and decision-making skills generally are in need of improvement.

Data are very important to make a decision or to develop an effective decision support system. Alternative solutions therefore must be introduced to improve on the paper-based methods by adoption of computerized systems. Provision for the following key data sets is fundamental to modelling a new system:

1. Patients' demographics information.
2. Patients' past/present entire medication histories.

Taking all these matters into account it is self-evident that there is a need and strong justification for designing and developing an appropriate and affordable decision support

system for ARF in Nepal. A computerised system that is able to accommodate all technical and socio-economic parameters will be able to meet the country's local requirements, country health policies, treatment practice and clinical procedures. The system to be developed of course must be geared to make best use of available resources, expert guidelines and acknowledged skills.

2.17. A New Hybrid Approach to Diagnosis of ARF

Our collaboration research discussed the approaches and methods that are used in clinical decision support systems based in Nepal. Currently in Nepal there is no computer-based application designed to help in the diagnosis and management of ARF. Our research aimed to provide better diagnosis of ARF through a computer-based decision support application. CDSS produce the results that could provide for diagnosis, prognosis, medication, therapy planning, and suggestion for further tests by analysing patient physical symptoms using laboratory test results. In Nepal sometimes the decision is solely based on limited knowledge, due to lack of laboratory records; incomplete information, uncertainty over issues, very often with doctors having a limited time to make a decision. Under such vague conditions, decisions can be harmful for patients on occasions. The challenges presented by the country's lack of resources, inadequate trained manpower, out-dated technology, socio-economic conditions, inappropriate local treatment and imprecise guidelines for clinical procedures need to be quantified and assessed carefully before designing and developing a new diagnosis model.

With regard specifically to diagnosis of ARF, two issues have been underlined by the Nepal Heart Foundation: 1) ARF in Nepal has created a lot of confusion in diagnosis and treatment, due to the lack of standard procedures and 2) the adoption of foreign guidelines is often not effective when they do not accord with the Nepali environment and life-style. Therefore, in our research we mainly focussed on investigating ARF signs and symptoms and the potential for using diagnosis processes from other more advanced countries. Rather than transfer the technology, our aim was to transfer the knowledge and information to diagnose ARF in Nepali and English versions. With this in mind, we studied the possibility of using a Hybrid Approach with a combination of knowledge-based, temporal theory and fuzzy logic techniques to develop a suitable model. The main functions of this model are firstly to collect the ARF's information and analyse it by NHF's experts and secondly to study the relationship between the symptoms, the time frame, uncertainty and other associated factors of ARF and finally to design and develop

an automated diagnostic application. A brief discussion on this topic is described under Research Methodology, Chapter 4.

2.18. Why a Hybrid Approach?

In our Hybrid Approach, Knowledge-based Temporal Theory and Fuzzy Logic are combined in order to model a CDSS system for the diagnosis of ARF. The reasons for selecting three different methods to design and develop this are as follows:

1. The purpose of applying a knowledge-based approach is to capture, organize, manipulate and represent the domain knowledge of ARF. It can facilitate production of systematic descriptions of ARFs that could lead to more useful and flexible guidelines for the ARF diagnosis process. The main goal of using KBS is collecting related ARF medical information from various international sources such as WHO, WHF, NHS Choice (UK), Australia, New Zealand, journals, books, conference papers and other guidelines for potential application in a new ARF diagnosis model suited to Nepal.

2. It is not necessary that all symptoms are present at the same time and same order. Thus, the use of temporal theory in this model will deal with the time variant of all ARF symptoms. In addition, the duration of a symptom's time may vary and this factor may be a crucial influence in diagnosis of ARF. Patients describe their problem in their own language, so it is necessary to capture a symptom's occurrence sequence and timeline accurately for effective diagnosis. Temporal Theory has the capacity to capture and process time-related data and place these in temporal order. In addition, in the clinical domain, time always play a vital role in the diagnosis process, prescribing medication, management of clinical data etc. so that Temporal Theory was one important facet to consider and develop in this model.

3. The reason for applying Fuzzy Logic is that some symptoms of ARF are unable to produce accurate numerical values. There are some uncertainties, for example over severity of pain, movement restriction, mild hotness in the joints, which raise the question of actually how severe pain the pain really is. This might depend upon individual perception and judgement fuzzy logic therefore offers techniques for dealing with such types of uncertainty.

The Hybrid Approach aims to apply knowledge-based, rule-based reasoning, which employs guidelines for diagnosing ARF within a Temporal Model. The fuzzy logic model aims to improve the precision of such diagnosis. ARF Diagnosis Applications would thus be a process for capturing and representing knowledge from experts in order to design and develop an application as well as provide assistance eventually for all users. The details of the Hybrid Approach including inference can be found in Research Methodology, Chapter 4.

In general, this model will assist inexperienced doctors and community rural health workers, to more effectively diagnose ARF at an early stage. Similarly, this model has a great potential not only to provide high quality diagnosis and better service but also to support reduction of healthcare costs and improve results.

2.19. Chapter Summary

After a review of literature, a conclusion can be drawn that, various CDSSs have been developed and are being used in developed countries. Most of them have great positive impact on health-care systems. At present, there is no effective DSS that has been developed for the diagnosis of ARF that is fit for the Nepalese environment and lifestyle.

Any type of computer-based system is obviously valuable for developing and under-developed countries where experts are either unavailable or excessively expensive. In the context of Nepal, the majority of people live in rural areas where proper medical facilities and experts are rare. Consequently, a system of this kind can be a tool with great potential for assisting community rural health workers or medical practitioners, especially for accurate recognition of disease at an early stage.

Clinical knowledge is huge and is changing frequently. It is estimated that doctors need to use up to two million pieces of information (Smith,R., 1996) to manage patients and are also required to keep their knowledge up to date. Textbooks, journals and other related information are not sufficient for answering many medical questions; textbooks and journals are often “out of date or not up-to-date”, (Smith R., 1996). Moreover, it is also not possible for doctors to memorise all the information for long periods. It is inevitable that old textbooks, guideline information, journals, treatment procedures are not up-to-date and thus may not be suitable for providing effective treatment for patients. By contrast, properly structured computer-based systems are invaluable tools for doctors to store, manipulate and retrieve medical knowledge. Unfortunately, in developing or under-

developed countries, doctors are not used to computer technology and the problem can be aggravated by the fact that a system might be developed that may not suit local requirements. We quickly realised that it is essential, to properly analyse local social and cultural values and existing treatment procedures to be able to develop an effective CDSS.

Analysis of these matters was provided by Wetter T. (2002), who emphasised that the following factors are essential for achieving successful implementation of CDSS: 1) timely advice; 2) workflow integration; 3) integration into IT environment; 4) flexibility; 5) response to user needs; 6) physician's ability to change the knowledge base and 7) maintenance and extension. It was accepted that these points must be considered and integrated during the analysis, design and development of ARF Diagnosis Application.

CDSS is evidently helpful in supporting medical decisions, but it is difficult to ensure that health providers actually use them, accordingly Bates *et al*., (2003), summarized ten rules for successful implementation of CDSS. These are: 1) speed is everything; 2) anticipate needs and deliver in Real Time; 3) fit into the user's workflow; 4) little things can make a big difference; 5) recognize that physicians will strongly resist stopping; 6) changing direction is easier than stopping; 7). simple interventions work best (fit a guideline on a single screen); 8) ask for additional information only when you really need; 9) monitor impact, get feedback, and respond and 10) manage and maintain your KBSs. We agreed to adopt the given points during the design phase and to adopt them ultimately for the system development phase.

Chapter 3: Acute Rheumatic Fever and Conceptual Framework

3.1. Introduction

This chapter describes a field visit for a feasibility study. It reports and discusses the collaborative work, data collection, country procedures needed to diagnose ARF and RHD and emphasises the position of important signs and symptoms of ARF. It also discusses Nepal's ARF and RHD prevention and control plan and its application. The chapter illustrates a conceptual framework for diagnosis of ARF in the Nepalese setting and closes with a focussed summary.

3.2. Field Visit Report

During this phase of my research, I visited Nepal three times to pursue various research tasks in (2011, 2014, and 2015). I first visited to establish the collaboration links between the NHF and UoG regarding the design and development of an affordable CDSS model to be designed for diagnosis of ARF in Nepal which needed to fit in with the Nepalese environment and lifestyle. The model had to be suitable and easy to use especially by community health workers and inexperienced doctors in rural areas. In addition, all the legal and ethical issues, data protection issues and communication channels between the university and NHF were set up in accordance with NHF and UoG's rules and regulations. The other main tasks were as follows:

- Understanding the treatment procedure and practice for diagnosis of ARF/RHD.
- Understanding the country-specific problems regarding diagnosis of ARF/RHD.
- Understanding the country's available technologies, manpower and national policy regarding ARF/RHD.
- Data collection *per se.*

With these in mind, we agreed upon a collaboration project between the NHF (Nepal) and UoG (UK), to design and develop an appropriate and mutually acceptable ARF diagnosis model.

In this research, NHF was to provide the data (patient registry), the country's guidelines, diagnosis procedures and practices for management of ARF together with other requisite expert support and information about ARF and RHD, beginning from the outset up to the

completion stage of my primary research. NHF thus fully participated in evaluation of the developed application and the evaluation and analysis of the application's results. Based on the final evaluation report, the application will be handed over to NHF. The training and implementation plan is to be setup by NHF in conjunction with the Nepal Ministry of Health and collaboratively to provide them appropriate training and support as required. The purpose of my second visit was to discuss the conceptual framework and development of a prototype for design and development in harmony with the Nepalese setting.

My third visit was for experimentation and evaluation of the proposed ARF model. Detailed descriptions are provided in the Experiment and Evaluation Chapter 5.

3.3. ARF/RHD Prevention and Control Plan

The government of Nepal has a program to provide the funding for valve replacement for low-income RHD patients. Each year, the government provides funds for about 300 valve replacements. The cost of each operation to replace a valve is approximately £2,500. Due to the high volume of RHD cases, the waiting list of operations is lengthy and many RHD patients die whilst waiting for surgery. The Government of Nepal indicated its interest in developing an ARF/RHD control and prevention programme with a view to decreasing the morbidity and mortality incidences in children in Nepal. This program was initiated by the NHF to fight ARF and RHD in Nepal. The NHF is an active member of the WHF and supports one of its most ambitious missions: "…*to unite members and lead the global fight against RHD through aligning around the World Health Organization (WHO)-related target of 25% reduction in ARF/RHD mortality by 2025 in under 25 years olds*" (Remeny B. *et al*., 2013). Since 2007, the NHF has been actively participated in designing and implementing this program.

The NHF gives high priority to raising awareness of ARF diseases in rural areas by applying various methods such as FM radio, interaction through communal dialogue, publications, mobile camps, clinical service provision, national, district and local level programs, health camps, monthly talk programs etc. (NHF Program Report (NHF), 2011). Despite this far-reaching and holistic programme, Nepal still faces a big challenge in the prevention of ARF/RHD. One of the major interventions is NHF's "**Save the Children Heart**" scheme in which the launch agenda included: 1) screening of school children; 2) confirmation of disease; 3) free supply of injection penicillin to ARF/RHD patients; 4)

support for surgery and 5) rehabilitation after surgery. Table 3.1 shows the NHF's management plan for ARF/RHD diseases (NHF Report 2011).

Table 3.1: Management Plan For ARF/RHD Diseases

Classification	Criteria	Review and Management Plan	Frequency
Low Risk (Priority level 3)	ARF with no evidence of RHD or trivial to mild valvular disease	Secondary prophylaxis	4 - Weekly
		Doctor review	Yearly
		Dental review	Yearly
		Echocardiogram (if available)	Children: 2 -Yearly Adults: 2-3 Yearly
Medium Risk (Priority level 2)	Any moderate valve lesion in the absence of symptoms and with normal left ventricular function or Mechanical prosthetic valves	Secondary prophylaxis	4 Weekly
		Doctor review	6 Monthly
		Influenza vaccination	Yearly
		ECG optional	Yearly
		Medical or Heart specialist review	Yearly
		Echocardiogram	Yearly
		Dental review	Yearly
		Polysaccharide pneumococcal vaccination	5 Yearly (max. 3 doses)
		Endocarditis prevention	As required
High Risk (Priority level 1)	Severe valvular disease, or Moderate / Severe valvular disease with symptoms, or Tissue prosthetic valves and valve repairs	Secondary prophylaxis	3-4 Weekly
		Doctor review	3-6 Monthly
		Influenza vaccination	Yearly
		ECG optional	Yearly
		Medical or Heart specialist review	3-6 Monthly
		Echocardiogram	3-6 Monthly
		Dental review	Within 3 months and yearly thereafter
		Polysaccharide pneumococcal vaccination	5 Yearly (max. 3 doses)
		Endocarditis prevention	As required
		Warfarin + Aspirin	As prescribed

The NHF's overall plan regarding the prevention and control of ARF are given below based on (Regmi P. R. and Wyber R., 2013):

Core program objectives:

The core program objectives are a) early detection and registration of RF/RHD patients; b) establishment of centres for safe administration of Benzathine Penicillin G (BPG) injection for secondary prophylaxis and c) establishment of a national strategy for RF/RHD prevention and control with development of RHD control toolkit.

Elements of the program:

The elements of the program are: 1) epidemiological studies; 2) awareness activities; 3) training of health workers; 4) case detection (heart screening); 5) registry of RF/RHD patients (hospital register, National (central) register, penicillin injection card); 6) delivery of medicines for secondary prophylaxis; 7) surveillance system and 8) evaluation and monitoring.

3.3.1. Primary Prophylaxis of ARF in Nepal

The primary prevention of ARF is "prevention of initial attack of Group A Streptococcal (GAS) infection". Therefore, prevention of ARF is required to recognise and accurately treat GAS Pharyngitis.

Methods used:

Table 3.2 shows specific antibiotic treatment of streptococcal throat infection, currently provided by the NHF.

Table 3.2: Treatment of Streptococcal Throat Infection

Medicine	Route	Dosage	Time period
Amoxicillin	PO (By mouth)	500 mg 3 times a day (If body weight > 30 Kg) 250 mg 3 times a day (If body weight < 30 kg)	7 days
Azithromycin	PO	500 mg once daily (If body weight > 30 Kg) 250 mg once daily (If body weight < 30 kg)	5 day

Future Plan:

A register-based pilot project on primary prevention of ARF is being carried out in Lalitpur district of Nepal. After completion of this project, a national strategy for primary prevention of ARF will be formulated and implemented.

3.3.2. Secondary Prophylaxis of ARF/RHD in Nepal

In secondary prophylaxis, the Benzathine Penicillin G (BPG) injection is being prescribed for treatment every 3 or 4 weeks to prevent recurrence of GAS infection (WHO, 2004). It is also recommended for patients who have a history of ARF or RHD. The lengthy treatment is required for secondary prophylaxis and is essential for proper administration of treatment. BPG is usually given by deep intramuscular injection every 4 weeks; it can be prescribed every 3 weeks in high prevalence areas in accordance with local guidelines (WHF, 2007). According to WHO, the standard doses of BPG are 1,200,000 units for all patients whose weights are greater than or equal to 30kg and 600,000 units for all patients whose weight is less than 30kg. An alternative oral penicillin (Penicillin V) can be prescribed if BPG injection's pain cannot be tolerated or the injection is not available. The standard dose is 250mg orally taken twice daily for all patients (WHO, 2004). In Nepal for secondary prophylaxis with Penicillin the does is given once every 3 weeks as recommended by the NHF. The alternative to penicillin injection is daily oral penicillin although it has been noted that there is a high risk of recurrence of ARF if receiving oral Penicillin rather than the preferred Benzathine BPG (Feinstein A.R *et al*., 1959).

3.3.3. ARF Secondary Prevention: Time Period

Table 3.3 shows the treatment timeframe of ARF, provided by the NHF.

Table 3.3: ARF Treatment Timeframe

RF without carditis	**5 years or until age 18 whichever is longer**
RF with carditis but no residual valvular disease	**10 years** or until age 25 whichever is longer
RF with residual valvular disease	At least **10 years** after last episode and at least until age 40. Sometimes lifelong.

In secondary prophylaxis, the Benzathine Penicillin G (BPG) injection is prescribed for repetition every 3 or 4 weeks to prevent of recurrent of GAS infections.

Methods used:

Registry of RHD patients and the prevention of recurrence and progression of ARF are aided if the prescription procedure set out in Table 3.4 is followed, based upon information provided by NHF.

Table 3.4: Medicine Benzathine Penicillin G

Medicine	Route	Dosage	Time period
Benzathine Penicillin G	IM(Intramuscular)	6 lakhs units (If body < 30 Kg) 12 lakhs units (If body weight > 30 kg)	Once every three WKs

Regarding secondary prophylaxis, NHF has identified some challenges namely: reluctance to administer BPG, pain of injection (5% of patients on secondary prophylaxis stopped taking BPG injections) and BPG quality. To address these issues the NHF has developed a guideline for penicillin skin testing. The steps for skin testing which are being used are outlined in Appendix 3.1. The NHF recommendations on safe Benzathine penicillin injection delivery are provided in Appendix 3.2. Information about anaphylactic reaction and vasovagal reaction is outlined in Appendix 3.3 and minimizing pain of BPG injections is described in Appendix 3.4), all based upon (Regmi, P. R. and Wyber, R., 2013).

3.3.4. Process and Practice for Recognition of ARF

The NHF is launching the program as an ARF screening plan for schools entitled "School Children Screening" for which they provide a questionnaire for schools and parents. The questionnaire in the ARF/RHD survey form is in both English and Nepali. This is shown in Appendix 3.5. The questions incorporated in the survey, English version only, is in Table 3.5. Parents complete the form and during the school screening phase doctors will use it to make an initial diagnosis. Based on the diagnosis they then prepare a treatment plan that may recommend a patient to attend hospital for testing or prescribe immediate treatment and medication etc.

Table 3.5: RF/RHD Survey Form Quessionnaire

Questionnaire for Parents / Teacher

Q.N.	Questions	Answer
1	Frequency of throat infection : one or more than one time in year	Y/N
2	Large joints pain with swelling or redness or hotness	Y/N
3	Joints pain only	Y/N
4	Breathing problem : walking or working	Y/N
5	Twitchy and jerking movements / restriction of movements	Y/N
6	Subcutaneous Nodules on bony prominences	Y/N
7	Painless flat pink patches on the skin	Y/N
8	Rheumatic heart disease / fever - taking any penicillin or tablet according to doctor advise.	Y/N
9	Any medicine taken for heart diseases	Y/N
10	Visit doctors or hospital for any other health problems	Y/N

3.3.5. NHF Diagnosis Process for ARF

Nepal follows WHO guidelines revised by the Jones criteria for use in diagnosis of ARF. These are given below (WHO, 2004):

1. A. The first episode of ARF can be confirmed if:
    a. 2 MAJOR or 1 MAJOR and 2 MINOR manifestations are present plus if there is evidence of preceding Group A streptococcal infection.
2. Recurrent ARF (with no RHD) can be confirmed if:
    a. 2 MAJOR or 1 MAJOR and 2 MINOR manifestations are present plus if there is evidence of preceding Group A streptococcal infection.
3. Recurrent ARF (with existing RHD) can be confirmed if:
    a. 2 MINOR manifestations are present plus if there is evidence of preceding Group A streptococcal infection.

3.3.6. ARF Case Analysis

The data from July 2011 to April 2014 was obtained from the NHF registry and was collated and analysed; data only collected from the Kathmandu valley. It was found that a total of 636 patients were screened; ARF was detected in 85 (13.36%) cases; ARF was suspected in 48 (7.55%) cases and ARF was not detected in 503 (79.09) cases. Table 3.6 shows the total number of patients; detected cases of ARF; suspected cases of ARF and not detected cases of ARF.

Table 3.6: ARF Case in Nepal

S.N.	ARF Case	No. of patients	In %
1	Detected	87	13.68
2	Suspected	74	11.64
3	Not detected	475	74.68
	Total	**636**	**100.00**

The Pie Chart, Figure 3.1, depicts the relative proportions ARF cases.

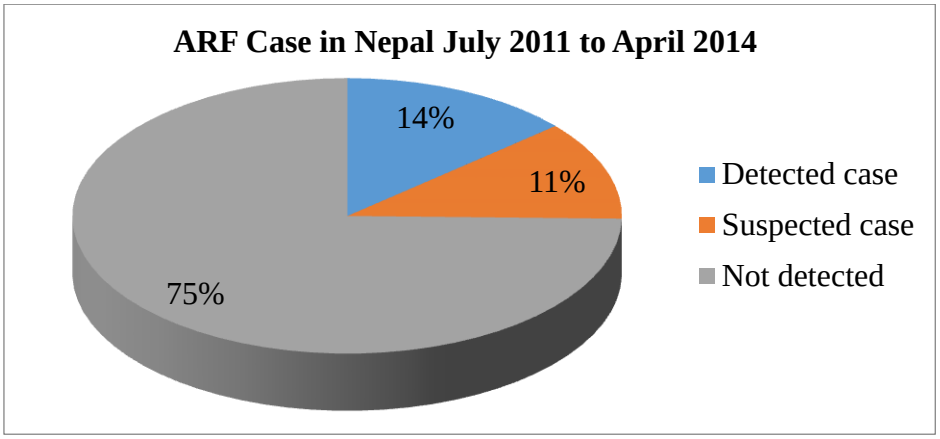


Figure 3.1: ARF Case in Nepal

Table 3.7 shows the ARF screening program output by gender.

Table 3.7: ARF Case in Gender Wise

Gender	No. of Patients	In %
Male	337	52.98
Female	299	47.01
Total	**636**	**100.00**

Pie Chart, Figure 3.2, illustrates the ARF screening program participation by gender.

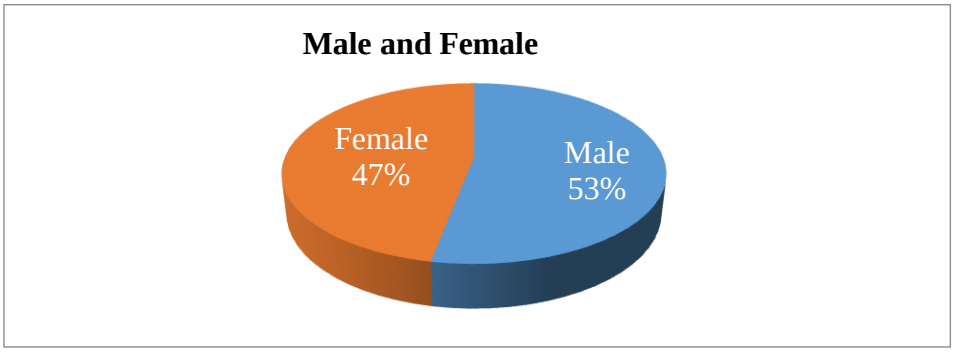


Figure 3.2: ARF Screening Program Participation by Gender

Table 3.8 shows detected and suspected cases of ARF in Nepal (2015).

Table 3.8: ARF Detected and Suspected Cases

ARF Case	No. of Patients	In %
Detected	87	54.04
Suspected	74	45.96
Total	**133**	**100.00**

Pie chart, Figure 3.3, illustrates detected and suspected cases of ARF in Nepal (2015).

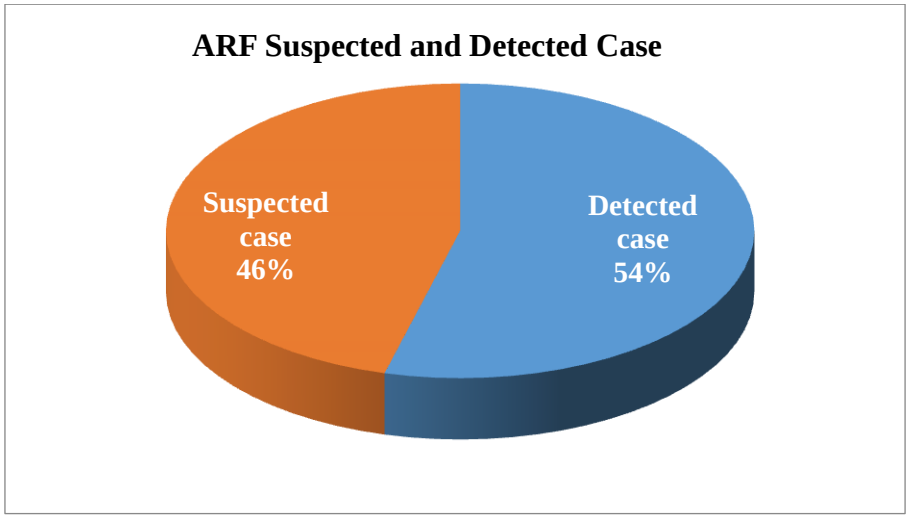


Figure 3.3: ARF Detected and Suspected Cases

Table 3.9 shows the male and female in detected and suspected cases of ARF in Nepal (2015).

Table 3.9: Detected and Suspected Cases Gender-wise

Gender	No. of Patients	In %
Male	87	54.04
Female	74	45.96
Total	**133**	**100.00**

Pie chart, Figure 3.4, illustrates gender for detected and suspected cases of ARF in Nepal.

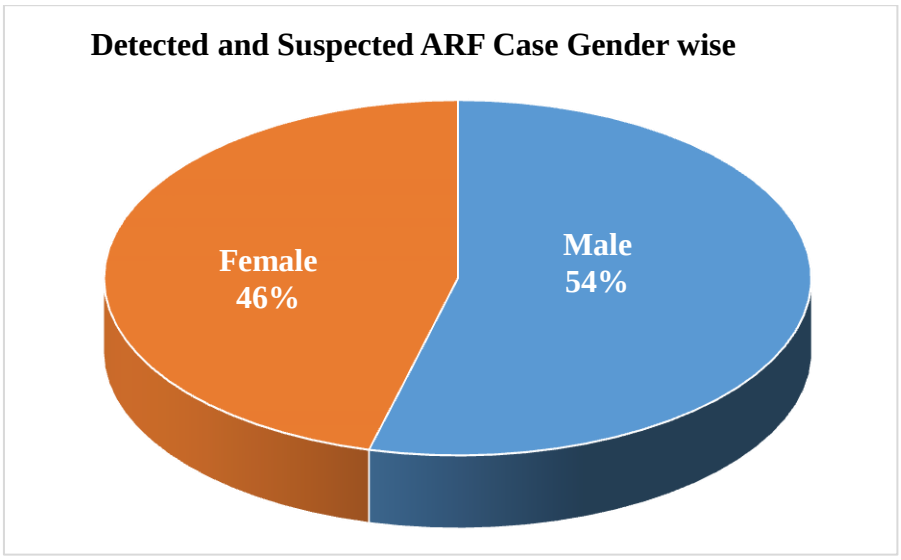


Figure 3.4: Detected and Suspected Cases Gender -wise

Table 3.10 shows the number of patients and their answer (Y/N) for each symptom included in the NHF questionnaire. Only detected and suspected ARF cases were analysed.

Table 3.10: No of Patients With Each Particular Symptom

Symptoms	Questions	No of Patients Response		In Percentage (%)	
		Yes	No	Yes	No
GAS Infection	Frequency of throat infection : one or more than one in year	133	28	82.61	17.39
Arthritis	Large joints pain with swelling or redness or hotness	85	76	52.80	47.20
Arthralgia	Joints pain only	121	40	75.16	24.84
Carditis	Breathing problem - walking or working	85	76	52.80	47.20
Chorea	Twitchy and jerking movements / Restriction of movements	49	112	30.43	69.57
SN	Subcutaneous Nodules on bony prominences	28	133	17.39	82.61
EM	Painless flat pink patches on the skin	34	127	21.12	78.88
RHD/Fever	Rheumatic heart disease / fever - taking any Penicillin or tablet according to dr. advise	6	155	3.73	96.27
Med/Heart	Any medicine taken for heart diseases	10	151	6.21	93.79
Visit Hospital	Visit doctors or hospital for any other problems	142	19	88.20	11.80

The Bar chart, Figure 3.5, shows patient responses with ARF symptoms.

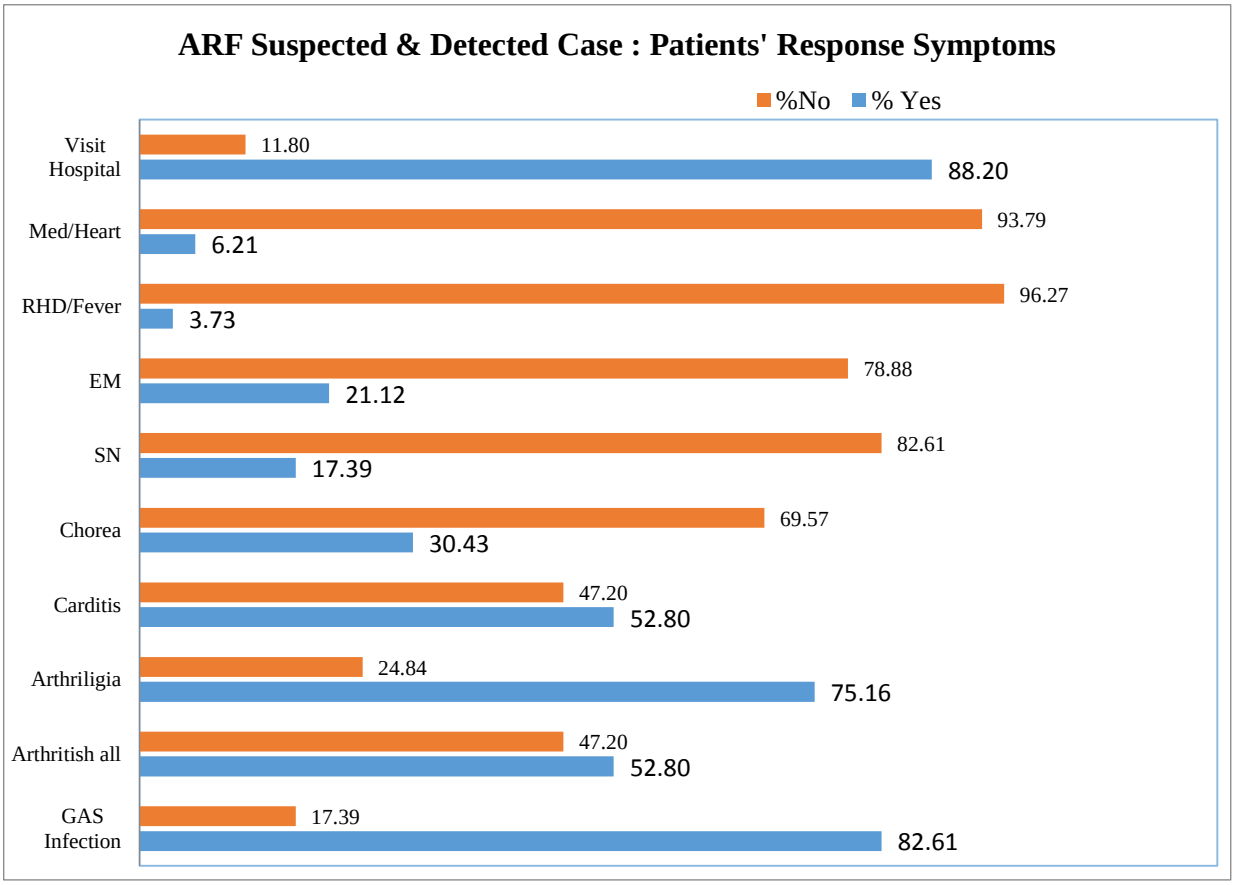


Figure 3.5: Patients and Symptoms

EM= Erythema Marginatum and SN= Subcutaneous Nodules

3.4. Conceptual Framework of Diagnosis of ARF in the Nepalese Setting

The WHO and WHF's guidelines alone were not comprehensive enough for the proper diagnosis for ARF applications in Nepal as we observed that there are cases of a peculiar nature, which may not be covered. Therefore, local country treatment procedures and practice, manpower, technology etc. are additional factors that need to be analysed adequately. Moreover, it is also not essential for every country to have the same guidelines and procedure for diagnosis and treatment of ARF. Other factors that require consideration include the country's topography and environmental situation that tend to have an impact on the signs and symptoms observable in patients. It is for this reason that local country procedures are deemed as essential requirements in the development of a CDSS model for diagnosing ARF. It was recognised that use of a combination of WHO and WHF's guidelines and the country's diagnosis and treatment procedures and practices, would form a much broader and more substantial basis for such diagnoses. As a consequence, we proposed a diagnosis process of ARF in Nepal, which is discussed in the Research Methodology, Chapter 4.

3.4.1. Signs and Symptoms of ARF

The required symptoms for diagnosis of ARF that are suitable for the Nepalese environment are given in Table 2.11. The list of symptoms was prepared and analysed based on the NHF expertise guidelines and support. During the symptoms selection process, the social, geographical, environment, lifestyles, technical and existing treatment practice of Nepal were given all due consideration. The WHO, World Heart Federation (WHF) and information from other developed countries reviewed systematically. The symptoms were ranked subsequently and listed with the lack of symptoms that are required and suitable for Nepalese lifestyle, notably arthritis pain being a common symptom that was presented in almost all ARF diagnoses. Hips and Shoulders were added in the arthritis pain group as well as palpitation in carditis. The overall list of symptoms is presented in Table 3.11.

Table 3.11: Signs and Symptoms of ARF

Coding	Signs and Symptoms of ARF	Remarks
A.	Major Manifestations	
Ar.	Arthritis (large joints pain or tenderness/inflamed)	Occurs in 75% of patients
Ar_1	Severe Pain (Ankles, Knees, Wrists, Elbows, Hips, Shoulders)	
Ar_2	Pain Associated with Swelling, Hotness, Redness, Movement Restriction (limitation of movements)	
Ar_3	Migratory / Shifting Severe Pain (shifting of arthritis between in the joints)	
Cr	Carditis : Inflammation of the Heart Valves	Occurs in 45% - 75% of patients
Cr_4	Currently Present Heart Murmur	
Cr_5	Chest Pain / Difficulty in Breathing/ Palpitation	
Ch	Sydenham's Chorea : (St. Vitus's Dance)	Common in female 10% of patients
Ch_6:	Muscle Weakness Hands and Feet	
Ch_7:	Twitchy and Jerking Movements of Hands, Feet, Facial Muscles, Tongue	
Sn	Subcutaneous Nodules	Rare in Nepal (Occurs in 2% - 20% of patients)
Sn_8:	Painless lumps on the outside surface of Wrists or Elbow or Ankles or Knees groups 3-4 (up to 12)	
$Sn_{9:}$	Lumps round / firm and freely movable size from 0.5-2.0 cm	
Em	Erythema Marginatum	Rare in Nepal (Occurs in 2% – 10% of patients)
Em_{10}: Em_{11}:	Painless, flat pink patches on the skin Not itchy or painful and has well-defined borders	
B.	**Minor Manifestations**	
Fe_{12}	Fever	Occurs in 90% of case
Art_{13}	Arthralgia (joints pain)	
Ecg_{14}	Prolonged P-R interval on ECG	
Crp_{15}	Raised or Positive CRP	
Esr_{16}	Raised ESR	
C.	Mandatory/Essential	
Prt_{17}	Positive Rapid Strep Test	
Ast_{18}	Raised (Positive) Anti-Streptolysin O tire (ASOT)	
Gs_{19}	Positive throat culture for GAS infection	

3.4.2. ARF's Symptoms and Descriptions

ARF signs and symptom descriptions are given below as provided by NHF and included in WHO guidelines. Group A streptococcal are the most common bacterial cause of pharyngitis, with a peak incidence in children 5–15 years of age (3, 5, 7, 9). Streptococcal pharyngitis is less frequent among children in the first three years of life and among adults. Group A Beta-Haemolytic Streptococcus (GABHS) is responsible for 30% of sore throat in children. Out of them 3% develop ARF. Figure 3.6 shows relevant images of sore throat as provided by the NHF (2014).

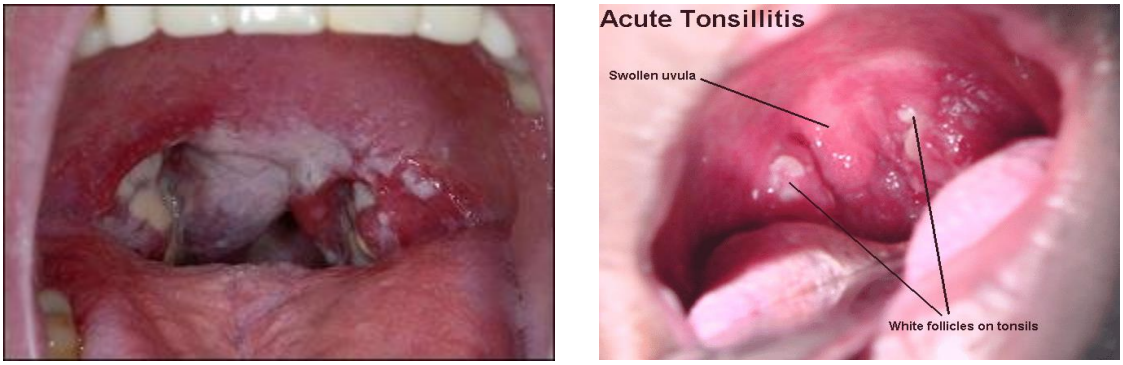


Figure 3.6: Images of Sore Throat

3.4.2.1. Tonsillitis and Pharyngitis: What are the causes?

The causes of tonsillitis and pharyngitis are shown in Table 3.12:

Table 3.12: Causes of Tonsillitis and Pharyngitis

Viral	Bacterial
Adenovirus	Group A Beta - Haemolytic Streptococci
Influenza virus	Neisseria gonorrhoeae
Epstein-Barr virus (mononucleosis)	Mycoplasma pneumonia
Herpes simplex virus	Chlamydia
Coxsackie virus	Corynebacterium diphtheria
Enterovirus (more common in children less than 3 years old.	Haemophilus

3.4.2.2. Tonsillitis and Pharyngitis Signs and Symptoms

Tonsillitis and pharyngitis symptoms are: Sore throat (pain), Fever (either high or low grade), Headache, and Decrease in appetite, Nausea, Vomiting, Stomachache, Painful swallowing and Visual redness or drainage in the throat. Streptococcal M protein and the

N-acetyl glucosamine of group A streptococcal carbohydrate are immunologically similar to molecules in human myocardium- myosin, tropomyosin, keratin, etc. Initial damage is due to inflammation caused by entry of antibodies into the cardiac valve endothelium. It affects the pharynx including the tonsils and possibly the larynx. Common symptoms include fever, sore throat, and enlarged lymph nodes. It is the cause of 37% of sore throats among children and 5-15% in adults in Nepal.

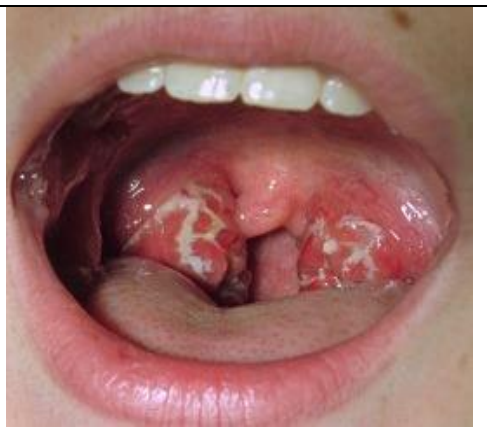
Signs and Symptoms

Tonsilo-pharyngitis

- Fever and Pain

The Centre criteria of bacterial throat infection

- Tonsillar exudates
- Tender anterior cervical adenopathy
- Fever by history
- Absence of cough



Note: Image provided by NHF (2014).

3.4.2.3. Guidelines for differentiation of Pharyngitis and Tonsillitis

The guidelines for differentiation of pharyngitis and tonsillitis are shown Table 3.13.

Table 3.13: Differentiation of Pharyngitis and Tonsillitis

Viral	Bacterial
Fever (moderate or low)	Fever (High grade)
Throat discomfort	Throat pain
Mildly enlarged, red tonsils	Severely enlarged, red tonsils
Erythema and swelling of pharynx	Erythema and swelling of pharynx
Tonsillar exudates	Petechiae of soft palate
Cough	Tonsillar exudate
Hoarseness	Anterior cervical lymphadenopathy
Red eyes	Erythematous “sandpaper” rash on tongue, gray furry tongue.
Running nose with Sneezing	Koplik spots (whitish)

Figure 3.7 shows the differentiation of pharyngitis and tonsillitis, images provided by NHF.

Image Viral	Image Bacterial

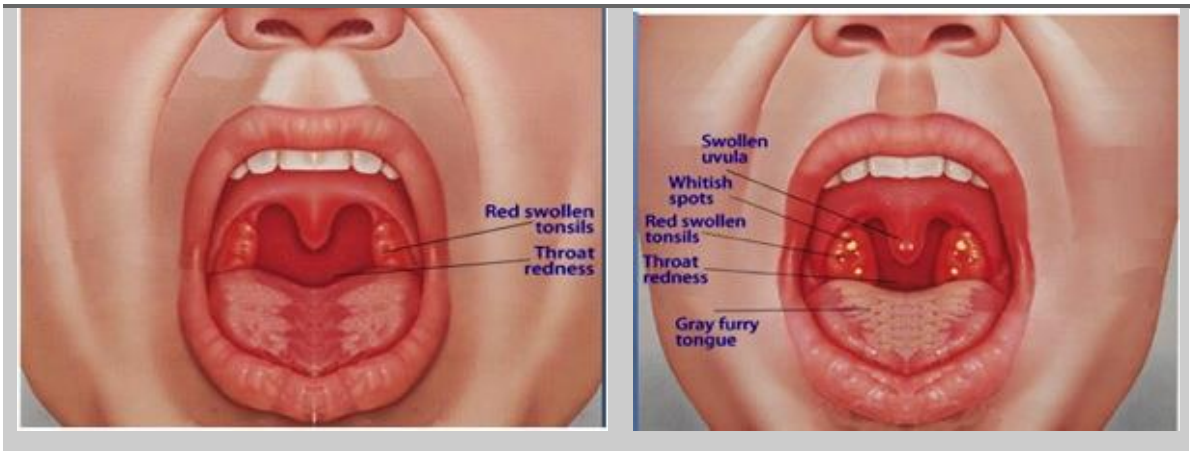


Figure 3.7 : Images of Viral and Bacterial Infection

3.4.2.4. Treatment

Non-pharmacological interventions:

- Rest and increased fluid intake.
- Avoidance of irritants (smoke) and cold.
- Saline gargles.
- Increase room humidity'

Pharmacological Interventions:

To relieve pain:

- Paracetamol.
- Ibuprofen.

Antibiotics:

- Injection BPG- single dose.
- Oral antibiotic therapy.
    - ❖ Pen V, Amoxicillin, Azithromycin, Cephalexin.
- For those with penicillin allergy
    - ❖ Erythromycin, Azithromycin.

Pregnant and breast feeding mothers:

1. Paracetamol, Injection BPG, penicillin VK, Erythromycin, Azithromycin and Cephalexin may be used.
2. Ibuprofen is not safe during pregnancy or while breastfeeding.

3.4.2.5. Arthritis Signs and Treatment

Arthritis is the most common symptom of ARF and occurs in 75% of patients. It may occur in large joints affected with very severe pain and one joint becoming inflamed as another subsides (migratory or movement restriction) but may be in multiple joints progressively becoming inflamed without warning. Arthritis is difficult to diagnose. The effect of Arthritis on hips and shoulders is also difficult to diagnose for positive symptoms for ARF because it is difficult to observe and measure the range of movement. Therefore, it is necessary that during the diagnosis of ARF (especially when arthritis is involved) differential diagnosis needs to be looked at. Community rural health workers especially need to seek advice and support or may need to contact physicians or surgeons.

Arthritis is the most frequent major manifestation of ARF, occurring in up to 75% of patients in the first attack of ARF. It occurs early in the course of the disease, as the presenting complaint. Carditis and arthritis frequently coexist during an ARF episode and demonstrate an inverse relationship between the severity of arthritis and carditis.

Arthritis Pain (Knees, Elbows, Wrists, Ankles, Hips, Shoulders)
Pain Associated with : Hotness (Knees, Elbows, Wrists, Ankles, Hips, Shoulders) Swelling (Knees, Elbows, Wrists, Ankles, Hips, Shoulders) Redness (Knees, Elbows, Wrists, Ankles, Hips, Shoulders)
Movement Restriction
Migrating Arthritis: • Most common feature: present in 80% of patients • Painful, migratory, short duration • Usually >5 joints affected and large joints preferred Knees, ankles, wrists, elbows, shoulders • Small joints and cervical spine less commonly involved
Treatment: Arthritis
• Salicylates or NSAIDs x 3 weeks • Usually excellent response • If poor response: diagnosis to be questioned

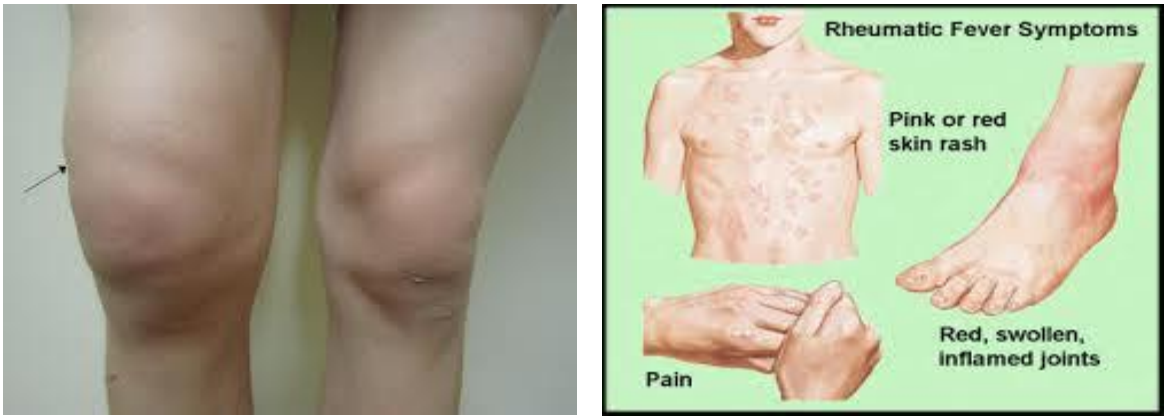


Figure 3.8 :Images of Arthritis (provided by NHF, 2014)

3.4.2.6. Carditis Signs and Treatment

It can be presented along with fever and arthritis usually within the first 2-6 weeks. Heart murmur, difficulty for breathing, pain, cardiac enlargement, palpitation etc. can also present.

- Most serious manifestation. Seen in 30-50% of patients with ARF.
- May lead to death in acute phase or at later stage.
- Any cardiac tissue may be affected.
- Valvular lesion most common: mitral and aortic.

Carditis clinical signs:

- High pulse rate
- Murmurs
- Cardiomegaly
- Rhythm disturbances (prolonged PR interval)
- Pericardial friction rubs
- Cardiac failure

Treatment: Carditis

- Potential for morbidity
- Steroid use compulsory
- Prednisone 1 -2 mg/kg/d (max 60 mg) x 10 - 15 days
- Taper 20 -25% each week
- Rest x 4 weeks
- If simultaneous arthritis and carditis: steroids alone sufficient

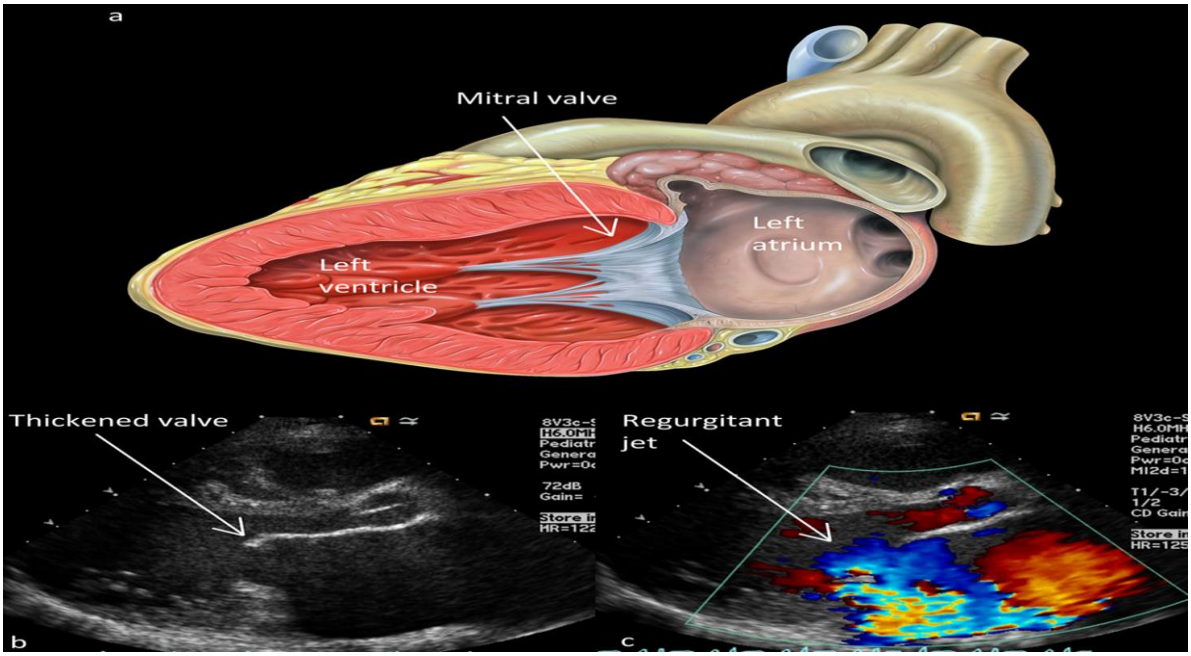


Figure 3.9 : Heart Scan (ECHO)

Figure 3.9 **a**) Artist rendition of normal left heart anatomy, demonstrating the left atrium connected to the left ventricle via a mitral valve.52 **b**) Two-dimensional echocardiogram of the left heart, demonstrating a thickened anterior leaflet of the mitral valve. **c**) Two-dimensional echocardiogram with colour Doppler, demonstrating moderate-to-severe mitral valve regurgitation (blue jet) adopted from (Michael D. S., 2011)

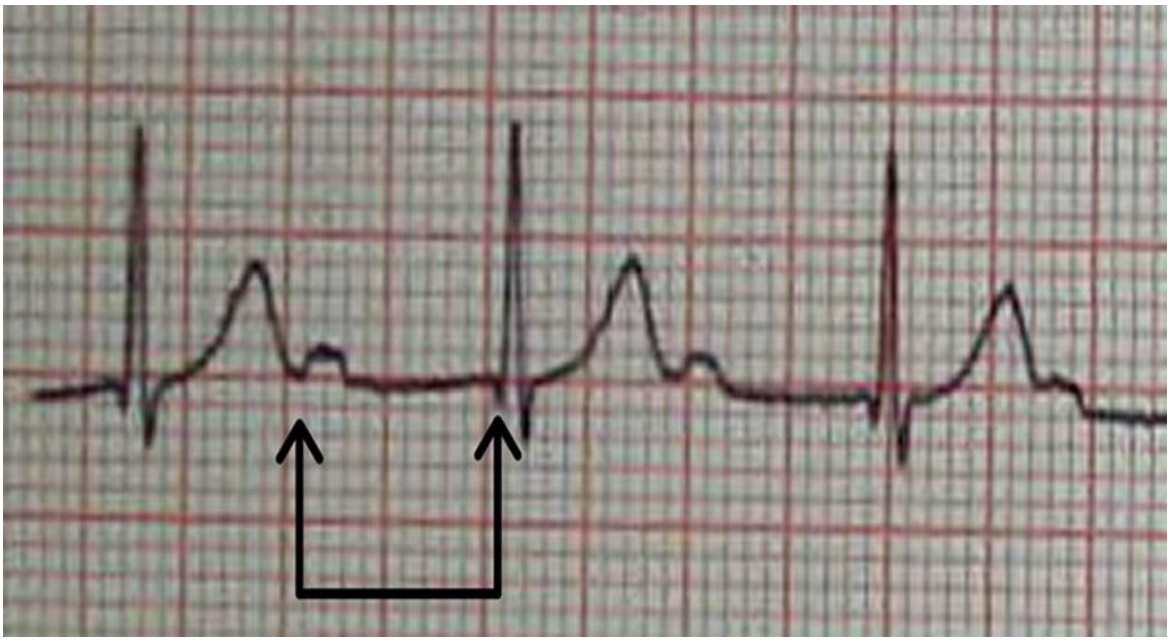


Figure 3.10 :ECG .

Figure 3.10, Electrocardiogram demonstrating first-degree heart block in a patient with acute rheumatic fever. The PR interval is noted by the arrows, and is markedly prolonged at 300 milliseconds (normal for an adult is less than 200 milliseconds), adopted from (Michael D Seckeler, 2011).

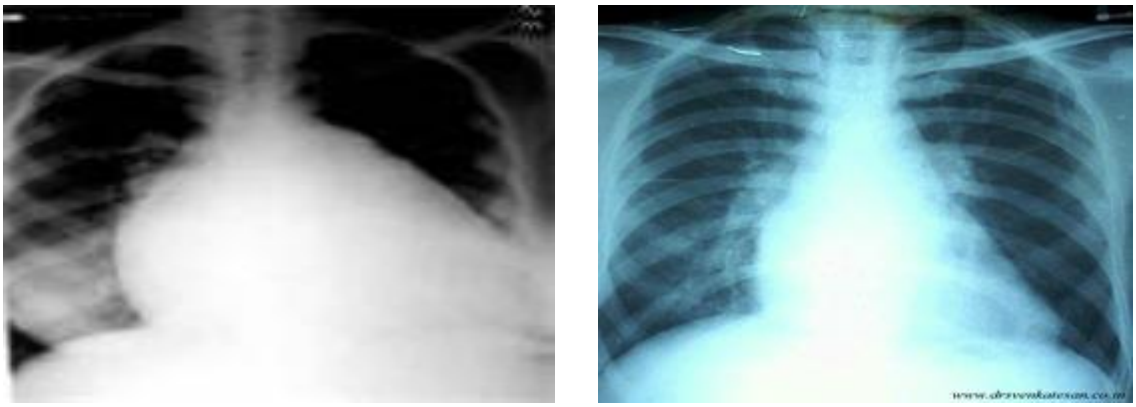


Figure 3.11: Chest X-ray heart enlarge

Figure 3.11 is provided by NHF (2014) which demonstrates chest X-ray reports.

3.4.2.7. Sydenham's Chorea Signs and Treatment

Chorea occurs primarily in children and is rare after the age of 20 years. It occurs primarily in females, and almost never occurs in post pubertal males. It consists of jerky and uncoordinated movements with the movements disappearing during sleep. The majority of cases can be resolved within 6 months although some cases can last for as long as 3 years.

- Extrapyramidal disorder.
- Fast, involuntary movements (especially face and limbs).
- Muscular hypotenuse and Emotional liability.
- First sign: difficulty walking, talking, writing.
- Usually a late manifestation: months after infection.
- Often the only manifestation of ARF.
- Occurs in 5-30% of patients with ARF.
- 1/2 of these also have carditis or arthritis.
- Usually benign and resolves in 2 - 3 months.
- Can last for more than 2 years.

Treatment: Sydenham's chorea

- Haloperidol 0.5 - 1 mg/kg.
- Add 0.5 mg every 3 days if not responding.
- Max 5 mg.
- Alternate: Sodium valproate 15 -20 mg/kg/d.
- No proven benefit of steroids.

3.4.2.8. Subcutaneous Nodules

This is a less common symptom. The incidence of subcutaneous nodules in patients with ARF varies widely in different studies and from country to country. These lesions have been reported in up to 20% of cases in Nepal. The subcutaneous nodules are round, firm, freely movable, painless lesions varying in size from 0.5–2.0 cm. Figure 3.12 shows an image of subcutaneous nodules (image provided by NHF, 2014).

- Firm, non-tender, isolated or in clusters.
- Most common: along extensor surfaces of joint.
- Knees, elbows, wrists.
- Also: on bony prominences, tendons, dorsi of feet, occiput or cervical spine.
- Last a few days only.
- Occur in 1 - 20% of cases.
- Often associated with carditis.

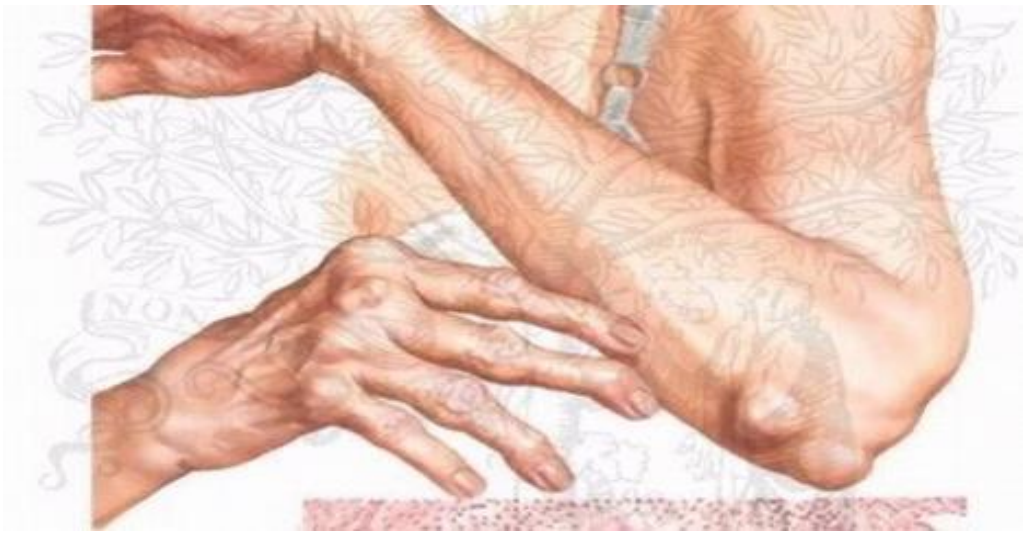


Figure 3.12: Image of Subcutaneous Nodules

3.4.2.9. Erythema Marginatum

It is also a less common symptom. The lesions of erythema marginatum appear first as a bright pink macule or papule, which spreads outward, in a circular or vertiginous pattern. The rash can be more visible after showering. The rash can be difficult to detect in dark-skinned people therefore proper and deep inspection is required. Figure 3.13 shows the image of erythema marginatum (image provided by NHF, 2014).

- Present in 1-7% of patients.
- Highly specific to ARF and Cutaneous lesion.

- Reddish pink border and pale centre.
- Round or irregular shape.
- Often on trunk, abdomen, inner arms, or thighs.
- Highly suggestive of carditis.

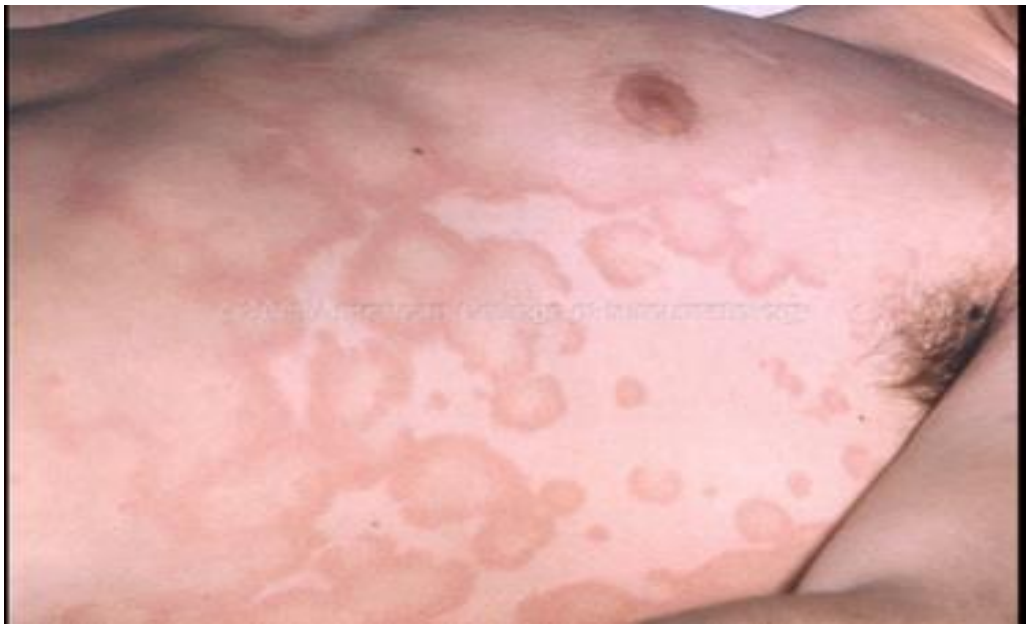


Figure 3.13: Image of Subcutaneous Nodules

3.4.2.10. Arthralgia

Arthralgia is different from arthritis. In arthralgia, pain exists in joint movement without evidence of swelling or hotness.

3.4.2.11. Rheumatic Heart Disease (RHD)

Untreated rheumatic fever permanently damages the heart, which can lead to heart failure or need for cardiac surgery. According to the WHF, "*Acute rheumatic fever primarily affects the heart, joints and central nervous system. The major importance of acute rheumatic fever is its ability to cause fibrosis of heart valves, leading to crippling valvular heart disease, heart failure and death"*. It is a very common disease in children in developing countries.

The symptoms of RHD are chest pain, heart palpitations, breathing problems when lying down, shortness of breath, fainting, swelling in feet and ankles and exercise intolerance. The frequency time of throat infection annually, electrocardiography (show the electrical activity of the heart), echocardiography and blood tests are required for the diagnosis of RHD (NHF unpublished report).

The primary prevention of RHD is treatment of Rheumatic Fever. Basically, 10 days of an oral antibiotic or single intramuscular penicillin injection can be applied as primary treatment (WHF, 2004). In our research, the focus was on RHD. It became clear that if any given symptoms appear in a patient then the patent must be referred to the nearest hospital as soon as possible.

3.5. Chapter Summary

This chapter describes brief information about ARF/RHD, its signs and symptoms, diagnosis processes. Nepal's ARF prevention and control plan and each ARF's symptom are discussed and supported by images and provides information on the medication that is applied to treat the patient after symptoms are recognised and assessed. The ARF situation was analysed and appropriate conceptual framework discussed in relation to diagnosis of ARF in the Nepalese setting. In Chapter 4, details of Research Methodology are presented and discussed.

Chapter 4: Research Methodology

"We cannot solve our problems with same thinking we used when we created them."

Albert Einstein

4.1. Introduction

This chapter describes our proposed diagnosis model for Acute Rheumatic Fever (ARF), and grouping the signs and symptoms that are required to build up an ARF Diagnosis Application. This chapter describes our proposed Hybrid Approach. This combines the Knowledge-Based System (KBS)/Boolean Rule Model, Temporal Model and Fuzzy Model. Each model entails processes to perform specific tasks, which are specifically illustrated. The chapter is organised as follows: section 4.2 describes a diagnosis model for ARF; in section 4.5 applied the Hybrid Approach; in section 4.6 the KBS/Boolean Rule Model; in section 4.7 the Temporal Model; in section 4.8 the Fuzzy Model and finally section 3.13 summarises the entire chapter.

4.2. Proposed Diagnosis Model of ARF

The proposed diagnosis process model was prepared based on the NHF's expertise guidelines. The main purpose of this model was to provide additional support for community rural health workers to recognise ARF cases at an early stage. Also to provide them with an indication of the severity level of ARF once a case has been recognised. Another aim was to deliver a fast track treatment service to patients, which will not only save time for patients' immediate treatment, but also protect them from further heart damage.

The model was designed as a symptoms-based approach. Based on observed symptoms, the model will determine the stage of an ARF. The ARF diagnosis process model is divided into three stages: 1) Detected ARF; 2) Suspected ARF and 3) Not-Detected ARF. If an ARF case is detected confirming that ARF is present the model should be able to detect the severity level of the case according to observed signs and symptoms after which it will be possible to classify it as a Severe Case, Moderate Case, Mild Case or Suspected Case. If an ARF case is suspected then the system will indicate required laboratory testing to acquire further clinical information. If ARF is not confirmed then the findings would likely point towards the possibility of another disease so that the community rural health worker can refer the patient to the nearest hospital or seek the

advice of senior doctors if available (Pandey S. *et al*., 2012). The diagnosis process model put forward will help provide a better and prompter treatment for patients. All the detected severe cases need immediate attention by referring the patient to the nearest hospital or by seeking expert advice as soon as possible. This task at present has to be done by a community rural health worker or inexperienced doctor. All moderate cases also need to visit the nearest hospital, with community rural health workers being able to prescribe medicines according to an expert's suggestion followed by referring cases to the nearest hospital for further treatment if necessary. The community rural health worker can deal with mild cases by prescribing the medication according to expert suggestions and they can then monitor the patients' progress until the ARF has been cured. All suspected cases need to visit hospital for laboratory tests and further treatment. If ARF is detected properly the case can then be confirmed and treatment prescribed. Figure 4.1 shows the proposed diagnosis model for diagnosis of ARF.

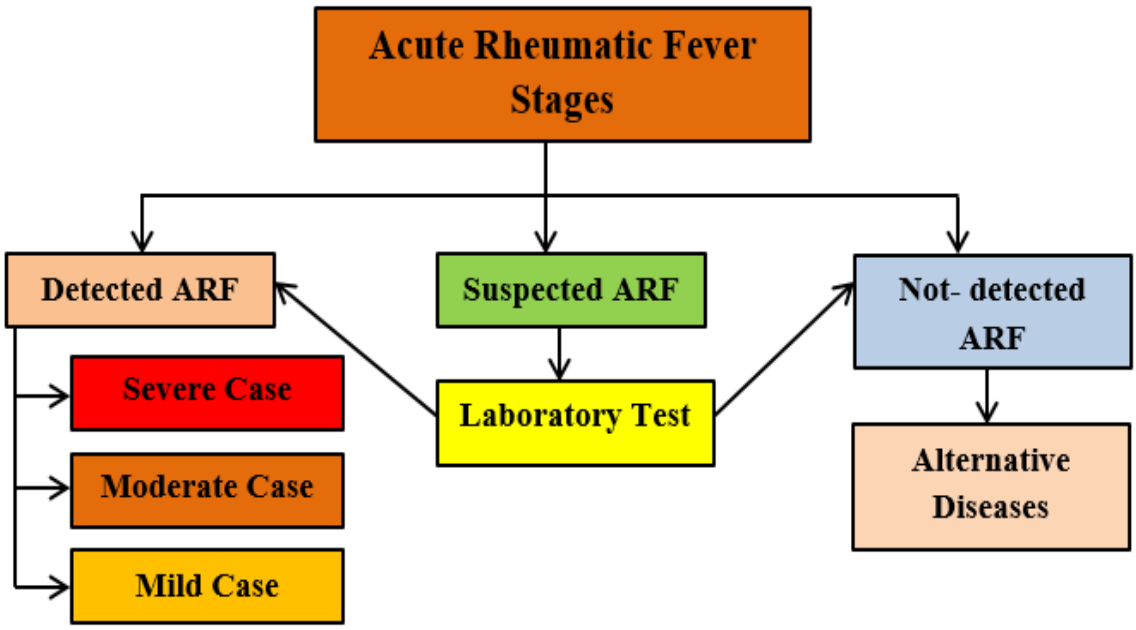


Figure 4.1: Proposed Diagnosis Model of ARF

Note: Detected ARF implies Acute Rheumatic Fever.

4.3. Signs and Symptoms for ARF Stages

Table 4.1 shows the symptoms of Detected ARF, Suspected ARF and Not-detected ARF.

4.3.1. Rules for Identification ARF Stages

The Nepal Heart Foundation (NHF) also follows the guidelines set by the WHO. The NHF overall diagnosis process for ARF is given in Table 4.1:

Table 4.1: Signs and Symptoms of ARF Stages

Detected ARF
➢ 1 Major sign + 2 Minor signs + 1 or more Essential sign(s)
➢ 2 or more Major signs + 0 Minor sign + 1 or more Essential sign(s)
➢ 1 Major sign - Chorea
➢ Arthralgia + Fever + CRP + 1 or more Essential sign(s)
➢ all Major signs (5) + 1 or more Essential sign(s)
➢ all Major signs (5) + all Minor signs (5) + all Essential sign (3)
Suspected ARF
➢ 1 Major (no Chorea) + 1 Minor sign + 1 or more Essential sign(s)
➢ Arthralgia + Fever + 1 or more Essential sign(s)
➢ Arthralgia + Fever + Prolonged P-R interval on ECG + 1 or more Essential sign(s)
➢ Arthralgia + Fever + Raised ESR + 1 or more Essential sign(s)
➢ Arthralgia + Fever + Prolonged P-R interval on ECG + Raised ESR + 1 or more Essential sign(s)
Laboratory Test: throat cultural, blood test, ECHO test etc. and diagnosis will be made based the result.
Not- detected ARF :
➢ 1 Major sign (no Chorea) + 0 sign + 1 or more Essential sign(s)
➢ 0 Major sign + all Minor signs (5) + 0 Essential sign
➢ 0 Major sign + 0 Minor sign + 1 or more Essential sign(s)
➢ 0 Major sign + Arthralgia or ECG or CRP or ESR + 1 or more Essential sign(s)
➢ 0 Major sign + Fever or ECG or CRP or ESR + 1 or more Essential sign(s)

All suspected cases require laboratory test i.e. blood test, throat test, ECHO etc. and diagnosis is made based on the laboratory result.

4.3.2. Symptoms for ARF Severity Level

Based on the NHF's expert guidelines, the signs and symptoms for different levels of severity have been separated and are presented in the Table 4.2. Based on these signs and symptoms the model is capable of identifying the severity level of ARF for target patients.

Table 4.2: Symptoms of ARF Level Severity

ARF : Severe Case
➢ Major symptoms 2 or more AND ➢ Minor symptoms 2 or more AND ➢ Carditis AND ➢ Mandatory/Essential symptom(s) 1 or more
ARF :Moderate Case
➢ Major symptoms 2 or more AND ➢ Minor symptoms 2 or more AND ➢ Mandatory/Essential symptom(s) 1 or more
ARF : Mild Case
➢ *Mild Case 1:* • Major symptom 1 AND • Minor symptoms 2 or more AND • Mandatory/Essential symptom(s) 1 or more ➢ *Mild Case 2:* • Major symptoms 2 AND • Mandatory / Essential symptom(s) 1 or more ➢ *Mild Case 3:* • Chorea ➢ *Mild Case 4* • Arthralgia + Fever + Positive CRP

4.4. ARF Diagnosis Model

In this section, I discuss knowledge acquisition, knowledge representation, and designing of rules for diagnosis of ARF model.

4.4.1. Knowledge Acquisition

Clinical knowledge acquisition is the process of acquiring, organizing, formulating, implementing and testing Knowledge. Various techniques have been developed for knowledge acquisition such as interview, description (information about solving the task,) and observation. Turban (1983), discussed a variety of techniques: the identification phase (problem), conceptualization phase, formulation phase, implementation phase,

testing phase and revision phase, which can all be applied in the knowledge acquisition process. During one, the field visits to Nepal, the local guidelines and diagnosis procedure s for ARF were studied and are set out in Table 4.1. The required knowledge was captured from various sources namely the WHO, WHF, revised Jones Criteria, NHS Choice (UK), the Internet, books, journals, Australian and New Zealand guidelines and experts from NHF. The required symptoms for diagnosis of ARF in a Nepali setting were prepared after analysis of the ARF medical information acquired from the sources listed in Table 3.11 and Table 3.4; inputs of experts from Nepal are given in Tables 4.1, and 4.2 and Figure 4.1. The applied knowledge acquisition method for ARF diagnosis model is illustrated in Figure 4.2.

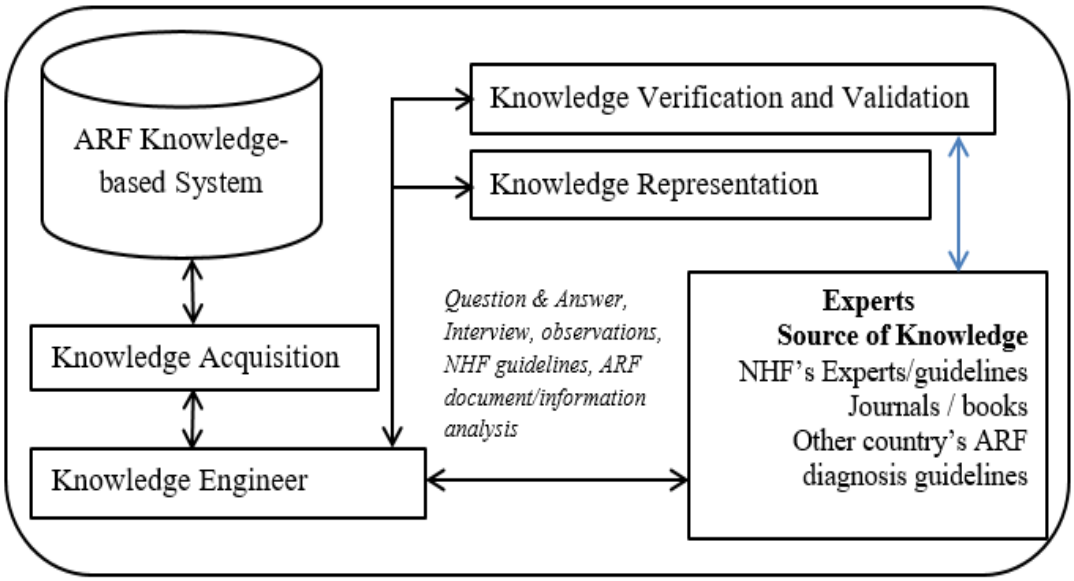


Figure 4.2: Knowledge Acquisition for ARF Diagnosis Model.

A knowledge-based model is responsible for identifying ARF stages, the severity level of ARF and the construction of the rules to identify them appropriately. Furthermore, the rules are also designed to identify the severity level of ARF from a patient's presented symptoms. Depending upon the observed traits in a detected ARF patient, the system can diagnose the level and severity of the case. This categorization (level of the severity) and associated symptoms are shown in Table 4.2.

4.4.2. Knowledge Representation

In the knowledge-based system, knowledge representation and management is a very important task for the proper delivery of the "*right knowledge to the right people in the right place from at the right time"* (Schreiber G *et al*., 2000). Knowledge representation is an important aspect of any type of CDSS and makes a big impact on the speed of the inference engine. Based on the literature review, it was confirmed that varying methods

are being used to represent the knowledge. Methods identified can be divided into two : 1) symbolic (natural language, frames, first order logic, fuzzy logic, Bayes networks, C/C++, C#, Java, Prolog, rules, hybrid system, sematic networks etc.) and 2) non-symbolic (neural network, genetic algorithm, etc.) methods. More detail about knowledge acquisition, knowledge representation/management and KBS development can be found in the knowledge-based system book (Akerkar and Sajja, 2009). The most frequently used knowledge representation methods are production rules, frames, cases, semantic networks and formal logic. Boolean logic was applied for formation of the rules for our research, which is discussed in the next section.

4.4.3. Designing the Rule-based

There are various types of rule design methods available that can be used to represent Knowledge as follows: traditional or Crisp logic rules (C-rules) for example; *IF <condition$_1$> AND/OR <condition$_2$>..... THEN <Conclusion>*. The C-rules provide the simplest and easiest way to understand how to represent Knowledge and it is easy to control the complexity of data. Fuzzy rule (F-rules) has smooth gradual changes rather than a true or false response that avoids the pitfalls inherent in Crisp logic. In the fuzzy rule predicate is replaced by membership functions to determine the belief of truth. M-of-N rules or Threshold rules (T-rules) is suitable when many alternative conditions need to be considered to make a conclusion. For example, *IF M <conditions> out of N conditions is true THEN Conclusion is TRUE.* The formation of (T – Rules) is: IF R(X_1, X_2, … X_m) THAN X_n (p%); where, logical function R (.), X_i, i=1…m is true then X_n appears in per cent (p) of cases. Another is Prototype-based rules (P-rules), the form of prototype-based rules is; If a case X and a prototype R a threshold P-rule = *IF D(X, R) ≥ Θ THEN Conclusion is True.* It also used in a nearest neighbour rule: *IF p = argminp D(X, P) THAN Class (X) = Class (P)*, where *D(X,P)* is a distance function. The distance function can be form $D(X,P) = \max_i|X_i,R_i|$ (Duch W, 2001). To generate the rules for describing data structures some other methods have been developed. For example a decision tree where rules are represented in a hierarchical structure (Rokach and Maimon, 2009), Machine Learning (Mitchel, 1997), Neural Networks, Nearest Neighbour Methods (Duch, 2000), Neuro-Fuzzy Method (Nauck *et al*., 1997) and Support Vector Machines (Diederich, 2008). The rules can be represented in various forms: relation, recommendation, directives, strategies and heuristics (Durkin, 1994). Selection of rules depends upon the nature of any particular problem. In the propositional logic, rules can be made in the form of:$sign_1 \wedge sign_2 \wedge sign_3 \wedge \ldots\ldots sign_n \rightarrow disease_1$, *where, sign$_1$,*

$sign_2$, $sign_3$ ..... $sign_n$ represent the symptoms plus laboratory test's result and $disease_1$ denote a particular disease. Then the reasoning process will search a rule in the rule-based system, if given antecedents part matches with the rule-based system then this fires a satisfied rule to determine the likely disease. Such type of reasoning process or medical diagnosis application is good because it has a variety of positive characteristics for example only matched rule can be fired based only on a determined fact. That means diagnosis can be made quickly helping to explain diagnosis information to the patient verifying how and why a certain diagnosis has been made.

In this research, the Boolean logic is applied to design and create the rules. The two-valued logic, based upon the assumption that every proposition is either true or false, was provided by originally by Aristotle in 400 B.C. In 1847 Boo, G. defined the calculus of deductive reasoning, which is now called "Boolean logic". In 1943 Post, E.L presented the *IF-THEN* rules to the solutions of enumerable problems (Note: Lecture 3: Logic and Rule-Based Reasoning, Roman V. B., BIS3226). Basically, Boolean logic is mathematics for manipulation of variables which can have either; '*True' and 'False'* in formal logic, or in digital form the values are '*On'* and '*Off', 1* and *0, 'high'* and *'low'*. The basic information of Boolean logic is explained below.

In the Boolean logic, any variable (x, y) that can only have two values:

$$x \in \{0,1\}, y \in \{False, True\}$$

Boolean function is a function *f:* $X \rightarrow Y$ between Boolean variables. The Boolean operations are: ¬ not (negation), ∧ and (conjunction), ∧ or (disjunction).

Let x be a Boolean variable then,

¬ NOT (negation) = the value of ¬x is 1 − x.

x	**¬ x**
0	1
1	0

∧ AND (conjunction) = the value of x ∧ y is the minimum of {x, y}. Conjunction is equivalent to the intersection of sets A ∩ B.

x	**y**	**x ∧ y**
0	0	0
1	0	0
0	1	0
1	1	1

$\vee$ OR (disjunction) = the value of x $\vee$ y is the maximum of {x, y}. Disjunction is equivalent to the union of sets A $\cup$ B.

x	**y**	**x $\vee$ y**
0	0	0
1	0	1
0	1	1
1	1	1

Implication ($\rightarrow, \Rightarrow$): the value of x $\Longrightarrow$ y is the same as $\neg$ x $\vee$ y. Disjunction is equivalent to set inclusion A $\subset$ B.

x	**y**	**x $\Longrightarrow$ y**
0	0	1
1	0	0
0	1	1
1	1	1

Equivalence ($\sim$): the value of x $\sim$ y is the same as (x $\vee$ y) $\wedge$ ($\neg$ x $\vee$ $\neg$ y). Logical equivalence is the same as set equivalence: A$\subset$B and A$\supset$B, A$\equiv$B

x	**y**	**x $\sim$ y**
0	0	1
1	0	0
0	1	0
1	1	1

The Boolean sum is OR and Boolean product is AND, for example,

Boolean sum = $1 + 1 = 1, \quad 1 + 0 = 1, \quad 0 + 1 = 1, \quad 0 + 0 = 0$

The complement is denoted by a bar (on the slides, we will use a minus sign). It is defined by: $-0 = 1$ and $-1 = 0$.

Boolean product **(.) =** $1 \cdot 1 = 1, \quad 1 \cdot 0 = 0, \quad 0 \cdot 1 = 0, \quad 0 \cdot 0 = 0$

The reason for choosing the Boolean logic is the formation of rules in my research is: if rules are associated with multiple conditions, the logical operators are required to represent the Knowledge. Such types of rules could be expressed as *IF <condition> is True, THEN take appropriate <action>*. The condition part has a pre-defined variable either in digital form, 1 and 0 or formal logic form (true and false, yes and no), or linguistic form (positive, negative; present, absent). Regarding the diagnosis of the ARF model, empirical knowledge exists as a set of definitions making it is easy to understand the information, for example:

IF *Arthritis = "Present"* AND *Chorea ="Present"* AND *Fever = "Present"* AND *Arthralgia ="Present"* AND *GAS infection="Present"* THEN *diagnosis DETECTED ARF*.

In this way, the knowledge for diagnosis of ARF is straightforward enabling every portion of knowledge to be formed into a rule. Further, the set of rules is easy to read, understand and maintain for non-IT related people, especially for inexperienced doctors or community rural health workers. Another reason for applying a Boolean logic or expression is that it can easily capture signs and symptoms for doctors and rural health workers as well as being easy to apply in rule formation. As stated by Hilden (2009) "*Boolean principles also underlie logical checking of rule-based decision support systems for inconsistencies, incompleteness and redundancy"* (Hilden J., 2009). The signs and symptoms captured by the ARF diagnosis system represent observable traits in ARF patients and use rules developed from experts guidelines within NHF criteria. Depending upon observed traits in ARF patients, the system can diagnose an ARF case defined with ARF's severity level index into three categories. This categorisation is shown in Figure 4.3. Rules were designed based on the signs and symptoms for detected and suspected cases. During the formation of rules, expert guidelines from NHF were used. The equations, Nos.1-11, are illustrated in Figure 4.3 which lists the rules. A New Rule Formation algorithm was later developed to produce a rule to be added if a particular rule is not already present in the rule-based system. This algorithm was designed and developed using the decision tree discussed in the New Rule Formation section.

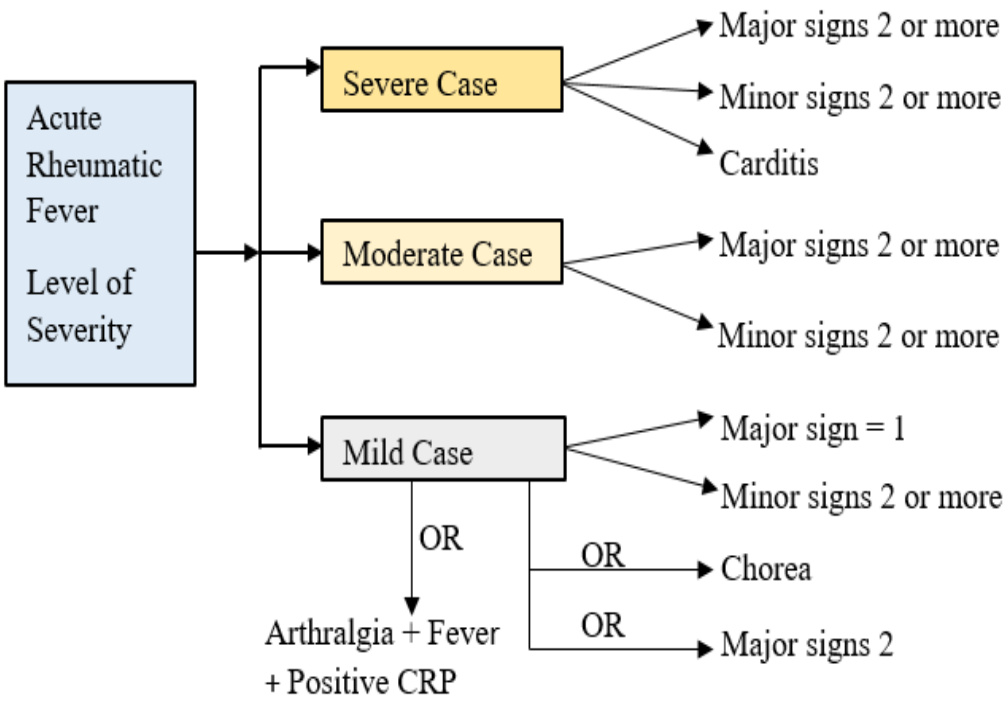


Figure 4.3 : Signs and Symptoms for Different Level of the Severity.

Again, it is an appropriate choice to apply the Boolean logic to the design rules where observations consist of logical forms: present or absent; positive or negative. Therefore,

in this model KBS consists of a set of Boolean rules for diagnosis of ARF and severity level. All ARF signs and laboratory results are facts. A set of rules is described by the respective expert's knowledge of diagnosing ARF based on the facts. The model rule engine (condition-action-rules or premise-consequence-rule e.g. *IF-THEN*) inference combines the rules and facts for application in the reasoning process. In addition, the reasoning process will match the pattern (matching the condition part of rules against facts stored) and fire the satisfied one with justification. The justification of each rule provides the WHO, WHF or NHF's information regarding diagnosis of ARF. The following equations Nos.1-11, have been created based on expert guidelines used to identify the severity level of ARF in confirmed cases.

$$\textbf{Severe} = \{carditis \wedge essential\ sign(s) \geq 1 \wedge major\ signs \geq 2 \wedge minor\ signs \geq 2\} \quad \text{.....(1)}$$

$$\textbf{Moderate} = \{essential\ sign(s) \geq 1 \wedge major\ signs \geq 2 \wedge minor \text{ signs} \geq 2\} \quad \text{.....(2)}$$

$$\textbf{Mild} = \{essential\ sign(s) \geq 1 \wedge major\ sign\ (\neg chorea) = 1 \wedge minor\ signs \geq 2\} \quad \text{.....(3)}$$

$$\textbf{Mild} = \{chorea\} \quad \text{.....(4)}$$

$$\textbf{Mild} = \{major\ signs\ (\neg chorea) \geq 2\ (\} \wedge \{essential\ sign(s) \geq 1\} \quad \text{.....(5)}$$

$$\textbf{Mild} = \{Art_{13} \wedge Fe_{12} \wedge Crp_{15} \wedge essential\ sign(s) \geq 1\} \quad \text{.....(6)}$$

$$\textbf{Suspected} = \{major\ sign\ (\neg chorea) = 1 \wedge minor\ sign = 1 \wedge essential\ sign(s) \geq 1\} \quad \text{.....(7)}$$

$$\textbf{Suspected} = \{Art_{13} \wedge Fe_{12} \wedge essential\ sing(s) \geq 1\} \quad \text{.....(8)}$$

$$\textbf{Suspected} = \{Art_{13} \wedge Fe_{12} \wedge Ecg_{14} \wedge essential\ sing(s) \geq 1\} \quad \text{.....(9)}$$

$$\textbf{Suspected} = \{Art_{13} \wedge Fe_{12} \wedge Esr_{16} \wedge essential\ sing(s) \geq 1\} \quad \text{.....(10)}$$

$$\textbf{Suspected} = \{Art_{13} \wedge Fe_{12} \wedge Esr_{16} \wedge Esr_{16} \wedge essential\ sing(s) \geq 1\} \quad \text{.....(11)}$$

A patient's symptoms are captured in a Boolean expression such as "True" or "False", "0" or "1" etc. We use "*P=present*" if verified signs are presented or observed and "*A=absent*" if signs are not presented or not observed. A set of rules have been created for all the severity levels of ARF. Each rule has symptoms in the condition part and corresponding severity levels of ARF with numbers of positive symptoms placed in the consequence part. The mixed reasoning methods (both backward and forward reasoning/chaining) have been applied. In the model, some of the rules were specially designed and used for forward reasoning and others used for backward reasoning. The purpose of applying the mixed reasoning process is to maximize the diagnosis efficiency

of ARF. Based on the above equations, we formulated *IF-THEN* rules, which the inference engine uses to diagnose cases of ARF, for example:

IF

Arthritis =*"P"* AND Carditis=*"P"* AND Chorea=*"A"* AND SN=*"A"* AND EM=*"A"* AND Fever=*"P"* AND Arthralgia=*"P"* AND Throat Infection=*"P"* AND GAS=*"P"*

THEN

ARF Stage: *"Detected ARF"*

Diagnosis: *"Acute Rheumatic Fever"*

Level of Severity: *"Severe Case"*

EXPLANATION:

Severe pain in the large joints with swelling or redness, movement restriction, carditis heart murmur presented with pain, current high temperature, small joints pain, GAS infection in the throat is positive including all throat infection. Based on the NHF guideline including timeframe of symptom appearance and development (Temporal Template) if this case is Acute Rheumatic Fever the level of severity is SEVERE. Immediate treatment required, follow medication guidelines. Seek advice from specialist or refer patient to nearest hospital as soon as possible if medication option currently not available.

NO. OF POSITIVE SYMPTOMS: 6

4.5. Hybrid Approach's Architecture

The current Hybrid Approach is a combination of Knowledge-based, Temporal theory and Fuzzy Logic. This approach involves defining three models: 1) KBS/Boolean Rule; 2) Temporal and 3) Fuzzy Model. Its components have unique tasks in designing the ARF Diagnosis Application. The Search and Match Stage of ARF, Rule Pattern Matching, New Rule Formation and Rule Selection Mechanism are the components of the KBS/Boolean Rule Model. This model is used for capture, management and representing ARF knowledge as well as for the construction of the Boolean rules. The detailed discussion of this model is given in the KBS/Boolean Model Section 4.6. The second model used is Temporal and is responsible for capturing the event and time from a patient's description (in his/her native language) during the explanation of symptoms. To simplify this task for doctors or rural health workers, we apply a standard electronic format that selects symptoms and the auto or manual method (user choice) will apply to capture the duration of symptoms. The descriptive explanation of ARF symptoms,

Temporal Lookup Table/Rule, Temporal Inference and Temporal Template, are the components of this model that are explained in the Temporal Model Section 4.7. The third model is Fuzzy, which is responsible for managing uncertainties, vagueness of signs and symptoms and for making a final diagnosis of ARF. Fuzzification, Fuzzy Inference and Defuzzification are components of this model that is explained Section 4.8. Figure 4.4 presents the Hybrid processes that are applied in the design and development of an ARF Diagnosis Application.

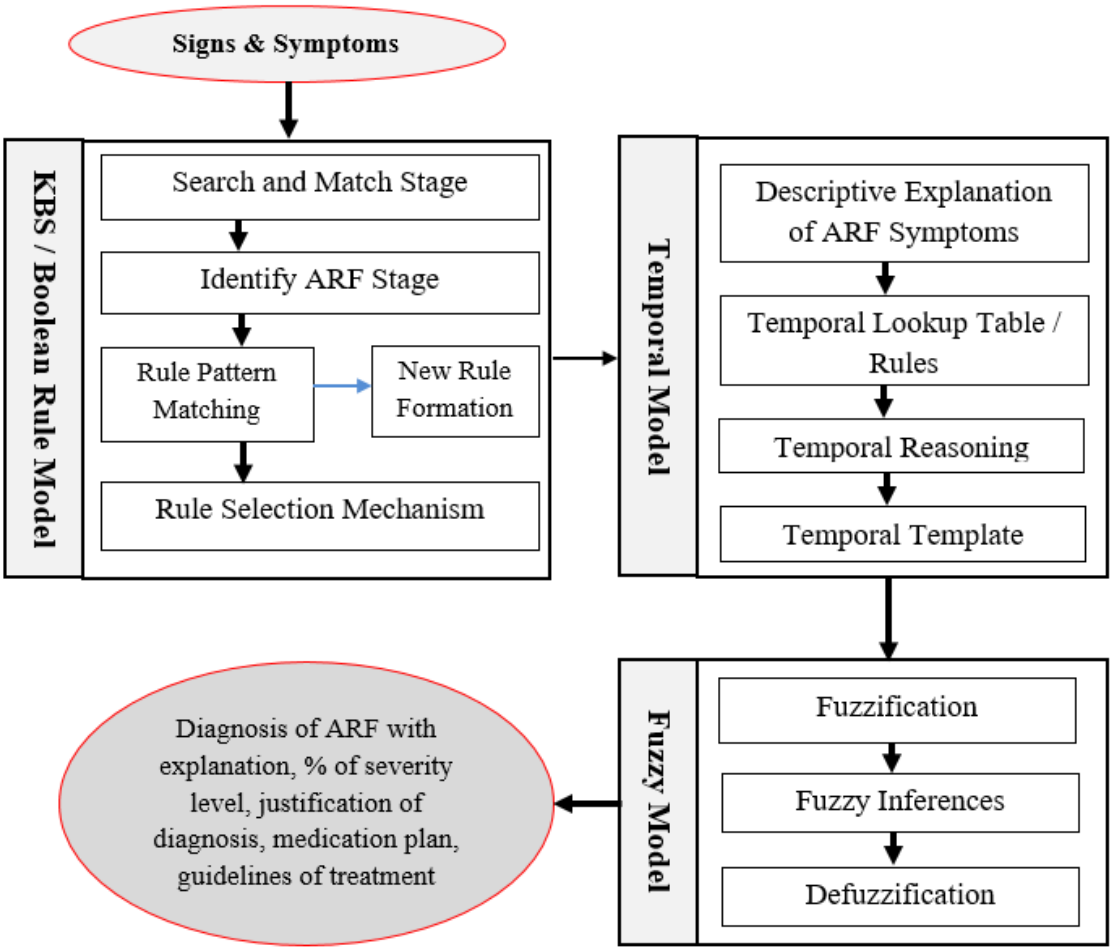


Figure 4.4: The Hybrid Process for ARF Diagnosis

The KBS/Boolean Rule Model reads the symptoms that are selected by users and goes through the components of the model providing us with knowledge of the stage of the ARF case severity level. The Temporal Model allows us to capture the time and duration of each symptom. The temporal reasoning processes produce a Temporal Template based on the presented signs and a temporal rule that explain the relation between the signs and ARF. The Fuzzy Model will make a final diagnosis of ARF.

Figure 4.5 provides an overall view of how an individual model works, how information/data follows from one model to another and produces the final output of ARF.

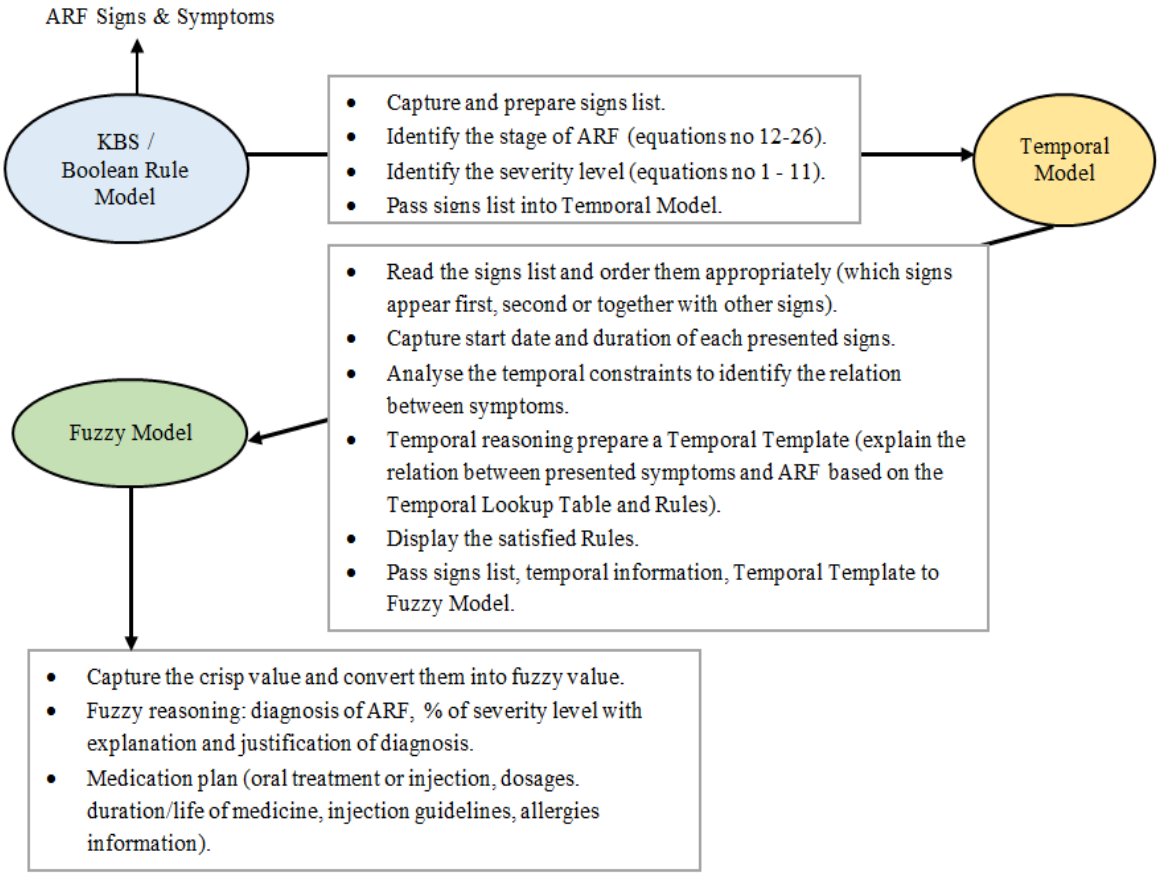


Figure 4.5: Overall View of Each Model's Work

The detailed discussion of each model is given below which describes with flowcharts how each component of a model performs its tasks.

4.6. Knowledge-Based / Boolean Rule Model

Some methodologies exist for the development of KBS for example, MIKE (Angele *et al.*, 1998), Common KADS (Scheiber *et al.*, 2000). These methodologies define three phases: 1) contextual analysis; 2) conceptual analysis and 3) design for development of KBS systems. This model is applied in various clinical domains (David S. and Vovel P., 2009). Another is PROTÉGÉ (Tu *et al.*, 1995). In 1987 Mark Musen built the Protégé meta tool for knowledge-based systems and aimed to build knowledge-acquisition tools. The current Protégé-2000 system is more advanced than the original version; it can run on a variety of platforms, incorporates the open knowledge base connectivity, and interacts with relational databases, XML etc. (Gennari J. H *et al.*, 2003). It was originally developed by Stanford Medical Informatics, and the Protégé method is a free open source

ontology editor. Protégé-Frames and Protégé-OWL editors are the main ways of modelling ontologies. "OpenKnoMe" is developed by GALEN project, GALEN-In-Use project, *Open* GALEN in 2001. *KnoME is designed to be a complete GRAIL knowledge management and ontological engineering environment.* This is an open-source resource available to the academic and not-for-profit clinical terminology community (Open Clinic: *Open*KnoME).

In the development of KBS systems, the most important part of it is knowledge acquisition and representation. These two activities are sometimes called knowledge engineering tasks or the KBS construction process. Reviewing various articles and lecturer notes it was noted that the decision model tasks can be represented as quantitative and qualitative. In the quantitative neural networks, Bayesian theory, fuzzy set etc. can be applied. In the qualitative decision model, truth table, Boolean logic, decision tree etc. can be applied. Knowledge acquisition and knowledge representation are described when designing the rules for the ARF diagnosis model. In our research, a decision matrix table (Truth Table) was applied for identification of ARF progress stages. A Decision Tree is used for development of New Rule Formation. All the components of KBS/Boolean Rule Model are discussed in this section below.

4.6.1. Search and Match Stage

Search and Match Stage (SMS) is designed and developed to identify the ARF stage and severity level, based on the observed patients' signs and symptoms. Each component of the KBS Model is implemented by a set of algorithms that are explained below.

4.6.2. The Identify Stage of ARF

To identify the stage of ARF, a decision matrix table is prepared and applied. The decision matrix table is formulated based on the equations 12-27 listed below. The equations were prepared based on the NHF experts' guidelines for diagnosis of ARF. The decision matrix table consists of major, minor and essential criteria and the number of symptoms associated with each criterion that represents the ARF stage. The decision matrix table is shown in Table 4.3.

$$(\{majorsigns, minorsigns, mandatorysigns\} \rightarrow \{detected\ ARF\ \vee suspected\ ARF\ \vee not-dtected\ ARF\}) \quad (12)$$

$$Detected\ ARF = (major\ sign \geq 1\ \wedge minor\ signs \geq 2\ \wedge essential\ sign(s) \geq 1) \quad (13)$$

$$Detected\ ARF = (major\ sign\ (Chorea)) \quad (14)$$

$$Detected\ ARF = (major\ signs \geq 2\ \wedge minor\ sign = 0\ \wedge\ essential\ sign(s) \geq 1) \ldots \ldots (15)$$

$$Detected\ ARF = (major\ signs = 5 \wedge minor\ signs = 5\ \wedge essential\ signs = 3) \ldots \ldots (16)$$

$$Detected\ ARF = (Art_{13} \wedge\ Fe_{12}\ \wedge Crp_{15} \wedge essential\ sign(s)\ \geq 1) \ldots \ldots (17)$$

$$Suspected\ ARF = (major\ sign = 1\ \wedge \neg Chorea\ \ \wedge\ minor\ sign = 1\ \wedge\ essential\ sign(s) \geq 1) \ldots \ldots (18)$$

$$Suspected\ ARF = (Art_{13} \wedge\ Fe_{12}\ \wedge essential\ sing(s)\ \geq 1) \ldots \ldots (19)$$

$$Suspected\ ARF = (Art_{13} \wedge\ Fe_{12}\ \wedge\ Ecg_{14}\ \wedge essential\ sing(s)\ \geq 1) \ldots \ldots (20)$$

$$Suspected\ ARF = (Art_{13} \wedge\ Fe_{12}\ \wedge\ Esr_{16}\ \wedge essential\ sing(s)\ \geq 1) \ldots \ldots (21)$$

$$Suspected\ ARF = (Art_{13} \wedge\ Fe_{12}\ \wedge\ \ Ecg_{14} \wedge Esr_{16}\ \wedge essential\ sing(s)\ \geq 1) \ldots \ldots (22)$$

$$Not - detected\ ARF = (majorsign = 1\ \wedge\ \neg Chorea\ \ \wedge\ \ 0\ \ minorsign(s) \wedge essential \geq 1) \ldots \ldots (23)$$

$$Not - detected\ ARF = (major\ sign = 0\ \wedge\ 1\ or\ all\ minor\ signs\ \wedge\ essential = 0) \ldots (24)$$

$$Not - detected\ ARF = (major\ sign = 0\ \wedge\ \ minor\ sign = 0\ \wedge\ essential\ signs \geq 1). (25)$$

$$Not - detected\ ARF = (major\ sign = 0\ \wedge\ \ (Art_{13} \vee\ Ecg_{14} \vee\ Crp_{15} \vee\ Esr_{16})\ \wedge\ essential\ signs \geq 1) \ldots \ldots (26)$$

$$Not - detected\ ARF = (major\ sign = 0\ \wedge\ \ (Fe_{12} \vee\ Ecg_{14} \vee\ Crp_{15} \vee\ Esr_{16})\ \wedge\ essential\ signs \geq 1) \ldots \ldots (27)$$

Table 4.3: Decision Matrix Table to Identify the ARF Stages

ARF Stage	Major Signs	Minor Signs	Mandatory Signs
Detected ARF	≥1	≥2	≥1
	Chorea	=0	=0
	≥2	=0	≥1
	=5	=5	=3
	=0	$Arth_{13}$+ Fev_{12}+Crp_{15}	≥1
Suspected ARF	=1 ∧ ¬ *Chorea*	=1	≥1
	=0	$Arth_{13}$+ Fev_{12}	≥1
	=0	$Arth_{13}$+ $Fev_{12} + Esr_{16}$	≥1
	=0	$Arth_{13}$+ $Fev_{12} + Ecg_{14}$	
	=0	$Arth_{13}$+ $Fev_{12} + Ecg_{14} + Esr_{16}$	≥1
Not-detected ARF	1 ∧ ¬*Chorea*	=0	≥1
	=0	≥1	=0
	=0	=0	≥1
	=0	$(Art_{13} \vee\ Ecg_{14} \vee\ Crp_{15} \vee\ Esr_{16}$	≥1
	=0	$(Fe_{12} \vee\ Ecg_{14} \vee\ Crp_{15} \vee\ Esr_{16}$	≥1

Identifying the stage of ARF is a reasoning process whereby community rural health workers or inexperienced doctors will observe / collect the ARF symptoms from a

patient's physical examination and feed them into the model. Then the model will reason the information based on the KBS guidelines in order to understand the ARF diagnosis stages, evaluate the information with the decision matrix table and display the result of the determined ARF stage. The decision matrix table that represents conditions required to identify the ARF stage either in Detected or Suspected or Not-detected ARF format. The flowchart in Figure 4.6 illustrates a comprehensive summary of the process.

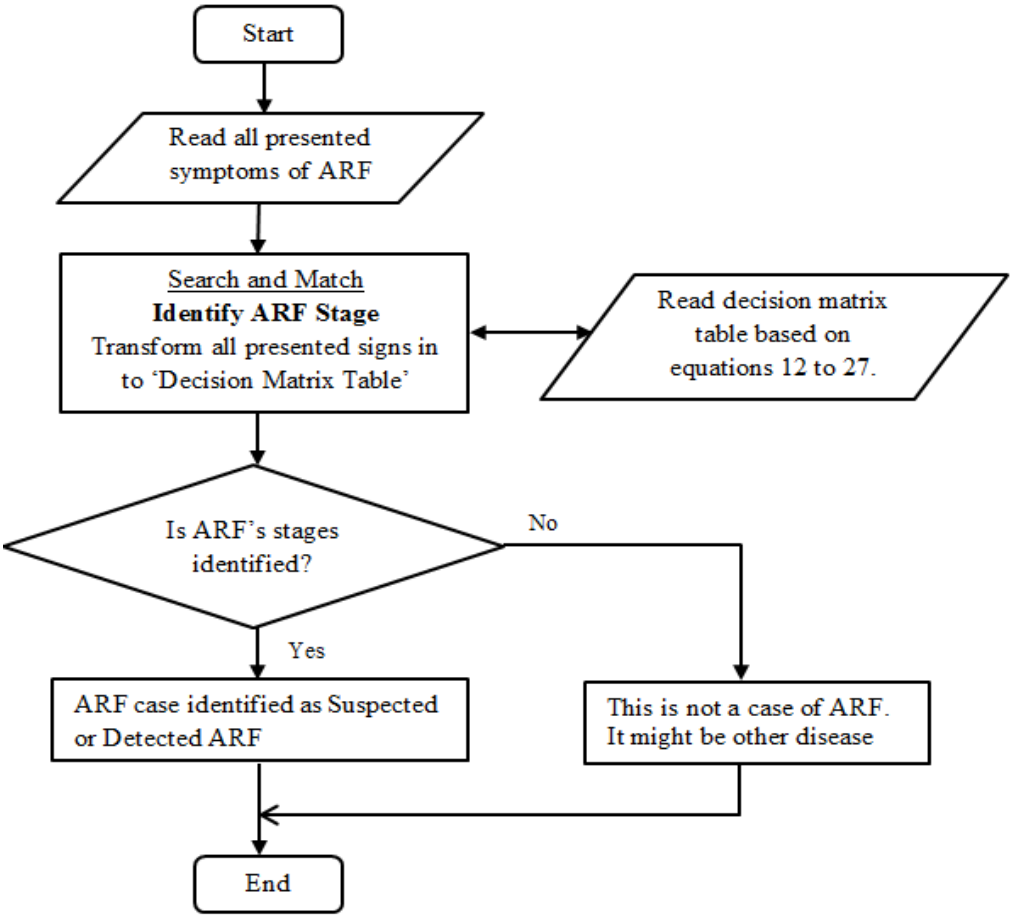


Figure 4.6: The Process of Identify the Stages of ARF

4.6.3. Rule Pattern Matching

Rule Pattern Matching (RPM) detects new or existing facts and matches them against the rule or search for a rule that in turn matches pattern in the data. There are various algorithms used for pattern matching Linear, Rete, Treat, Leaps etc. Here, we use a simple pattern matching strategy. The inference engine performs the pattern-matching task. The pattern matching process will help to fire the exact matching rule by eliminating any unsuitable rules and facts. After identifying the ARF stage, the RPM will automatically activate and identify the exact rule that matches between the pattern and fact (observed signs and symptoms). If the pattern of the rule matches the facts in working memory then the activation of the rule will be fired. However, in firing the rule

or deciding which rule needs to be fired this will be done by conflict resolution, which the first satisfied rule will fire. During the literature review, some strategies were found relating to conflict resolution: Refractoriness (the rule saying do not fire twice on the same data); Recency (select the recently arrived data in working memory and identify a rule that uses this data) and the Specificity (use most conditions attached). In this application, conflict resolving is managed by first applicable strategy meaning that if the rules are in order, fire the first match satisfied rule and stop the rule for further execution. The rule must match all the condition parts. Figure 4.7 is a flowchart illustrating the detailed process of Rule Pattern Matching.

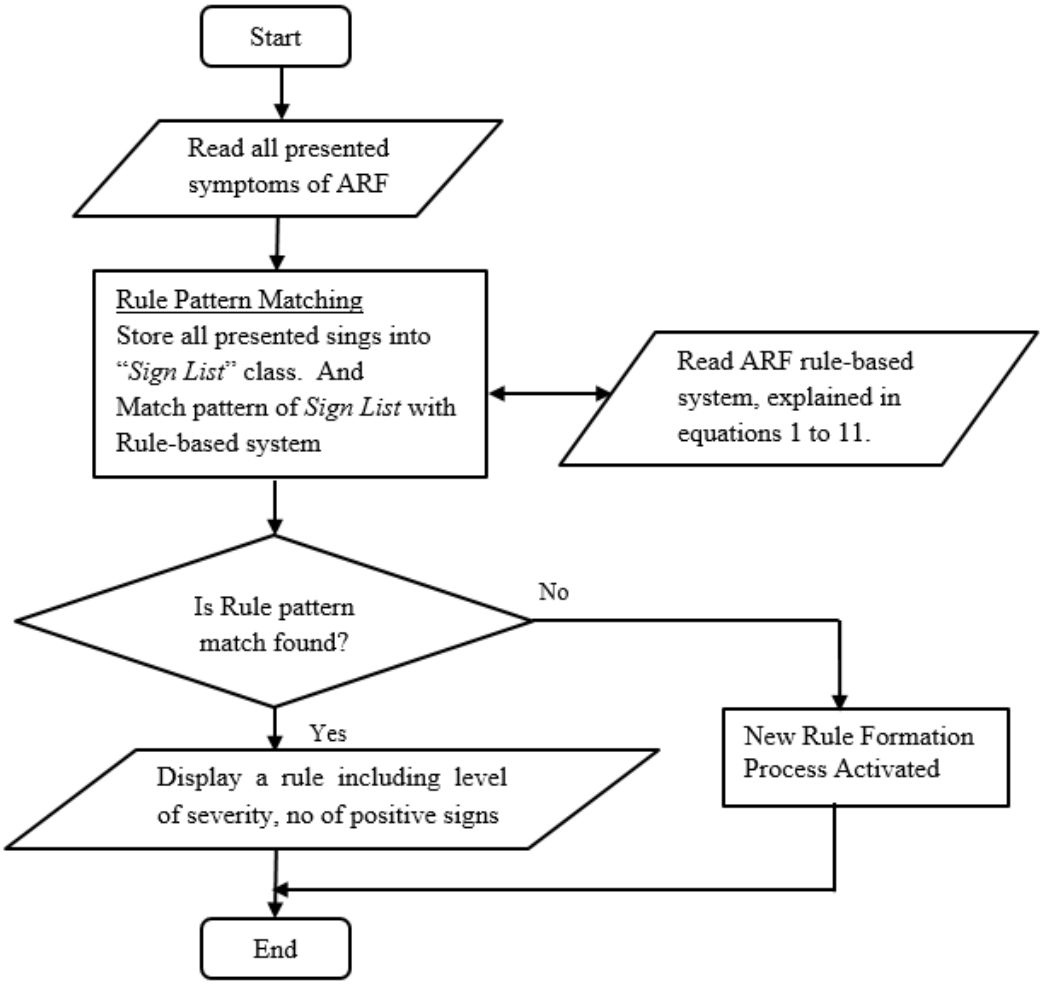


Figure 4.7: The Process of Rule Pattern Matching

4.6.4. New Rule Formation

During the process of Rule Pattern Matching, if a rule has not been found in the rule-base then the New Rule Formation (NRF) is activated which has process for generating a new rule. NRF is a self-developing algorithm that is applied in this system for construction of any new rule. The algorithm was developed based on the Decision Tree. There is scope for experts to revise, delete or add new parameters in an added rule if necessary. The

benefit of using this algorithm is that it assists whenever adding a new rule requires domain expertise, knowledge engineering and a programmer, which can be a time consuming process and dependent upon the availability of all experts. The NRF process helps by performing all tasks such as those pertaining to expertise, knowledge engineer and programmer by adding a new Rule using the rule-based system.

Quinlan introduced an algorithm for inducing the Decision Tree ID3 in 1986 and later it was upgraded with ID3 in an improved algorithm C4.5 (Quinlan 1993). Both algorithms (ID3 and C4.5) use a statistical calculation to build a Decision Tree function. The Decision Tree is generally easy to understand and is able to be used for management of both numerical and linguistic or categorical data. Furthermore, it does not require a big volume of data for its creation. It is also able to validate models using statistical tests.

The Decision Tree was created based on the signs and symptoms for different severity levels of ARF and made use of NHF's expert guidelines. The Decision Tree was applied in the NRF process of application, which is given below:

4.6.4.1. Decision Tree for Severe Cases

The Decision Tree for a severe case of ARF is shown in Figure 4.8. The process and equations are shown in Figure 4.9.

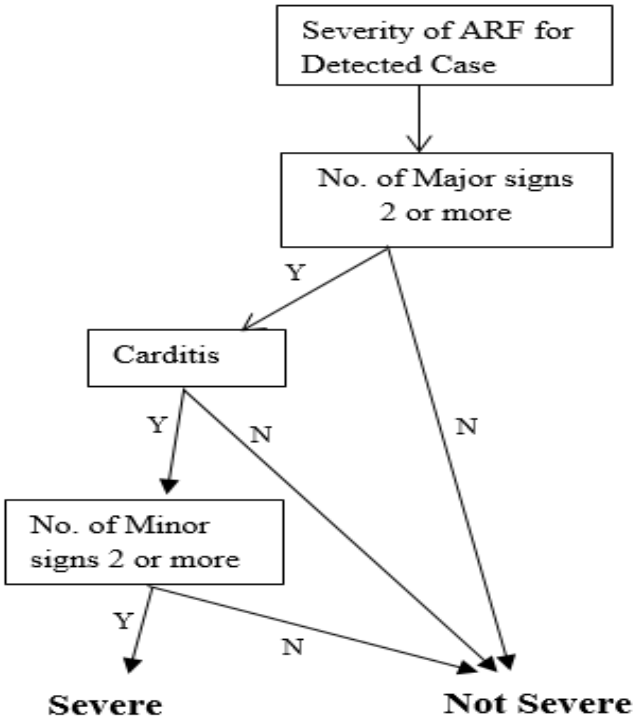


Figure 4.8: Decision Tree for Severe Case

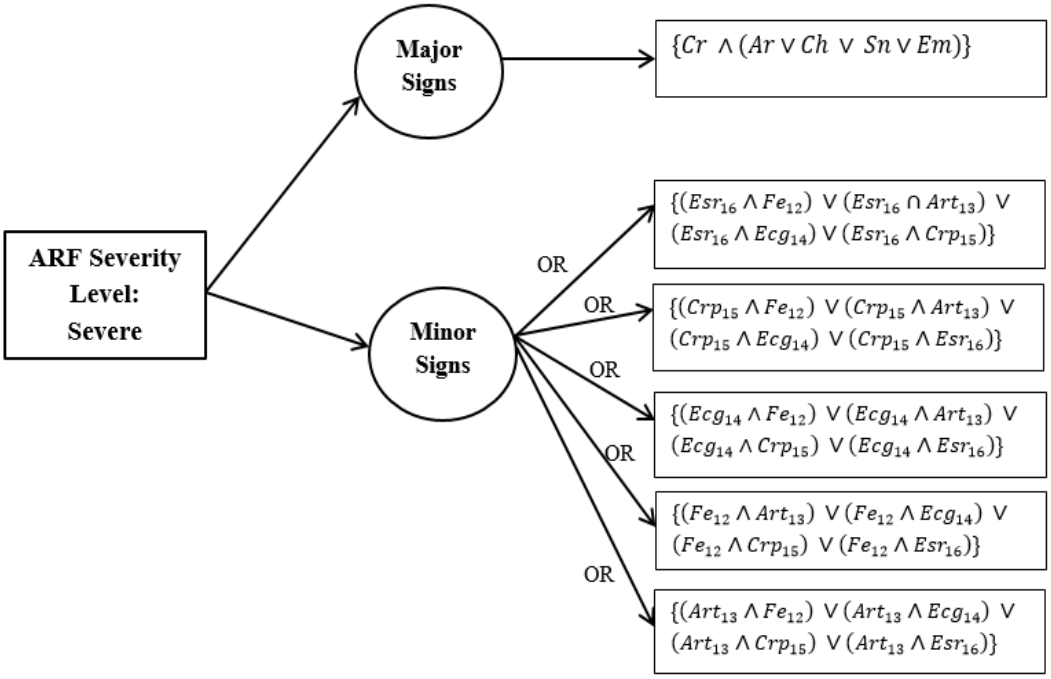


Figure 4.9 : New Rule Formation Process and Equations for Severe Cases

4.6.4.2. Decision Tree for Moderate Cases

The Decision Tree for a Moderate case of ARF is illustrated in Figure 4.10 and the process and equations are shown in Figure 4.11.

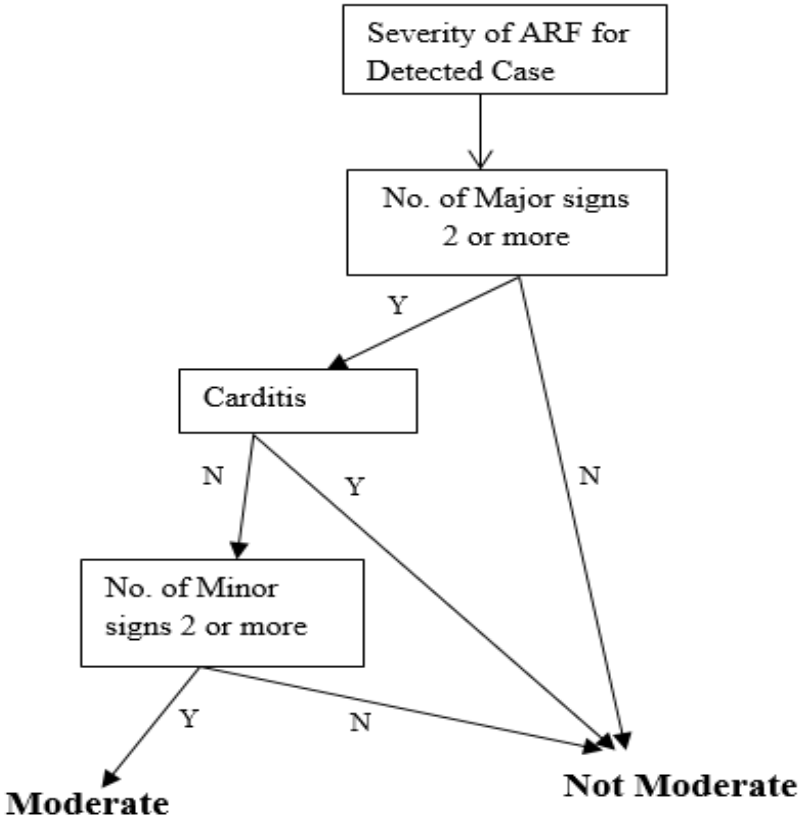


Figure 4.10: Decision Tree for a Moderate Case

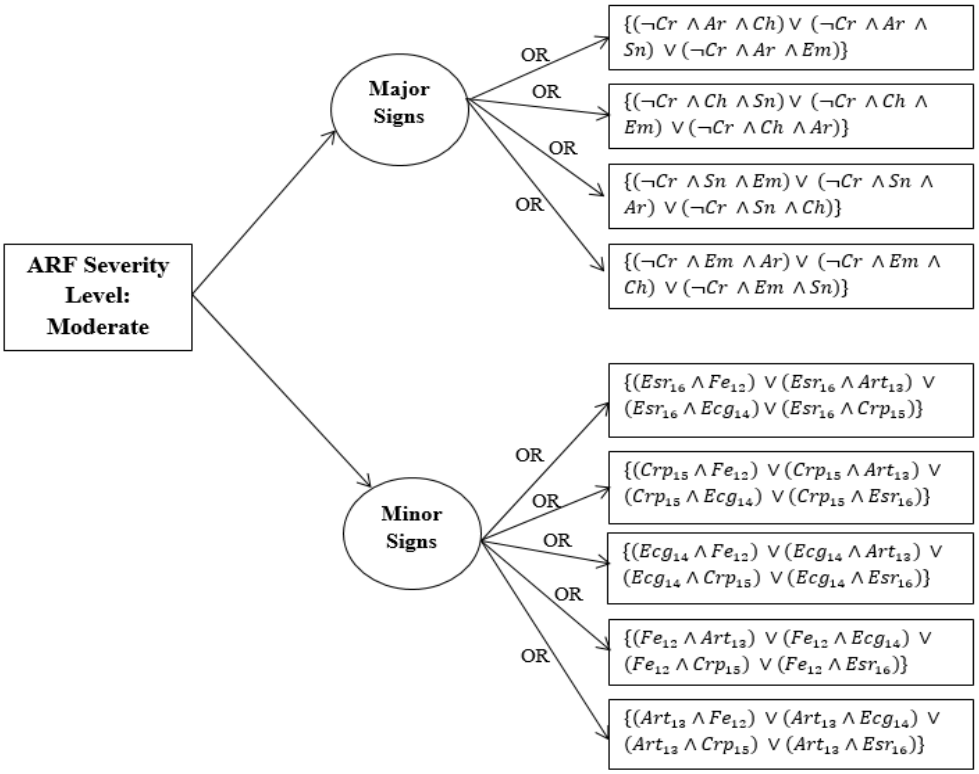


Figure 4.11 : New Rule Formation Process and Equations for Moderate Cases

4.6.4.3. Decision Tree for Mild Cases

The Decision Tree for a mild case of ARF is illustrated in Figure 4.12 and the process and equations are shown in Figure 4.13.

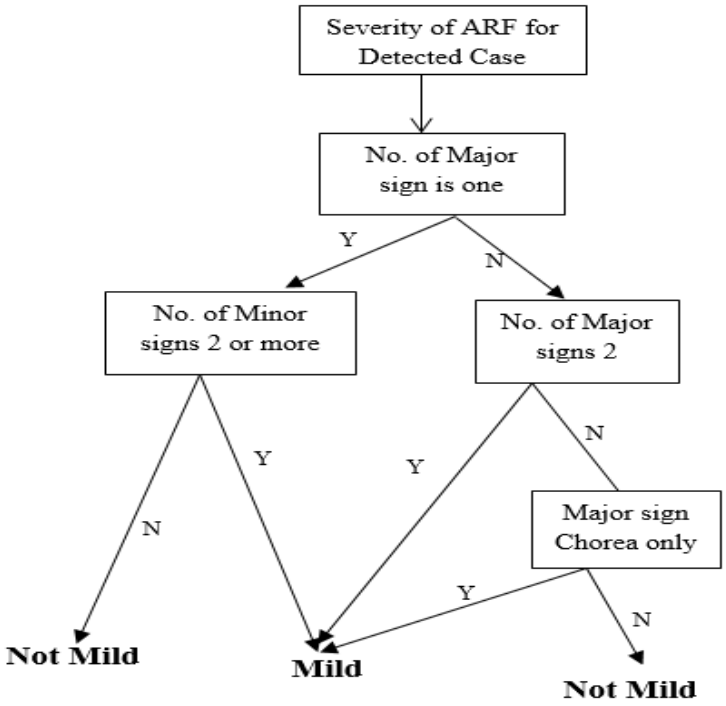


Figure 4.12: Decision Tree for Mild Cases

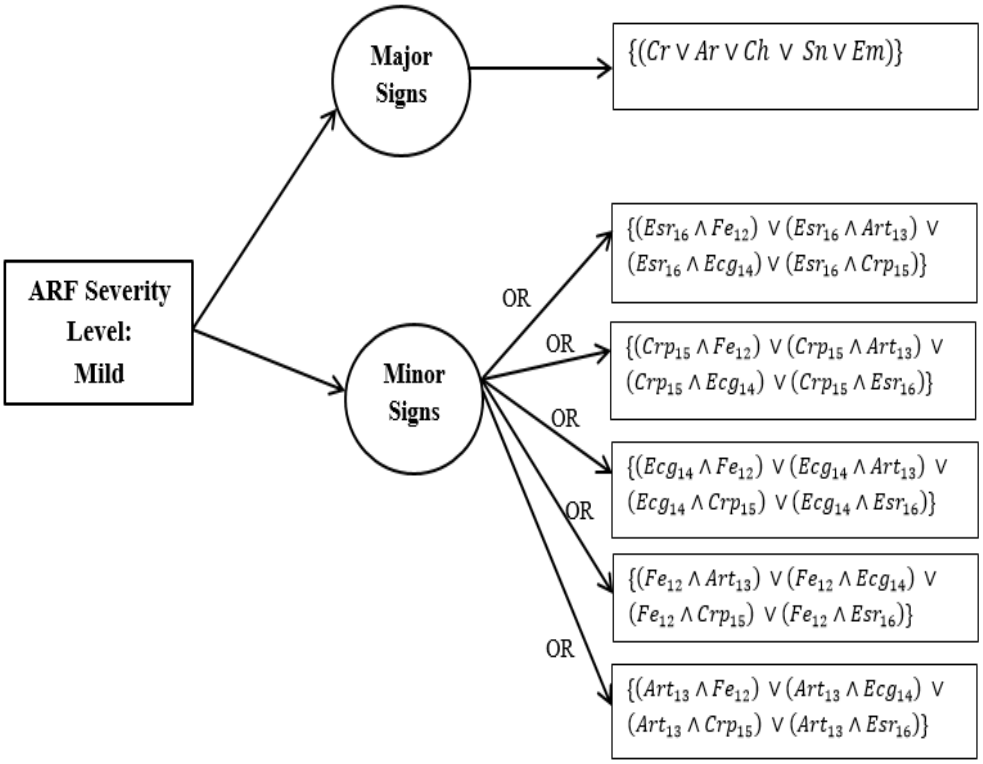


Figure 4.13: New Rule Formation Process and Equations for Mild Cases

4.6.5. Rule Selection Mechanism

The Rule Selection Mechanism (RSM) concept is simple but very important for the diagnosis of ARF. During the RPM process, it will show only matching rules and based on that help make a decision which may not be accurate enough for the ARF diagnosis model. Therefore, the main objective for developing and implementing this RSM is to be able to diagnose ARF more effectively. RSM is responsible for searching and selecting the appropriate rules from every level of ARF severity, based on a given total number of positive signs. The number of positive signs is a value obtained by using the RPM process. The algorithm of RSM is defined in Figure 4.14 to enable a better understanding of the process of RSM in ARF diagnosis model.

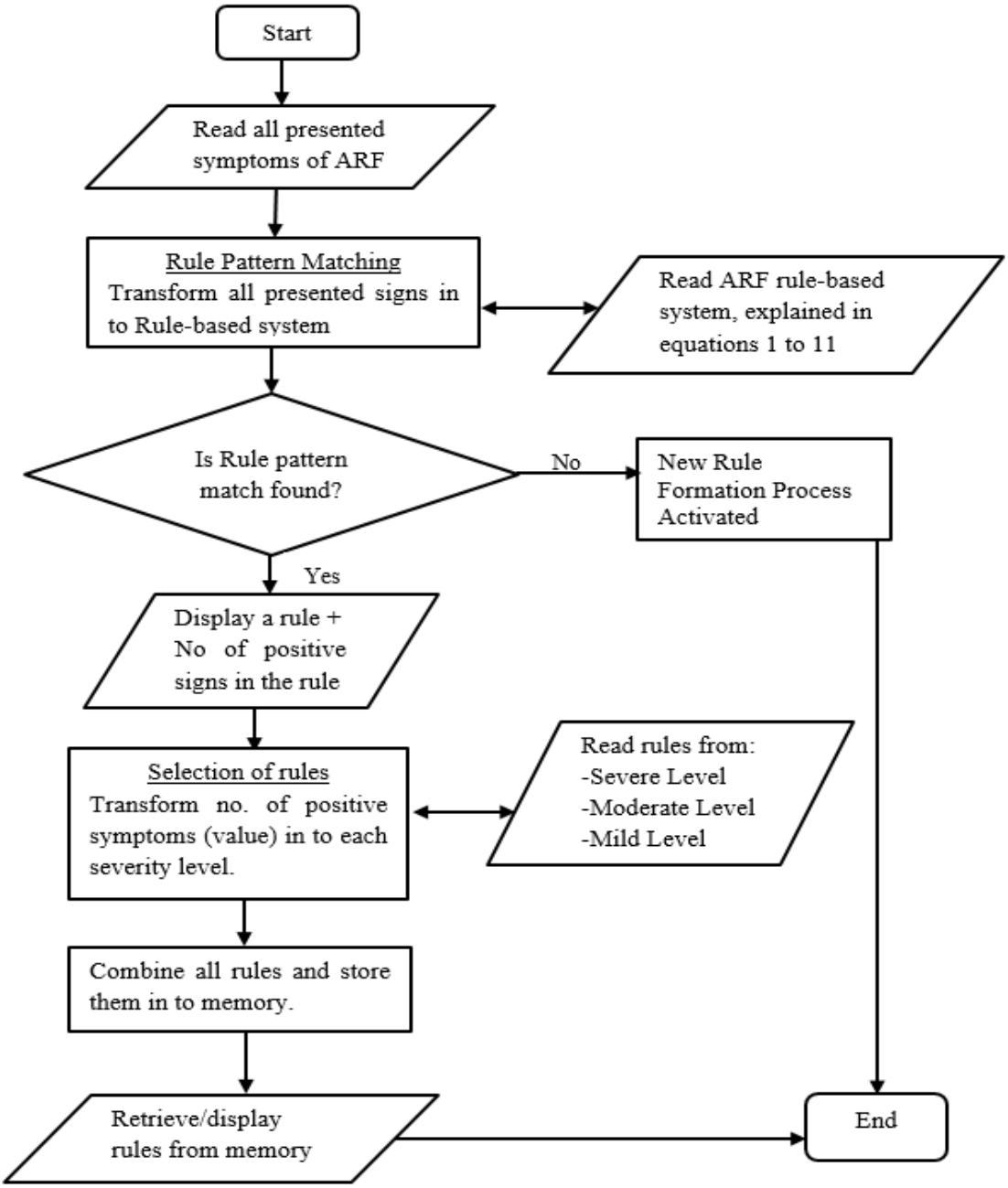


Figure 4.14: The Rules Selection Mechanism Process

This process reads all presented symptoms that are captured during the patient screening stage. The Rule Pattern Matching process transfers captured symptoms to a rules-based system and searches for pattern matching with the rule-based process. If found then it displays the satisfied rule and the number of positive symptoms (which can be obtained by counting a patient's presented symptoms). In addition, this process passes the number of positive symptoms (value) in each level of an ARF severity determined as Severe, Moderate, Mild and Suspected and captures all the rules from each level that match with the number of positive symptoms. Having analysed these data it combines all the satisfied rules from each level and stores them into its memory. Eventually the fuzzy process uses these rules to make a final diagnosis of ARF.

4.7. The Temporal Model and ARF Diagnosis

Time is an essential component of clinical decision support systems that is strongly related to medical data sets in diagnosis, therapy or medical knowledge. The representation and reasoning of time function is obviously a vital requirement for proper medical diagnosis systems. Time factors help clarify the picture of a patient's problems, but how to model time varies and is often depends on the specific medical domain. Application of temporal logic is growing generally in the medical domain. In medical diagnosis systems, temporal logic plays an important role in understanding temporal constraints between the symptoms and diseases. Temporal logic has been used in medical science for a long time. Clinical decision support systems need to capture different temporal features applying different types of data modelling approach. Most medical informatics system applications were developed based on the point-based approach. The point-based method is similar to McDermott's point's concept rather than time interval concept proposed by Allen (Carlo C, Yuval and Shahar, 1997),

It is accepted in medical diagnosis that an event occurs at some time point; certain facts hold during a time period and temporal relationships exist between facts and/or events (Ozsoyoglu G. and Snodgrass R. T., 1995). Modelling time is a key factor in abstraction for medical diagnosis processes and clinical database management. Various choices are available for instance transaction and valid time; time domain; instants and intervals; circular, branching and linear time; parallel time; relative and absolute times; temporal relationships, etc. Most of system presented time is linear where all time elements are ordered along a single time line. Other non-linear temporal structures are also presented such as McDermott's temporal logic, which allows time to branch into the future contrasting with Allen's intervals, which are not allowed to branch into the future (Ma J. and Knight B., 1994). It can be seen therefore that there is a wide difference between using point-based and interval-based temporal theory. Allen's interval-based concept allows for a natural representation that can occur in natural language in clinical information systems for example a "*child felt the severe pain in his ankles sometimes after walking*". But the point-based temporal primitives is more appropriate in domains where time stamped data occur automatically for example *ICU patient's blood pressure value was 180/200 at 9:30 PM on March 2014*. Another example, *Ramu had suffering from arthritis pain start from 5/9/2015 to 5 days* making it is easy to determine the duration of pain. But, *Ramu had suffering from arthritis pain sometimes last year in September,* makes it difficult to estimate the duration as there is an obvious degree of

uncertainty: how to define sometimes, few hours, 5 hours, 9 hours, 2 hours or 1 days or 2 days. Thus, point-based temporal primitives are better for computation and seem more practical to apply in the medical reasoning process. ARF symptoms can present a set of a time points and can provide the real numbers that can help further the diagnostic process. In the reasoning process, it also important to analyse the symptom and disease relations as well as symptom to symptom relations for example *X* can cause *Y*, *Y causes X* (more details are given in the section below). The most popular method is the point-based one in medical diagnosis processes (Kahn M. G. and Marrs K. A., 1995). The *IF-THEN* rules can be applied to the point-based Temporal Model in the diagnosis of disease and the form for a rule can be presented as:

IF *evidence of GAS infection on throat is present during the last 3 days with* fever
AND
Arthritis pain time stamp is present for 7 or more days with movement restriction, hotness, swelling, redness in the large joints
THEN *Rheumatic Fever can be* SUSPECTED,
SUGGESTION: *go for laboratory test.*

The point-based temporal abstract is used in our research was based on the Jixin Ma and Brain Knight's model (Ma J. and Knight B., 1994). Consider the interpretation in which the set of time points, **P**, is the set of all real numbers; and the set of time intervals, **I**, is the set of periods which are constructions over all possible point-pairs, $p_1,p_2 \in \mathbf{P}$ such that $p_1 < p_2$, with the following structures:

$$(p_1,p_2, \text{open}, \text{open}) =_{def} \{ r \in \mathbf{R} \mid p_1 < r < p_2 \},$$
$$(p_1, p2, \text{open}, \text{closed}) =_{def} \{ r \in \mathbf{R} \mid p_1 < r \leq p_2 \},$$
$$(p_1,p_2, \text{closed}, \text{open}) =_{def} \{ r \in \mathbf{R} \mid p_1 \leq r < p_2 \},$$
$$(p_1, p2, \text{closed}, \text{closed}) =_{def} \{ r \in \mathbf{R} \mid p_1 \leq r \leq p_2 \},$$

Where "<" and "≤" are the ordinary ordering relations over the set, **R**, of real numbers. They define the duration assignment function d as:

$$d((p_1,p_2,\_,\_)) = p_2 - p_1.$$

Interested readers can refer to "Jixin Ma and B Knight's, *"A General Temporal Theory*", *The Computer Journal* 37 (2), 1994, for further details.

Let us say *(P, ≤)*, derived objects, so interval can be defined as the type (left-open and right-open, left-closed and right-open, left-open and right-closed, left-closed and right-

closed) subsets of the set of primitive points that must be in one of the following forms (Guralnik V. and Srivastava J., 1999)

$$(p1, p2) = \{ p| \ p \in R \wedge p1 < p < p2\}$$

$$[p1, p2) = \{p| \ p \in R \wedge p1 \leq p < p2\}$$

$$(p1, p2] = \{p| \ p \in R \wedge p1 < p \leq p2\}$$

$$[p1, p2] = \{p| \ p \in R \wedge p1 \leq p \leq p2\}$$

During the process of literature review we identified that various choices are available to model the time: absolute or relative description of time; discrete or continuous time; linear, parallel or branching time; quantitative or qualitative time approach; time points or intervals; event, process or states etc. The following Point types are summarized.

- Temporal object – Points, start and end with events.
- Time period that events occur can hold during class that is indicated by a.m. – a.m., OR a.m. - p.m., OR p.m. – a.m. OR p.m. – p.m. , for example *"patient suffering from pain 7am to 8 am on 12/9/2015"*
- Temporal constraints can be divided into qualitative or quantitative. Point Algebra (PA) and Interval Algebra (IA) are two frameworks that are using for qualitative temporal reasoning. Thus in qualitative situations, the is relation between intervals and this can be use Interval Algebra (Allen's Algebra) which indicates start, during, before etc.
- Point Algebra is proposed by Vilain M. and Kautz H.A. (1986), which describes time points and binary relation over them. Point Algebra shows the three basic relations are <, =, >. In quantitative, number format is used for duration of an event i.e. Intentional relations e.g. $x - y < 11$ and constraints of bounded differences e.g. $6 < x - y < 8$.
- In PI, the primitive relations *p* between in two instants t_1 and t_2: $p = \{<,=,>\}$, so,

$$t1 \text{ before } t2: [t1<t2]$$

$$t1 \text{ equal to } t2: [t1=t2]$$

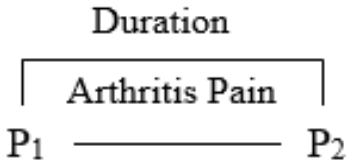
$$t1 \text{ after } t2: [t1>t2]$$

In PI, the qualitative constraints R between instants can be defined by:

Sets of the above relations (interpret as disjunction)

- $R = 2^P = \{\emptyset, \{<\}, \{=\}, \{>\}, \{<,=\}, \{<,>\}, \{=,>\}, P\}$

In this research work, each symptom of ARF can represent a set of a time points and can obtain real numbers. ARF symptoms express the relative positions of 2 points and this point can be expressed in the following relation: $P_i < P_j$, $P_i = P_j$, $P_i > P_j$. Here, constraints can be expressed in metrics by calculating the distances between two time points. As an example, let us examine symptoms of an ARF Arthritis.



The time duration of arthritis pain can be identified by, arthritis starting point = P_1, arthritis end point = P_2, and duration = P_2 - P_1. For Example: "*Sarmila has been suffering from arthritis pain starting from 1/9/2015 and ending on 5/9/2015 or 5 days"*, the arthritis pain can be expressed by:

$$occurs(arthritis, P_1, P_2) \wedge (1 < P_2 - P_1 \leq 5) \Longrightarrow Arthritis\ diseases_1$$

In this ARF diagnosis system, the Temporal Model is responsible for determining the relation between symptoms as well on a Temporal Template, which provides the linguistic information about how closely related a particular symptom is with ARF. A temporal constraint is used to analyse the links between the symptoms, absolute-time granularity captured the temporal dimension of symptoms, and its relationship with ARF is analysed. We created point-based time patterns of ARF symptoms and based on these time dimension, the research introduced how precisely related are particular signs of ARF. The components of the Temporal Model are explained below.

4.7.1. Descriptive Explanation of Symptoms

Temporal abstraction is used to describe patients' stages, which hold over particular time periods. This process captures the date and time when the patient explains about his/her problems. During the explanation of each symptom, doctors or community rural health workers could ask questions for patients to understand the time pattern of individual symptoms such as start date, how long symptoms continue, which symptom appeared first and for how long. For our ARF Diagnosis Model it was recognised that time considerations are vital when designing and developing the temporal rule and Temporal Template. It was therefore necessary to represent times for each recognised symptom and

place these in temporal order. The descriptive explanation of the ARF symptom process is demonstrated by the flowchart in Figure 4.15.

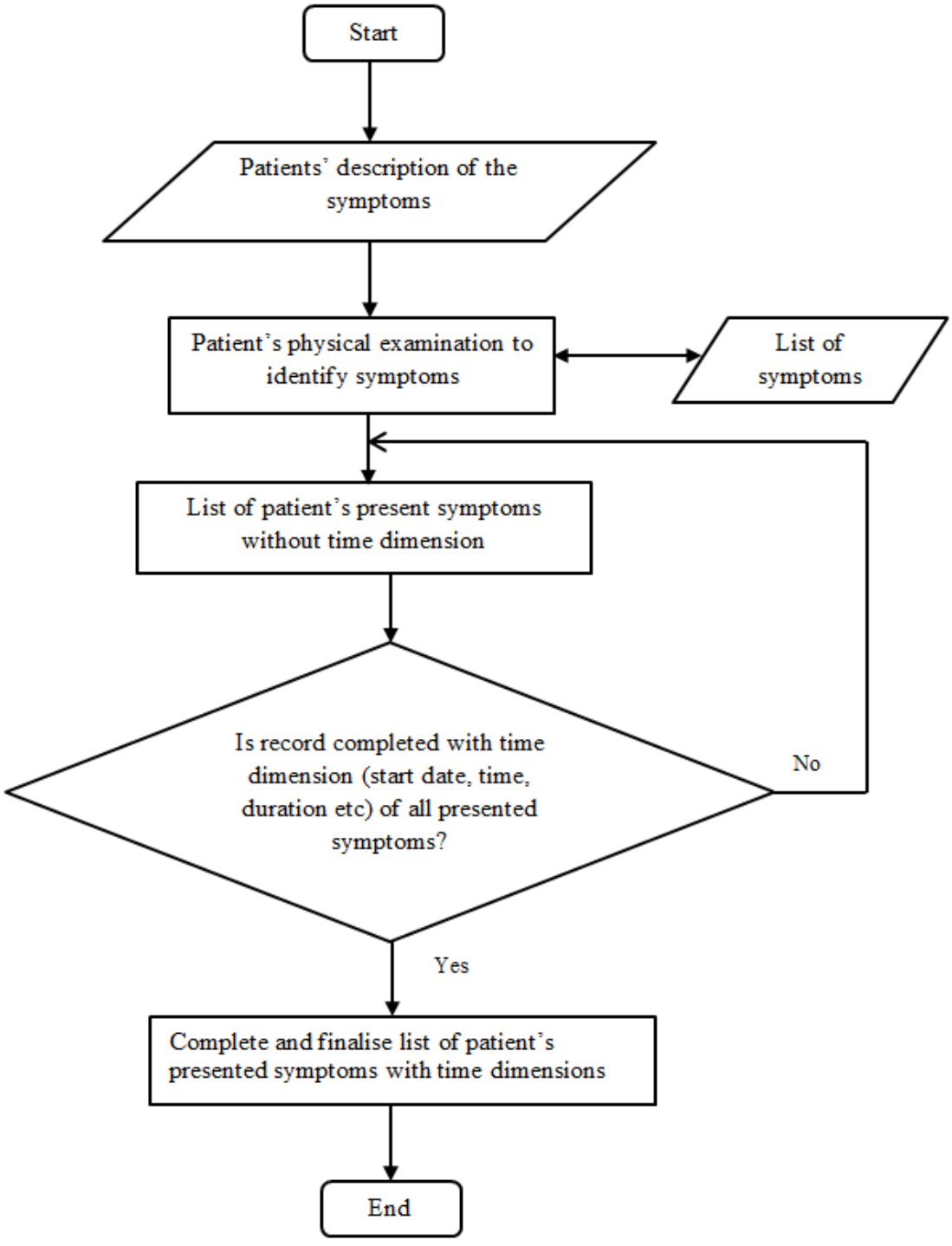


Figure 4.15 : Temporal Process of Descriptive Explanation of of an ARF case

4.7.2. Temporal Knowledge for ARF

Our research designed and generated a time-oriented temporal knowledge-based system, which consists of a Temporal Lookup Table. The Temporal Lookup Table reflects the

time span (in days) of ARF symptoms and their relationship with ARF disease. Temporal reasoning analyses the relationship between the symptoms and was designed based on the Temporal Lookup Table/Rules, which defines the absolutely positive, very positive, relatively positive and suspected timeframe of all ARF symptoms. Figure 4.16, provided by the NHF shows the clinical manifestations and ARF development timeframe.

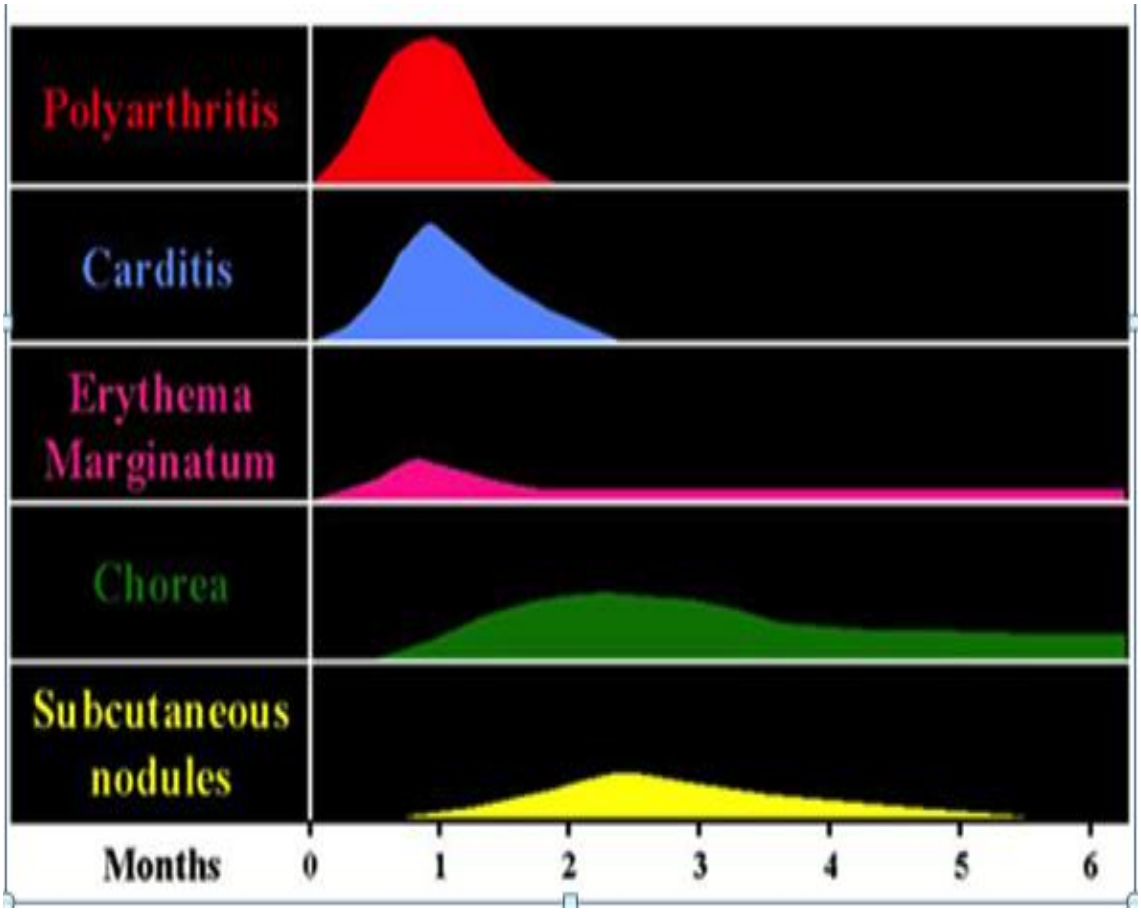


Figure 4.16: Clinical Manifestations of ARF

The timeframe of each symptom was provided by NHF experts. We created a rule based on this precise timeframe as well as their guidelines. We thus generated a new way to diagnose ARF, which will help in the development of a robust and much more accurate diagnosis application for ARF in Nepal.

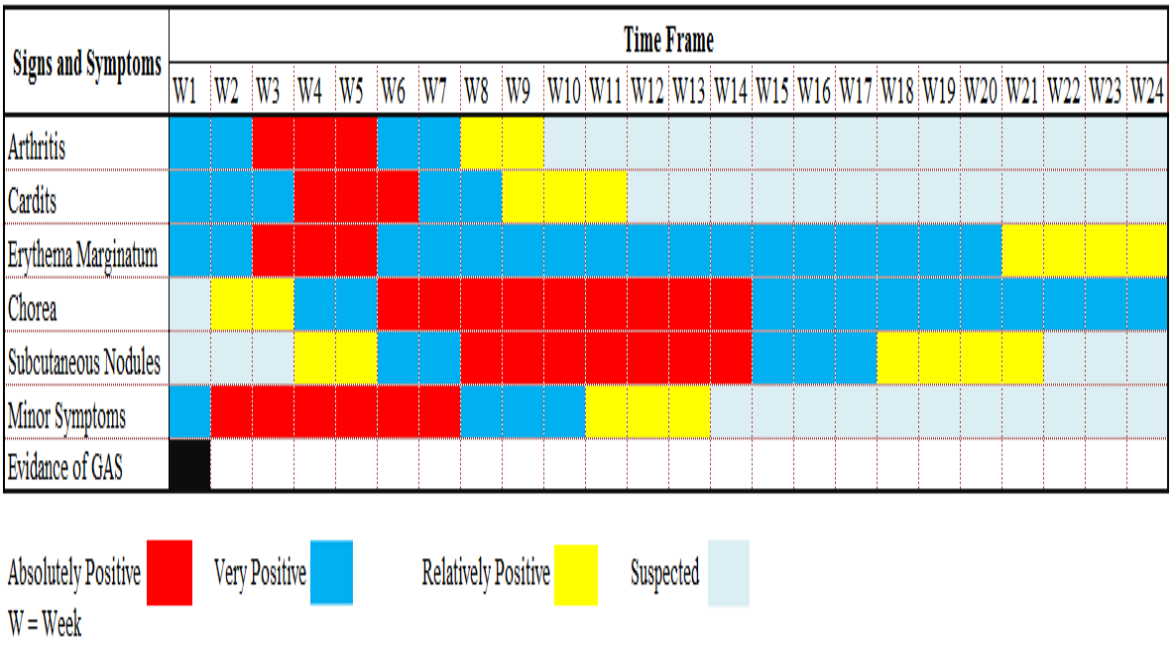
Table 4.5 defines the symptoms of ARF and a time period of a week. There are 24 weeks, which represent the relationship between the symptoms and ARF disease. For example arthritis pain start point is W1 (W1 indicates one week, 7 days) and the end point is W2. The relation between the arthritis and ARF is "Very positive". If arthritis pain occurrence time is 7 – 14 days after throat infection, the relation of arthritis with ARF is very positive. Examples of other relations between arthritis and ARF are shown in Table 4.4.

Table 4.4: Example of Arthritis Pain and Time

Start point	*End Point*	*Time (in days)*	*Relation with ARF*
W3	W5	15 - 35	Absolutely positive
W6	W7	36 - 49	Very positive
W8	W9	50 - 63	Relatively positive
W10	W24	64 - 168	Suspected

The symptoms of ARF do not all appear at the same time. It was noted in case studies that symptom often present themselves at very different times. Therefore, to make an ARF diagnosis model more reliable and accurate, it is necessary to capture, represent and analyse the symptoms with accurately recorded times of occurrence. We recognised that because ARF symptom presenting times can make a difference to diagnosis of severity levels (shown in Figure 4.16), we ensured the inclusion of time setting (temporal dimension) and its relation with ARF in our model based on time setting information kindly provided by NHF experts. The temporal dimension and its relationship with ARF are shown in Table 4.5.

Table 4.5: ARF's Symptoms and Temporal Dimension



In the table, the temporal dimension for each symptom's development time is divided up into 24 weeks or 168 days. The sign "GAS infection on the throat" is a starting time point or time of origin for each patient. Other captured development times for symptoms are calculated from origin of time. This is then used to determine where the particular

symptom occurs within the Temporal Lookup Table. Equations are used to show the temporal dimension and create a temporal knowledge-based function. The equation for construction of a “Temporal Lookup Table” is given below:

sm = $\{s_1 \ldots\ldots s_n\}$

T = $\{p_1 \ldots\ldots p_n\}$

The definition of temporal rule base (Lj) will extend as:

P_i = Symptom’s start point

P_j= Symptom’s end point

O_i = output (P_j - P_i) {“Absolutely Positive”, “Very Positive”, “Relatively Positive”, “Suspected” }

sm = input signs and symptoms

L_i = Temporal Rule

$$L_i, p_i, p_j, o_i = \{\, sm, p_i, p_j, \big(sm, (p_j - p_i) = o_1 \vee o_2 \vee o_3 \vee o_4\big)\},$$

$$where \begin{cases} o_1 = \text{"}Absolutely\ Positive\ (AP)_{sm}\text{"} \\ o_2 = \text{"}Very\ Positive\ (VP)_{sm}\text{"} \\ o_3 = \text{"}Relatively\ Positive\ (RP)_{sm}\text{"} \\ o_4 = \text{Suspected (S)}_{sm} \end{cases} \ldots\ldots(28)$$

Temporal knowledge is contained in the Temporal Lookup Table. The Temporal Lookup Table is created based on the temporal dimension of ARF symptoms and equation no. 28. The temporal dimension development is based on the functions set out in Table 4.6. The Temporal Lookup Table was designed on a grid format where ARF’s symptoms, time period (temporal dimension), absolutely positive, very positive, relatively positive and suspected are the linguistic variables which show how closely related symptoms are to any given ARF case. A temporal rule was created based on a Temporal Lookup Table that presents the time span of ARF case symptoms in days.

Table 4.6: Temporal Knowledge-based: Lookup Table

Signs and Symptom	Time Period	Absolutely positive	Very Positive	Relatively Positive	Suspected
Arthritis	$(P_{11},P_{12}]$ $x = P_{12} - P_{11}$	$x>14 \wedge x\leq35$	$(x\geq0 \wedge x\leq14) \vee (x>35 \wedge x\leq49)$	$x>49 \wedge x\leq63$	$x>63 \wedge x\leq168$
Carditis	$(P_{21},P_{22}]$ $x = P_{22} - P_{21}$	$x>21 \wedge x\leq42$	$(x\geq0 \wedge x \leq 21) \vee (x>42 \wedge x \leq 56)$	$x>56 \wedge x \leq77$	$x>77 \wedge x \leq 168$
EM	$(P_{31},P_{32}]$ $x = P_{32} - P_{31}$	$x>14 \wedge x\leq35$	$(x\geq0 \wedge x \leq14) \vee (x>35\wedge x \leq140)$	$x> 140 \wedge x \leq 168$	$x> 168$
Chorea	$(P_{41},P_{42}]$ $x = P_{42} - P_{41}$	$x>35 \wedge x\leq98$	$(x>21 \wedge x \leq35) \vee (x>98 \wedge x \leq168)$	$x>7 \wedge x\leq21$	$x\geq0 \wedge x\leq7$
Subcutaneous Nodules	$(P_{51},P_{52}]$ $x = P_{52} - P_{51}$	$x>49 \wedge x\leq98$	$(x>35 \wedge x \leq49) \vee (x>98 \wedge x \leq119)$	$(x>21 \wedge x\leq35) \vee (x>119 \wedge x \leq 147)$	$(x\geq0 \wedge x\leq21) \vee (x>147 \wedge x \leq 168)$
Minor Symptoms	$(P_{61},P_{62}]$ $x = P_{62} - P_{61}$	$x> 7 \wedge x \leq49$	$(x\geq 0 \wedge x \leq7) \vee (x> 49 \wedge x \leq70)$	$x>70 \wedge x\leq91$	$x > 91 \wedge x \leq 168$

For example, a child had arthritis pain about 4-5 days after throat infection/pain (about 2 days). He/she had complained that the chest pain was exacerbated by a breathing problem (Carditis) occurring at the same time with arthritis pain for 5-7 days. He/she had complained of weakness in hands and feet (Chorea) for about 6 days after chest pain. He/she had also complained of fever and arthralgia together with throat pain for about 4-5 days. Thus, the temporal abstraction of the above statement is given in Figure 4.17.

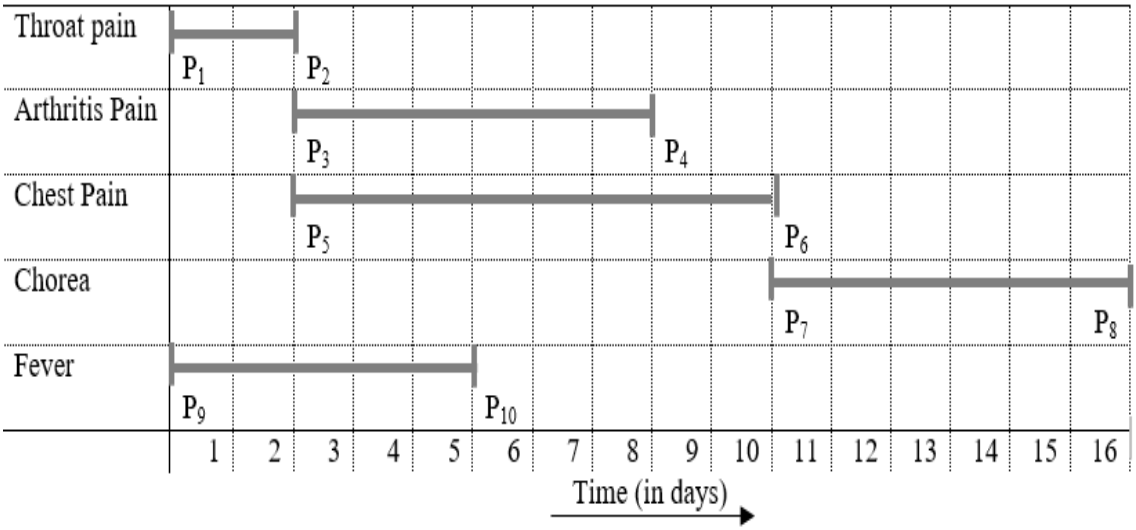


Figure 4.17 : Example of Temporal Abstraction

The given statement can infer that:

1. Throat pain duration was 2 days, so, $0<P_2 - P_1 \leq 2$

2. Arthritis pain start point (end point of throat pain) which means that the arthritis pain start point is equal to the throat pain end point indicating that the arthritis pain end point will be (3+5 =8). So, $P_2=P_3 \wedge 2 <P_4 - P_3 \leq 8$ and based on the temporal knowledge-based look-up table and concludes that the relation between ARF and arthritis pain is **very positive.**

3. Carditis symptom for 5-7 days, presented together with arthritis, which means that the Carditis start point, is equal to the arthritis pain start point and throat pain end point. Carditis pain end point will be 3+7=10. So, $P_2=P_5 \wedge P_3=P_5 \wedge 2<P_6 - P_5 \leq 10$ and based on the temporal knowledge-based look-up table the relation between ARF and Carditis is **very positive.**

4. Chorea symptom for 6 days but presented after Carditis. The start point of chorea is the end point of Carditis and thus the stop point of chorea will be 10+6=16. So, $P_6=P_7 \wedge 10 <P_8 - P_7 \leq 16$ and based on the temporal knowledge-based look-up table the relation between ARF and Carditis is **relatively positive.**

5. Fever and arthralgia symptoms appeared together with throat pain and before arthritis pain. The fever and arthralgia start point is equal to that of the throat pain. The fever and arthralgia end point is 3. So, $P1=P_9 \wedge 0 <P_{10} - P_9 \leq 5$ and based on the temporal knowledge-based look-up table the relation between ARF and Carditis is **absolutely positive.**

4.7.3. Temporal Abstraction, Relationship with ARF Symptoms

The following abstraction and equations show the time dimension and temporal relation of each ARF symptom then it is either Absolutely Positive ARF or Very Positive ARF or Relatively Positive ARF or Suspected ARF.

4.7.3.1. Temporal Abstraction for Absolutely Positive ARF

The temporal abstraction of absolutely positive for ARF is shown in Figure 4.18.

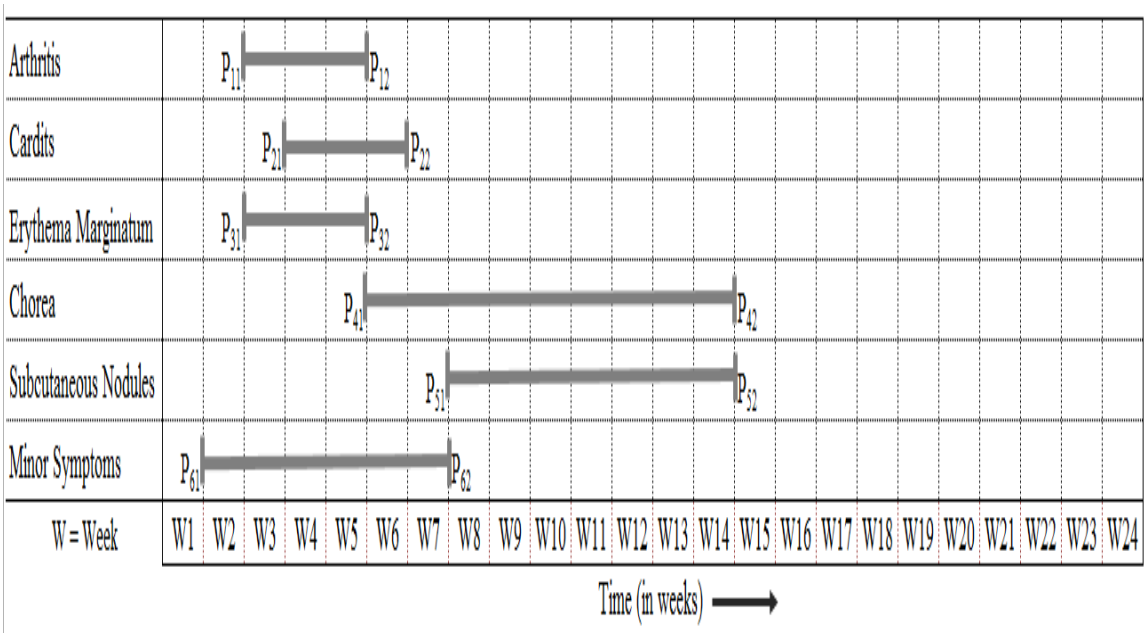


Figure 4.18 : Temporal Abstraction of Absolutely Positive for ARF

The above temporal abstraction can be presented by following temporal constraints (equations 29 to 34) which are designed to identify the absolutely positive relationship between symptoms and ARF.

Arthritis

$$Occurs(arthritis, p_{11}, p_{12}) \wedge (14 < p_{12} - p_{11} \leq 35) \Longrightarrow AP_{arthritis} \ldots\ldots\ldots\ldots\ldots (29)$$

Carditis

$$Occurs(carditis, p_{21}, p_{22}) \wedge (21 < p_{22} - p_{21} \leq 42) \Longrightarrow AP_{carditis} \ldots\ldots\ldots\ldots (30)$$

Erythema Marginatum (EM)

$$Occurs(EM, p_{31}, p_{32}) \wedge (14 < p_{32} - p_{31} \leq 35) \Longrightarrow AP_{EM} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (31)$$

Chorea

$$Occurs(chorea, p_{41}, p_{42}) \wedge (35 < p_{42} - p_{41} \leq 98) \Longrightarrow AP_{chorea} \ldots\ldots\ldots\ldots\ldots (32)$$

Subcutaneous Nodules (SN)

$$Occurs(SN, p_{51}, p_{52}) \wedge (49 < p_{52} - p_{51} \leq 98) \Longrightarrow AP_{SN} \ldots\ldots\ldots\ldots\ldots (33)$$

Minor Symptoms (MS)

$$Occurs(MS, p_{61}, p_{62}) \wedge (7 < p_{62} - p_{61} \leq 49) \Longrightarrow AP_{MS} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (34)$$

4.7.3.2. Temporal Abstraction for Very Positive ARF

The temporal abstraction of very positive for ARF is shown in Figure 4.19.

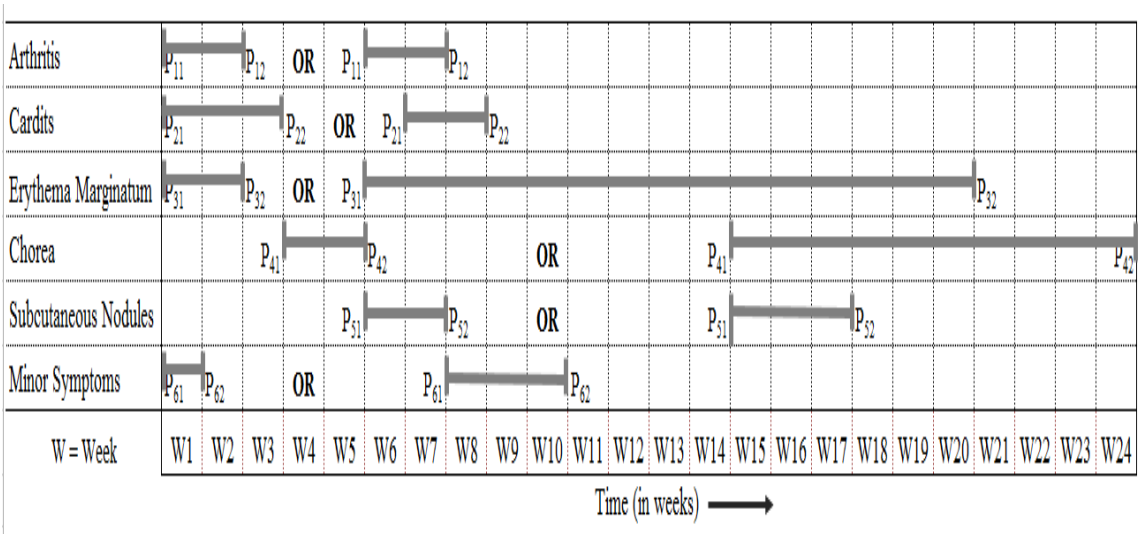


Figure 4.19 : Temporal Abstraction of Very Positive for ARF

The temporal abstraction can be presented by following temporal constraints (equations 35 to 40) which are designed to identify the very positive relationship between symptoms and ARF.

Arthritis

$$Occurs(arthritis, p_{11}, p_{12}) \wedge ((0 \leq p_{12} - p_{11} \leq 14) \vee (35 < p_{12} - p_{11} \leq 49)) \Longrightarrow VP_{arthritis} \quad \text{.....(35)}$$

Carditis

$$Occurs(carditis, p_{21}, p_{22}) \wedge \big((0 \leq p_{22} - p_{21} \leq 21) \vee (42 < p_{22} - p_{21} \leq 56)\big) \Longrightarrow VP_{carditis} \quad \text{.....(36)}$$

Erythema Marginatum (EM)

$$Occurs(EM, p_{31}, p_{32}) \wedge ((0 \leq p_{32} - p_{31} \leq 14) \vee (35 < p_{32} - p_{31} \leq 140)) \Longrightarrow VP_{EM} \quad \text{.....(37)}$$

Chorea

$$Occurs(chorea, p_{41}, p_{42}) \wedge ((21 < p_{42} - p_{41} \leq 35) \wedge (98 < p_{42} - p_{41} \leq 168)) \Longrightarrow VP_{chorea} \quad \text{.....(38)}$$

Subcutaneous Nodules (SN)

$$Occurs(SN, p_{51}, p_{52}) \wedge ((35 < p_{52} - p_{51} \leq 49) \vee (98 < p_{52} - p_{51} \leq 119)) \Longrightarrow VP_{SN} \quad \text{.....(39)}$$

Minor Symptoms (MS)

$$Occurs(MS, p_{61}, p_{62}) \wedge \big((0 \leq p_{62} - p_{61} \leq 7) \vee (49 < p_{62} - p_{61} \leq 70)\big) \Longrightarrow VP_{MS} \quad \text{.....(40)}$$

4.7.3.3. Temporal Abstraction for Relatively Positive ARF

The temporal abstraction for relatively positive ARF is shown in Figure 4.20.

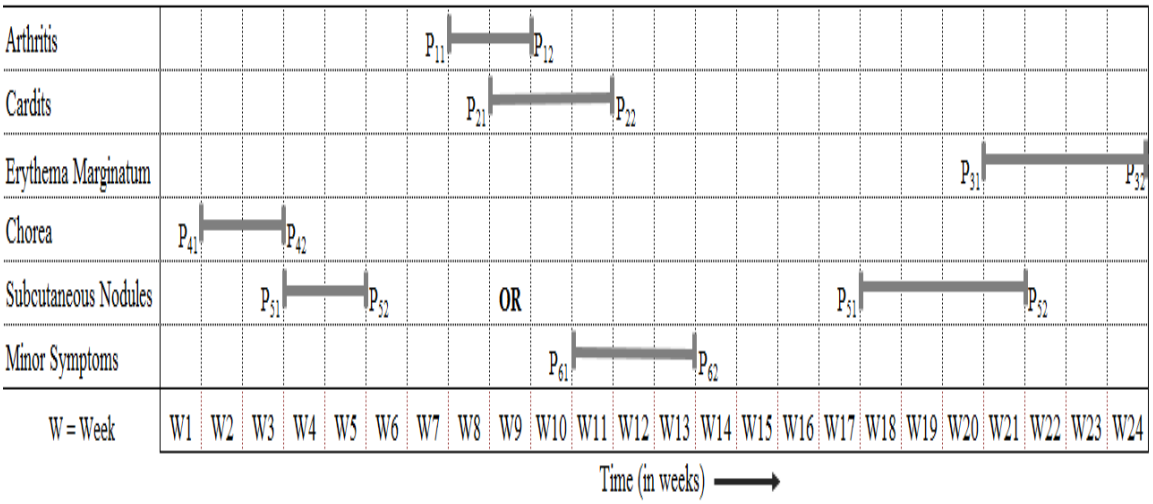


Figure 4.20 : Temporal Abstraction of Relatively Positive ARF

The temporal abstraction can be presented by following temporal constrains (equations 41 to 46) which is designed to identify the relatively positive relation between symptoms and ARF.

Arthritis

$$Occurs(arthritis, p_{11}, p_{12}) \wedge (49 < p_{12} - p_{11} \leq 63) \Longrightarrow RP_{arthritis} \quad (41)$$

Carditis

$$Occurs(carditis, p_{21}, p_{22}) \wedge (56 < p_{22} - p_{21} \leq 77) \Longrightarrow RP_{carditis} \quad (42)$$

Erythema Marginatum (EM)

$$Occurs(EM, p_{31}, p_{32}) \wedge (140 < p_{32} - p_{31} \geq 168) \Longrightarrow RP_{EM} \quad (43)$$

Chorea

$$Occurs(chorea, p_{41}, p_{42}) \wedge (7 < p_{42} - p_{41} \leq 21) \Longrightarrow RP_{chorea} \quad (44)$$

Subcutaneous Nodules (SN)

$$Occurs(SN, p_{51}, p_{52}) \wedge ((21 < p_{52} - p_{51} \leq 35) \vee (119 < p_{52} - p_{51} \leq 147)) \Longrightarrow RP_{SN} \quad (45)$$

Minor Symptoms (MS)

$$Occurs(MS, p_{61}, p_{62}) \wedge (70 < p_{62} - p_{61} \leq 91) \Longrightarrow RP_{MS} \quad (46)$$

4.7.3.4. Temporal Abstraction for Suspected ARF

The temporal abstraction of suspected for ARF is shown in Figure 4.21.

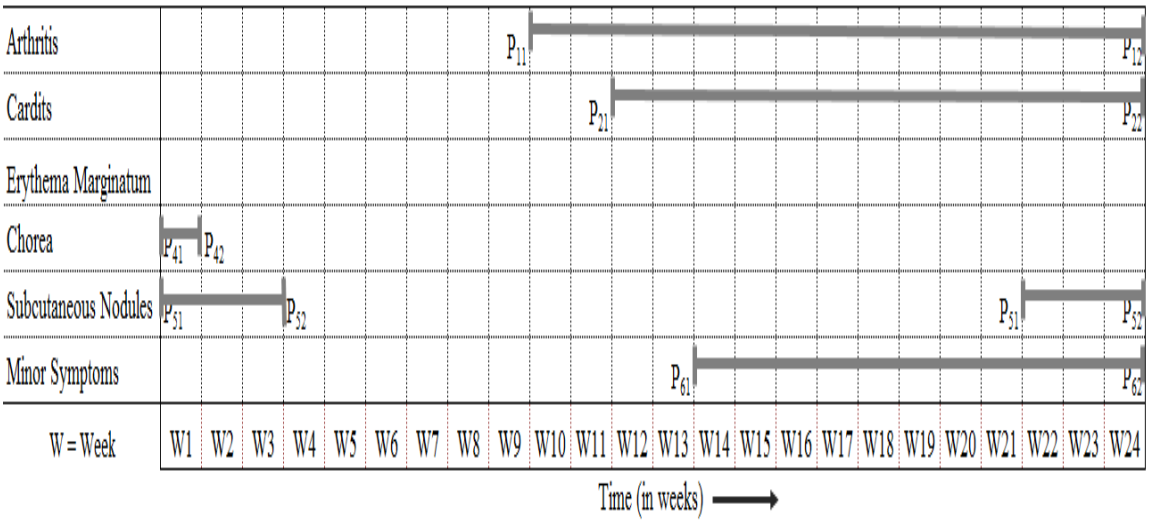


Figure 4.21: Temporal Abstraction of Suspected ARF

The indicated temporal abstraction can presented by following temporal constraints (equations 47 to 52) which is designed to identify the suspected positive relation between symptoms and ARF.

Arthritis

$$\text{Occurs}(\text{arthritis}, p_{11}, p_{12}) \wedge (63 < p_{12} - p_{11} \leq 168) \Longrightarrow S_{\text{arthritis}} \quad \text{.....(47)}$$

Carditis

$$Occurs(carditis, p_{21}, p_{22}) \wedge (77 < p_{22} - p_{21} \leq 168) \Longrightarrow S_{carditis} \quad \text{.....(48)}$$

Erythema Marginatum (EM)

$$Occurs(EM, p_{31}, p_{32}) \wedge (p_{32} - p_{31} > 168) \Longrightarrow S_{EM} \quad \text{.....(49)}$$

Chorea

$$Occurs(chorea, p_{41}, p_{42}) \wedge (0 < p_{42} - p_{41} \leq 7) \Longrightarrow S_{chorea} \quad \text{.....(50)}$$

Subcutaneous Nodules (SN)

$$Occurs(SN, p_{51}, p_{52}) \wedge ((0 \leq p_{52} - p_{51} \leq 21) \vee (147 < p_{52} - p_{51} \leq 168)) \Longrightarrow S_{SN} \quad \text{.....(51)}$$

Minor Symptoms (MS)

$$Occurs(MS, p_{61}, p_{62}) \wedge (91 < p_{62} - p_{61} \leq 168) \Longrightarrow S_{MS}, where\ p_{61} < p_{62} \quad \text{..... (52)}$$

4.7.4. Temporal Relation with ARF Symptoms for Absolutely Positive

A. Temporal relations between Arthritis and other symptoms

- ***Arthritis and Carditis***

$$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(carditis, p_{21}, p_{22}) \wedge p_{21} - p_{11} = 7 \wedge p_{22} - p_{12} = 7 \wedge p_{12} - p_{21} = 14 \wedge p_{22} - p_{11} = 28, therefore \begin{cases} p_{12} - p_{11} = 21 \\ p_{22} - p_{21} = 21 \end{cases} \quad \text{.....(53)}$$

- ***Arthritis and Erythema Marginatum (em)***

$$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(em, p_{31}, p_{32}) \wedge p_{11} = p_{31} \wedge p_{12} = p_{32} \wedge p_{12} - p_{31} = 21 \wedge p_{32} - p_{11} = 21, therefore \begin{cases} p_{12} - p_{11} = 21 \\ p_{32} - p_{31} = 21 \end{cases} \quad \text{.....(54)}$$

- ***Arthritis and Chorea***

$$Occurs(arthritis, p_{11}, p_{12}) \wedge Occours(chorea, p_{41}, p_{42}) \wedge p_{41} - p_{11} = 21 \wedge p_{12} = p_{41} \wedge p_{42} - p_{12} = 63, threfore \begin{cases} p_{12} - p_{11} = 21 \\ p_{42} - p_{41} = 63 \end{cases} \quad \text{.....(55)}$$

- ***Arthritis and Subcutaneous Nodules (SN)***

$$Occurs(arthritis, p_{11}, p_{12}) \wedge Occours(sn, p_{51}, p_{52}) \wedge p_{51} - p_{12} = 14 \wedge p_{51} - p_{11} = 35 \wedge p_{52} - p_{12} = 63, \ therefore \begin{cases} p_{12} - p_{11} = 21 \\ p_{52} - p_{51} = 49 \end{cases} \quad \text{.....(56)}$$

- ***Arthritis and Minor Symptoms (ms)***

$$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(ms, p_{41}, p_{42}) \wedge p_{11} - p_{61} = 7 \wedge p_{62} - p_{12} = 14 \wedge p_{12} - p_{61} = 28, where \begin{cases} p_{12} - p_{11} = 21 \\ p_{62} - p_{61} = 42 \end{cases} \quad \text{.....(57)}$$

B. Temporal relations between Carditis and other symptoms

- ***Carditis and Erythema Marginatum***

em=Erythema Marginatum

$$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(em, p_{31}, p_{32}) \wedge p_{21} - p_{31} = 7 \wedge p_{22} - p_{32} = 7 \wedge p_{32} - p_{21} = 14 \wedge p_{22} - p_{31} = 28, \ therefore \begin{cases} p_{22} - p_{21} = 21 \\ p_{32} - p_{31} = 21 \end{cases} \quad \text{.....(58)}$$

- ***Carditis and Chorea***

$$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{41} - p_{21} = 14 \wedge p_{22} - p_{41} = 7 \wedge p_{42} - p_{22} = 56, \ therefore \begin{cases} p_{22} - p_{21} = 21 \\ p_{42} - p_{41} = 63 \end{cases} \quad \text{.....(59)}$$

- ***Carditis and Subcutaneous Nodules***

sn=Subcutaneous Nodules

$$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{51} - p_{21} = 28 \wedge p_{51} - p_{22} = 7 \wedge p_{52} - p_{22} = 56, therefore \begin{cases} p_{22} - p_{21} = 21 \\ p_{52} - p_{51} = 49 \end{cases} \quad \text{.....(60)}$$

- ***Carditis and Minor Symptoms***

ms=Minor Symptoms

$$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(ms, p_{51}, p_{52}) \wedge p_{21} - p_{61} = 14 \wedge p_{62} - p_{21} = 28 \wedge p_{62} - p_{22} = 7 \wedge p_{22} - p_{61} = 35, therefore \begin{cases} p_{22} - p_{21} = 21 \\ p_{62} - p_{61} = 42 \end{cases} \quad \text{.....(61)}$$

C. Temporal relation between Erythema Marginatum and other symptoms

- ***Erythema Marginatum (em) and Chorea***

em=Erythema Marginatum

$$Occurs(em, p_{31}, p_{32}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{41} - p_{31} = 21 \wedge p_{32} = p_{41} \wedge p_{42} - p_{32} = 63, therefore \begin{cases} p_{32} - p_{31} = 21 \\ p_{42} - p_{41} = 63 \end{cases} \quad \text{.....(62)}$$

- ***Erythema Marginatum and Subcutaneous Nodules***

em=Erythema Marginatum; sn=Subcutaneous Nodules

$$Occurs(em, p_{31}, p_{32}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{51} - p_{32} = 14 \wedge p_{52} - p_{32} = 63 \wedge p_{51} - p_{31} = 35, therefore \begin{cases} p_{32} - p_{31} = 21 \\ p_{52} - p_{51} = 49 \end{cases} \quad \text{.....(63)}$$

- ***Erythema Marginatum and Minor Symptoms***

em=Erythema Marginatum; ms=Minor Symptoms

$$Occurs(em, p_{31}, p_{32}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{31} - p_{61} = 7 \wedge p_{62} - p_{32} = 14 \wedge p_{62} - p_{31} = 35 \wedge p_{32} - p_{61} = 28, therefore \begin{cases} p_{32} - p_{31} = 21 \\ p_{62} - p_{61} = 42 \end{cases} \quad \text{.....(64)}$$

D. Temporal relation between Chorea and other symptoms

- ***Chorea and Subcutaneous Nodules***

sn=Subcutaneous Nodules

$$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{51} - p_{41} = 14 \wedge p_{42} = p_{52} \wedge p_{42} - p_{51} = 49 \wedge p_{52} - p_{41} = 63, therefore \begin{cases} p_{42} - p_{41} = 63 \\ p_{52} - p_{51} = 49 \end{cases} \quad \text{.....(65)}$$

- ***Chorea and Minor Symptoms***

ms=Minor Symptoms

$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{41} - p_{61} = 28 \wedge p_{62} - p_{41} = 14 \wedge p_{42} - p_{62} = 49$, $therefore \begin{cases} p_{42} - p_{41} = 63 \\ p_{62} - p_{61} = 42 \end{cases}$ ……..……(66)

E. Temporal relation between Subcutaneous Nodules and Minor Symptoms

sn=Subcutaneous Nodules, ms=Minor Symptoms

$Occurs(sn, p_{51}, p_{52}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{51} - p_{61} = 42 \wedge p_{51} = p_{62} \wedge p_{52} - p_{62} = 49$, $therefore \begin{cases} p_{52} - p_{51} = 49 \\ p_{62} - p_{61} = 42 \end{cases}$ ……..……(67)

4.7.5. Temporal Relation with ARF's Symptoms for Very Positive

A. Temporal Relation between Arthritis and Other Symptoms

- ***Arthritis and Carditis***

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(carditis, p_{21}, p_{22}) \wedge p_{11} = p_{21} \wedge p_{22} - p_{12} = 7 \wedge p_{12} - p_{21} = 14, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{22} - p_{21} = 21 \end{cases}$ ……..……(68)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(carditis, p_{21}, p_{22}) \wedge p_{21} - p_{12} = 28 \wedge p_{21} - p_{11} = 42 \wedge p_{22} - p_{12} = 42, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{22} - p_{21} = 14 \end{cases}$ ……..……(69)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(carditis, p_{21}, p_{22}) \wedge p_{11} - p_{22} = 14 \wedge p_{11} - p_{21} = 35 \wedge p_{12} - p_{22} = 28, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{22} - p_{21} = 21 \end{cases}$ ……,……(70)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(carditis, p_{21}, p_{22}) \wedge p_{21} - p_{11} = 7 \wedge p_{22} - p_{12} = 7 \wedge p_{22} - p_{11} = 21, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{22} - p_{21} = 14 \end{cases}$ ……..……(71)

- ***Arthritis and Erythema Marginatum***

em = Erythema Marginatum

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(em, p_{31}, p_{32}) \wedge p_{11} = p_{31} \wedge p_{12} = p_{32} \wedge p_{32} - p_{12} = 0 \wedge p_{32} - p_{11} = 14 \wedge p_{12} - p_{31} = 14 \; therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{32} - p_{31} = 14 \end{cases}$ ……..(72)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(em, p_{31}, p_{32}) \wedge p_{31} - p_{12} = 21 \wedge p_{32} - p_{12} = 126 \wedge p_{31} - p_{11} = 35, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{32} - p_{31} = 105 \end{cases}$ ……(73)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(em, p_{31}, p_{32}) \wedge p_{11} = p_{31} \wedge p_{32} - p_{12} = 91 \wedge p_{12} - p_{31} = 14, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{32} - p_{31} = 140 \end{cases}$ ……(74)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(em, p_{31}, p_{32}) \wedge p_{12} - p_{32} = 35 \wedge p_{11} - p_{31} = 35 \wedge p_{11} - p_{31} = 21, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{32} - p_{31} = 14 \end{cases}$ ……(75)

- ***Arthritis and Chorea***

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occours(chorea, p_{41}, p_{42}) \wedge p_{42} - p_{12} = 21 \wedge p_{41} - p_{11} = 21 \wedge p_{42} - p_{11} = 35, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{42} - p_{41} = 14 \end{cases}$ ……(76)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occours(chorea, p_{41}, p_{42}) \wedge p_{12} - p_{41} = 28 \wedge p_{11} = p_{42} \wedge p_{12} - p_{42} = 14, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{42} - p_{41} = 14 \end{cases}$ ……(77)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occours(chorea, p_{41}, p_{42}) \wedge p_{42} - p_{12} = 154 \wedge p_{41} - p_{11} = 98 \wedge p_{41} - p_{12} = 84, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{42} - p_{41} = 70 \end{cases}$ ……(78)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occours(chorea, p_{41}, p_{42}) \wedge p_{42} - p_{12} = 119 \wedge p_{41} - p_{11} = 63 \wedge p_{41} - p_{12} = 49, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{42} - p_{41} = 70 \end{cases}$ ……(79)

- ***Arthritis and Subcutaneous Nodules***

sn=Subcutaneous Nodules

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occours(sn, p_{51}, p_{52}) \wedge p_{51} - p_{12} = 21 \wedge p_{52} - p_{12} = 35 \wedge p_{52} - p_{11} = 49, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{52} - p_{51} = 14 \end{cases}$ ……(80)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occours(sn, p_{51}, p_{52}) \wedge p_{51} - p_{12} = 84 \wedge p_{52} - p_{12} = 105 \wedge p_{51} - p_{11} = 98, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{52} - p_{51} = 21 \end{cases}$ ……(81)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occours(sn, p_{51}, p_{52}) \wedge p_{11} = p_{51} \wedge p_{12} = p_{52} \wedge p_{12} - p_{51} = 14, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{52} - p_{51} = 14 \end{cases}$ ……(82)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occours(sn, p_{51}, p_{52}) \wedge p_{51} - p_{12} = 49 \wedge p_{51} - p_{11} = 63 \wedge p_{52} - p_{12} = 70, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{52} - p_{51} = 21 \end{cases}$ ……(83)

- ***Arthritis and Minor Symptoms***

ms = Minor Symptoms

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(ms, p_{41}, p_{42}) \wedge p_{11} = p_{61} \wedge p_{12} - p_{62} = 7 \wedge p_{62} - p_{11} = 7, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{62} - p_{61} = 7 \end{cases}$ ……(84)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(ms, p_{41}, p_{42}) \wedge p_{61} - p_{12} = 35 \wedge p_{61} - p_{11} = 49 \wedge p_{62} - p_{12} = 56, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{62} - p_{61} = 21 \end{cases}$ ……(85)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(ms, p_{41}, p_{42}) \wedge p_{12} - p_{61} = 49 \wedge p_{12} - p_{62} = 42 \wedge p_{11} - p_{62} = 28, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{62} - p_{61} = 7 \end{cases}$ ……(86)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(ms, p_{41}, p_{42}) \wedge p_{61} = p_{12} \wedge p_{61} - p_{11} = 14 \wedge p_{62} - p_{12} = 21, therefore \begin{cases} p_{12} - p_{11} = 14 \\ p_{62} - p_{61} = 21 \end{cases}$ ……(87)

B. Relation between Carditis, Erythema Marginatum, Chorea, Subcutaneous Nodules and Minor Symptoms

- ***Carditis and Erythema Marginatum***

em = Erythema Marginatum

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(em, p_{31}, p_{32}) \wedge p_{21} = p_{31} \wedge p_{22} - p_{32} = 7 \wedge p_{32} - p_{21} = 14, therefore \begin{cases} p_{22} - p_{21} = 21 \\ p_{32} - p_{31} = 14 \end{cases}$ ……(88)

OR

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(em, p_{31}, p_{32}) \wedge p_{31} - p_{22} = 14 \wedge p_{32} - p_{22} = 119 \wedge p_{31} - p_{21} = 35, therefore \begin{cases} p_{22} - p_{21} = 21 \\ p_{32} - p_{31} = 105 \end{cases}$ ……(89)

OR

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(em, p_{31}, p_{32}) \wedge p_{22} - p_{32} = 42 \wedge p_{21} - p_{31} = 42 \wedge p_{22} - p_{21} = 14, therefore \begin{cases} p_{22} - p_{21} = 14 \\ p_{32} - p_{31} = 14 \end{cases}$ ……(90)

OR

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(em, p_{31}, p_{32}) \wedge p_{21} - p_{31} = 7 \wedge p_{32} - p_{22} = 84 \wedge p_{22} - p_{31} = 21, \ therefore \begin{cases} p_{22} - p_{21} = 14 \\ p_{32} - p_{31} = 105 \end{cases}$ ……(91)

- ***Carditis and Chorea***

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{21} = p_{41} \wedge p_{42} - p_{22} = 14 \wedge p_{41} - p_{21} = 14, therefore \begin{cases} p_{22} - p_{21} = 21 \\ p_{42} - p_{41} = 14 \end{cases}$ ……(92)

OR

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{42} - p_{22} = 147 \wedge p_{41} - p_{21} = 98 \wedge p_{41} - p_{22} = 77, therefore \begin{cases} p_{22} - p_{21} = 21 \\ p_{42} - p_{41} = 70 \end{cases}$ ……(93)

OR

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{42} - p_{22} = 112 \wedge p_{41} - p_{21} = 56 \wedge p_{41} - p_{22} = 42, where \begin{cases} p_{22} - p_{21} = 14 \\ p_{42} - p_{41} = 70 \end{cases}$ ……(94)

OR

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{22} - p_{42} = 21 \wedge p_{21} - p_{41} = 21 \wedge p_{21} - p_{42} = 7, where \begin{cases} p_{22} - p_{21} = 14 \\ p_{42} - p_{41} = 14 \end{cases}$ ……(95)

- ***Carditis and Subcutaneous Nodules***

sn = Subcutaneous Nodules

$$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{52} - p_{22} = 28 \wedge p_{51} - p_{21} = 35 \wedge p_{51} - p_{22} = 14, where \begin{cases} p_{22} - p_{21} = 21 \\ p_{52} - p_{51} = 14 \end{cases} \quad \text{.....(96)}$$

OR

$$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{52} - p_{22} = 98 \wedge p_{51} - p_{21} = 98 \wedge p_{51} - p_{22} = 77, where \begin{cases} p_{22} - p_{21} = 21 \\ p_{52} - p_{51} = 21 \end{cases} \quad \text{.....(97)}$$

OR

$$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{22} - p_{52} = 7 \wedge p_{21} - p_{51} = 7 \wedge p_{22} - p_{51} = 21, where \begin{cases} p_{22} - p_{21} = 14 \\ p_{52} - p_{51} = 14 \end{cases} \quad \text{.....(98)}$$

OR

$$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{52} - p_{22} = 63 \wedge p_{51} - p_{21} = 56 \wedge p_{51} - p_{22} = 42, where \begin{cases} p_{22} - p_{21} = 14 \\ p_{52} - p_{51} = 21 \end{cases} \quad \text{.....(99)}$$

- ***Carditis and Minor Symptoms***

sm = Minor Symptoms

$$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(sm, p_{61}, p_{62}) \wedge p_{21} = p_{61} \wedge p_{22} - p_{62} = 14 \wedge p_{22} - p_{61} = 21, where \begin{cases} p_{22} - p_{21} = 21 \\ p_{62} - p_{61} = 7 \end{cases} \quad \text{.....(100)}$$

OR

$$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(sm, p_{61}, p_{62}) \wedge p_{62} - p_{22} = 49 \wedge p_{61} - p_{21} = 49 \wedge p_{61} - p_{22} = 28, where \begin{cases} p_{22} - p_{21} = 21 \\ p_{62} - p_{61} = 21 \end{cases} \quad \text{.....(101)}$$

OR

$$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(sm, p_{61}, p_{62}) \wedge p_{22} - p_{62} = 49 \wedge p_{21} - p_{61} = 42 \wedge p_{21} - p_{62} = 35, where \begin{cases} p_{22} - p_{21} = 14 \\ p_{62} - p_{61} = 7 \end{cases} \quad \text{.....(102)}$$

OR

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(sm, p_{61}, p_{62}) \wedge p_{62} - p_{22} = 14 \wedge p_{61} - p_{21} = 7 \wedge p_{22} - p_{61} = 7, where \begin{cases} p_{22} - p_{21} = 14 \\ p_{62} - p_{61} \leq 21 \end{cases}$ .....(103)

C. Relation between Erythema Marginatum, Chorea, Subcutaneous Nodules and Minor Symptoms

- ***Erythema Marginatum and Chorea***

em = Erythema Marginatum

$Occurs(em, p_{31}, p_{32}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{42} - p_{32} = 21 \wedge p_{41} - p_{31} = 21 \wedge p_{41} - p_{32} = 7, where \begin{cases} p_{32} - p_{31} = 14 \\ p_{42} - p_{41} = 14 \end{cases}$ .....(104)

OR

$Occurs(em, p_{31}, p_{32}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{42} - p_{32} = 154 \wedge p_{41} - p_{31} = 98 \wedge p_{41} - p_{32} = 84, where \begin{cases} p_{32} - p_{31} = 14 \\ p_{42} - p_{41} = 70 \end{cases}$ .....(105)

OR

$Occurs(em, p_{31}, p_{32}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{32} - p_{42} = 105 \wedge p_{31} - p_{41} = 14 \wedge p_{31} = p_{42}, where \begin{cases} p_{32} - p_{31} = 105 \\ p_{42} - p_{41} = 14 \end{cases}$ .....(106)

OR

$Occurs(em, p_{31}, p_{32}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{42} - p_{32} = 28 \wedge p_{41} - p_{31} = 63 \wedge p_{32} - p_{41} = 42, where \begin{cases} p_{32} - p_{31} = 105 \\ p_{42} - p_{41} = 70 \end{cases}$ .....(107)

- ***Erythema Marginatum and Subcutaneous Nodules***

sn = Subcutaneous Nodules

$Occurs(em, p_{31}, p_{32}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{52} - p_{32} = 35 \wedge p_{51} - p_{31} = 35 \wedge p_{51} - p_{32} = 21, where \begin{cases} p_{32} - p_{31} = 14 \\ p_{52} - p_{51} = 19 \end{cases}$ .....(108)

OR

$Occurs(em, p_{31}, p_{32}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{52} - p_{32} = 105 \wedge p_{51} - p_{31} = 98 \wedge p_{51} - p_{32} = 84, where \begin{cases} p_{32} - p_{31} = 14 \\ p_{52} - p_{51} = 21 \end{cases}$ .....(109)

OR

$Occurs(em, p_{31}, p_{32}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{31} = p_{51} \wedge p_{32} - p_{52} = 91 \wedge p_{52} - p_{31} = 7, where \begin{cases} p_{32} - p_{31} = 105 \\ p_{52} - p_{51} = 14 \end{cases}$ ……(110)

OR

$Occurs(em, p_{31}, p_{32}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{32} - p_{52} = 21 \wedge p_{51} - p_{31} = 63 \wedge p_{32} - p_{51} = 42, where \begin{cases} p_{32} - p_{31} = 105 \\ p_{52} - p_{51} = 21 \end{cases}$ ……(111)

- ***Erythema Marginatum and Minor Symptoms***

ms = Minor Symptoms ; em=Erythema Marginatum

$Occurs(em, p_{31}, p_{32}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{31} = p_{61} \wedge p_{32} - p_{62} = 7 \wedge p_{32} - p_{61} = 14, \ where \begin{cases} p_{32} - p_{31} = 14 \\ p_{62} - p_{61} = 7 \end{cases}$ ……(112)

OR

$Occurs(em, p_{31}, p_{32}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{62} - p_{32} = 56 \wedge p_{61} - p_{31} = 49 \wedge p_{61} - p_{32} = 35, \ where \begin{cases} p_{32} - p_{31} = 14 \\ p_{62} - p_{61} = 21 \end{cases}$ ……(113)

OR

$Occurs(em, p_{31}, p_{32}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{32} - p_{62} = 133 \wedge p_{31} - p_{61} = 35 \wedge p_{31} - p_{62} = 28, \ where \begin{cases} p_{32} - p_{31} = 105 \\ p_{62} - p_{61} = 7 \end{cases}$ ……(114)

OR

$Occurs(em, p_{31}, p_{32}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{32} - p_{62} = 70 \wedge p_{61} - p_{31} = 14 \wedge p_{32} - p_{61} = 91, \ where \begin{cases} p_{32} - p_{31} = 105 \\ p_{62} - p_{61} = 21 \end{cases}$ ……(115)

D. Relation between Chorea, Subcutaneous Nodules and Minor Symptoms

- ***Chorea and Subcutaneous Nodules***

sn = Subcutaneous Nodules

$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{52} - p_{42} = 14 \wedge p_{51} - p_{41} = 14 \wedge p_{51} = p_{42}, \ where \begin{cases} p_{42} - p_{41} = 14 \\ p_{52} - p_{51} = 14 \end{cases}$ ……(116)

OR

$$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{52} - p_{42} = 84 \wedge p_{51} - p_{41} = 77 \wedge p_{51} - p_{42} = 63, \; where \begin{cases} p_{42} - p_{41} = 14 \\ p_{52} - p_{51} = 21 \end{cases} \quad \text{……(117)}$$

OR

$$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{42} - p_{52} = 119 \wedge p_{41} - p_{51} = 63 \wedge p_{42} - p_{51} = 133, \; where \begin{cases} p_{42} - p_{41} = 70 \\ p_{52} - p_{51} = 14 \end{cases} \quad \text{……(118)}$$

OR

$$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{41} = p_{51} \wedge p_{42} - p_{52} = 49 \wedge p_{42} - p_{51} = 70, \; where \begin{cases} p_{42} - p_{41} = 70 \\ p_{52} - p_{51} = 21 \end{cases} \quad \text{……(119)}$$

- ***Chorea and Minor Symptoms***

ms = Minor Symptoms

$$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{42} - p_{62} = 28 \wedge p_{41} - p_{61} = 21 \wedge p_{41} - p_{62} = 14, \; where \begin{cases} p_{42} - p_{41} = 14 \\ p_{62} - p_{61} = 7 \end{cases} \quad \text{……(120)}$$

OR

$$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{62} - p_{42} = 35 \wedge p_{61} - p_{41} = 28 \wedge p_{61} - p_{42} = 14, \; where \begin{cases} p_{42} - p_{41} = 14 \\ p_{62} - p_{61} = 21 \end{cases} \quad \text{……(121)}$$

OR

$$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{42} - p_{62} = 161 \wedge p_{41} - p_{61} = 98 \wedge p_{41} - p_{62} = 91, \; where \begin{cases} p_{42} - p_{41} = 70 \\ p_{62} - p_{61} = 7 \end{cases} \quad \text{……(122)}$$

OR

$$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{42} - p_{62} = 98 \wedge p_{41} - p_{61} = 49 \wedge p_{41} - p_{62} = 28, \; where \begin{cases} p_{42} - p_{41} = 70 \\ p_{62} - p_{61} = 21 \end{cases} \quad \text{……(123)}$$

E. Relation between Subcutaneous Nodules and Minor Symptoms

sn = Subcutaneous Nodules; ms = Minor symptoms

$$Occurs(sn, p_{51}, p_{52}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{52} - p_{62} = 42 \wedge p_{51} - p_{61} = 35 \wedge p_{51} - p_{62} = 28, \; where \begin{cases} p_{52} - p_{51} = 14 \\ p_{62} - p_{61} = 7 \end{cases} \quad \text{……(124)}$$

OR

$Occurs(sn, p_{51}, p_{52}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{52} = p_{61} \wedge p_{62} - p_{52} = 21 \wedge p_{61} - p_{51} = 14,\ where \begin{cases} p_{52} - p_{51} = 14 \\ p_{62} - p_{61} = 21 \end{cases}$ ……(125)

OR

$Occurs(sn, p_{51}, p_{52}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{52} - p_{62} = 112 \wedge p_{51} - p_{61} = 98 \wedge p_{61} - p_{52} = 119,\ where \begin{cases} p_{52} - p_{51} = 21 \\ p_{62} - p_{61} = 7 \end{cases}$ ……(126)

OR

$Occurs(sn, p_{51}, p_{52}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{52} - p_{62} = 49 \wedge p_{51} - p_{61} = 49 \wedge p_{51} - p_{62} = 28,\ where \begin{cases} p_{52} - p_{51} = 21 \\ p_{62} - p_{61} = 7 \end{cases}$ ……(127)

4.7.6. Temporal Relation with ARF's Symptoms for Relatively Positive

A. Temporal relation between Arthritis, Carditis, EM, Chorea, Subcutaneous Nodules and Minor Symptoms

- ***Arthritis and Carditis***

  $Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(carditis, p_{21}, p_{22}) \wedge p_{21} - p_{11} = 7 \wedge p_{22} - p_{12} = 14 \wedge p_{12} - p_{56} = 7,\ where \begin{cases} p_{12} - p_{11} = 14 \\ p_{22} - p_{21} = 21 \end{cases}$ ……(128)

- ***Arthritis and Erythema marginatum***

  em = Erythema marginatum

  $Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(em, p_{31}, p_{32}) \wedge p_{31} - p_{11} = 91 \wedge p_{32} - p_{12} = 105 \wedge p_{31} - p_{12} = 77,\ where \begin{cases} p_{12} - p_{11} = 14 \\ p_{32} - p_{31} = 28 \end{cases}$ ……(129)

- ***Arthritis and Chorea***

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{41} - p_{11} = 42 \wedge p_{42} - p_{12} = 42 \wedge p_{11} - p_{42} = 28,\ where \begin{cases} p_{12} - p_{11} = 14 \\ p_{42} - p_{41} = 14 \end{cases}$ ……(130)

- ***Arthritis and Subcutaneous Nodules***

  sn = Subcutaneous Nodules

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(sm, p_{51}, p_{52}) \wedge p_{11} - p_{51} = 28 \wedge p_{12} - p_{52} = 28 \wedge p_{11} - p_{52} = 14,\ where \begin{cases} p_{12} - p_{11} = 14 \\ p_{52} - p_{51} = 14 \end{cases}$ ……(131)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(sm, p_{51}, p_{52}) \wedge p_{51} - p_{11} = 70 \wedge p_{52} - p_{12} = 84 \wedge p_{51} - p_{12} = 56,\ where \begin{cases} p_{12} - p_{11} = 14 \\ p_{52} - p_{51} = 28 \end{cases}$ ……..…(132)

- ***Arthritis and Minor Symptoms***

ms = minor symptoms

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{61} - p_{11} = 21 \wedge p_{62} - p_{12} = 28 \wedge p_{61} - p_{12} = 7,\ where \begin{cases} p_{12} - p_{11} \leq 14 \\ p_{52} - p_{51} \leq 21 \end{cases}$ ……..(133)

B. Temporal relation between Carditis, Erythema marginatum, Chorea, Subcutaneous Nodules and Minor Symptoms

- ***Carditis and Erythema marginatum***

  em = Erythema marginatum

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(em, p_{31}, p_{32}) \wedge p_{31} - p_{21} = 84 \wedge p_{32} - p_{22} = 91 \wedge p_{31} - p_{22} = 63,\ where \begin{cases} p_{22} - p_{21} = 21 \\ p_{32} - p_{31} = 28 \end{cases}$ ……..(134)

- ***Carditis and Chorea***

  $Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{21} - p_{41} = 49 \wedge p_{22} - p_{42} = 56 \wedge p_{22} - p_{41} = 70,\ where \begin{cases} p_{22} - p_{21} = 21 \\ p_{42} - p_{41} = 14 \end{cases}$ ……..(135)

- ***Carditis and Subcutaneous Nodules***

  sn = Subcutaneous Nodules

  $Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{21} - p_{51} = 35 \wedge p_{22} - p_{52} = 42 \wedge p_{21} - p_{52} = 21,\ where \begin{cases} p_{22} - p_{21} = 21 \\ p_{52} - p_{51} = 14 \end{cases}$ ……..(136)

OR

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{51} - p_{22} = 42 \wedge p_{51} - p_{21} = 63 \wedge p_{52} - p_{22} = 70,\ where \begin{cases} p_{22} - p_{21} = 21 \\ p_{52} - p_{51} = 28 \end{cases}$ ……..(137)

- ***Carditis and Minor Symptoms***

  ms = Minor Symptoms

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{61} - p_{21} = 14 \wedge p_{62} - p_{22} = 14 \wedge p_{22} - p_{61} = 7,\ where \begin{cases} p_{22} - p_{21} = 21 \\ p_{62} - p_{61} = 21 \end{cases}$ ……(138)

C. Temporal relation between Erythema marginatum, Chorea, Subcutaneous Nodules and Minor Symptoms

- ***Erythema marginatum and Chorea***

em = Erythema marginatum

$$Occurs(em, p_{31}, p_{32}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{31} - p_{41} = 133 \wedge p_{32} - p_{42} = 147 \wedge p_{31} - p_{42} = 119, \; where \begin{cases} p_{32} - p_{31} = 28 \\ p_{42} - p_{41} = 14 \end{cases} \quad \text{.....(139)}$$

- **Erythema marginatum and Subcutaneous Nodules**

em=Erythema marginatum

sn = Subcutaneous Nodules

$$Occurs(em, p_{31}, p_{32}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{31} - p_{51} = 119 \wedge p_{32} - p_{52} = 133 \wedge p_{31} - p_{52} = 105, \; where \begin{cases} p_{32} - p_{31} = 28 \\ p_{52} - p_{51} = 14 \end{cases} \quad \text{.....(140)}$$

OR

$$Occurs(em, p_{31}, p_{32}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{31} - p_{51} = 21 \wedge p_{32} - p_{52} = 21 \wedge p_{52} - p_{31} = 7, \; where \begin{cases} p_{32} - p_{31} = 28 \\ p_{52} - p_{51} = 28 \end{cases} \quad \text{.....(141)}$$

- ***Erythema marginatum and Minor Symptoms***

ms = Minor Symptoms

em=Erythema marginatum

$$Occurs(em, p_{31}, p_{32}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{31} - p_{61} = 70 \wedge p_{32} - p_{62} = 77 \wedge p_{31} - p_{62} = 49, \; where \begin{cases} p_{32} - p_{31} = 28 \\ p_{62} - p_{61} = 21 \end{cases} \quad \text{.....(142)}$$

D. Temporal relation between Chorea, Subcutaneous Nodules and Minor Symptoms

- ***Chorea and Subcutaneous Nodules***

sn= Subcutaneous Nodules

$$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{51} - p_{41} = 14 \wedge p_{52} - p_{42} = 14 \wedge p_{42} - p_{61}, \; where \begin{cases} p_{42} - p_{41} = 14 \\ p_{52} - p_{51} = 14 \end{cases} \quad \text{.....(143)}$$

OR

$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{51} - p_{41} = 112 \wedge p_{52} - p_{42} = 126 \wedge p_{51} - p_{42} = 98,\ where \begin{cases} p_{42} - p_{41} = 14 \\ p_{52} - p_{51} = 28 \end{cases}$ ……(144)

- ***Chorea and Minor Symptoms***

ms = Minor Symptoms

$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{61} - p_{41} = 63 \wedge p_{62} - p_{42} = 70 \wedge p_{61} - p_{42} = 49,\ where \begin{cases} p_{42} - p_{41} = 14 \\ p_{62} - p_{61} = 21 \end{cases}$ ……(145)

E. Temporal relation between Subcutaneous Nodules and Minor Symptoms

sn = Subcutaneous Nodules

ms= Minor Symptoms

$Occurs(sn, p_{51}, p_{52}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{61} - p_{51} = 49 \wedge p_{62} - p_{52} = 56 \wedge p_{61} - p_{52} = 35,\ where \begin{cases} p_{52} - p_{51} = 14 \\ p_{62} - p_{61} = 21 \end{cases}$ ……(146)

OR

$Occurs(sn, p_{51}, p_{52}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{51} - p_{61} = 49 \wedge p_{52} - p_{62} = 56 \wedge p_{51} - p_{62} = 28,\ where \begin{cases} p_{52} - p_{51} = 28 \\ p_{62} - p_{61} = 21 \end{cases}$ ……(147)

4.7.7. Temporal Relation with ARF's Symptoms for Suspected Cases

A. Temporal relation between Arthritis, Carditis, EM, Chorea, Subcutaneous Nodules and Minor Symptoms

- ***Arthritis and Cardits***

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(carditis, p_{21}, p_{22}) \wedge p_{21} - p_{11} = 14 \wedge p_{12} = p_{22} \wedge p_{12} - p_{21} = 91, where \begin{cases} p_{12} - p_{11} = 105 \\ p_{22} - p_{21} = 91 \end{cases}$ ……(148)

- ***Arthritis and Erythema marginatum***

em=Erythema Marginatum

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(em, p_{31}, p_{32}) \wedge p_{12} = p_{31} \wedge p_{12} - p_{21} > 168, where \begin{cases} p_{12} - p_{11} = 105 \\ p_{22} - p_{21} > 168 \end{cases}$ ……(149)

- ***Arthritis and Chorea***

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{11} - p_{41} = 63 \wedge p_{12} - p_{42} = 161 \wedge p_{11} - p_{42} = 56, where \begin{cases} p_{12} - p_{11} = 105 \\ p_{42} - p_{41} = 7 \end{cases}$ ……(150)

- ***Arthritis and Subcutaneous Nodules***

  sn =Subcutaneous Nodules

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{11} - p_{51} = 63 \wedge p_{12} - p_{52} = 106 \wedge p_{11} - p_{52} = 46, where \begin{cases} p_{12} - p_{11} = 105 \\ p_{52} - p_{51} = 21 \end{cases}$ ……(151)

OR

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{51} - p_{11} = 84 \wedge p_{52} = p_{12} \wedge p_{12} - p_{51} = 21, where \begin{cases} p_{12} - p_{11} = 105 \\ p_{52} - p_{51} = 21 \end{cases}$ ……(152)

- ***Arthritis and Minor Symptoms***

ms = Minor Symptoms

$Occurs(arthritis, p_{11}, p_{12}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{61} - p_{11} = 28 \wedge p_{62} = p_{12} \wedge p_{12} - p_{61} = 67, where \begin{cases} p_{12} - p_{11} = 105 \\ p_{62} - p_{61} = 77 \end{cases}$ ……(153)

B. Temporal relation between Carditis, Erythema Marginatum, Chorea, Subcutaneous Nodules and Minor Symptoms

- ***Carditis and Erythema marginatum***

  em=Erythema marginatum

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(em, p_{31}, p_{32}) \wedge p_{22} = p_{32} \wedge p_{32} - p_{31} = 68, where \begin{cases} p_{22} - p_{21} = 91 \\ p_{32} - p_{31} > 168 \end{cases}$ ……(154)

- ***Carditis and Chorea***

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{21} - p_{41} = 77 \wedge p_{22} - p_{42} = 161 \wedge p_{21} - p_{42} = 70, where \begin{cases} p_{22} - p_{21} = 91 \\ p_{42} - p_{41} = 7 \end{cases}$ ……(155)

- ***Carditis and Subcutaneous Nodules***

  sn =Subcutaneous Nodules

$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{21} - p_{51} = 77 \wedge p_{22} - p_{52} = 147 \wedge p_{21} - p_{52} = 56, where \begin{cases} p_{22} - p_{21} = 91 \\ p_{52} - p_{51} = 21 \end{cases}$ ……(156)

OR

$$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{51} - p_{21} = 70 \wedge p_{52} = p_{22} \wedge p_{22} - p_{51} = 21, where \begin{cases} p_{22} - p_{21} = 91 \\ p_{52} - p_{51} = 21 \end{cases} \quad \text{.....(157)}$$

- ***Carditis and Minor Symptoms***
  ms =Minor Symptoms

$$Occurs(carditis, p_{21}, p_{22}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{61} - p_{21} = 14 \wedge p_{22} = p_{62} \wedge p_{22} - p_{61} = 77, where \begin{cases} p_{22} - p_{21} = 91 \\ p_{62} - p_{61} = 77 \end{cases} \quad \text{.....(158)}$$

C. Temporal relation between Erythema Marginatum, Chorea, Subcutaneous Nodules and Minor Symptoms

- ***Erythema Marginatum and Chorea***
  em=Erythema marginatum

$$Occurs(em, p_{31}, p_{32}) \wedge Occurs(chorea, p_{41}, p_{42}) \wedge p_{32} - p_{42} = 125 \wedge p_{32} - p_{31} > 168, where \begin{cases} p_{32} - p_{31} > 168 \\ p_{42} - p_{41} = 7 \end{cases} \quad \text{.....(159)}$$

- ***Erythema Marginatum and Subcutaneous Nodules***
  sn =Subcutaneous Nodules

$$Occurs(em, p_{31}, p_{32}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{52} - p_{32} = 147 \wedge p_{32} - p_{31} > 168, where \begin{cases} p_{32} - p_{31} > 168 \\ p_{52} - p_{51} = 21 \end{cases} \quad \text{.....(160)}$$

OR

$$Occurs(em, p_{31}, p_{32}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{52} = p_{32} \wedge p_{32} - p_{31} > 168, where \begin{cases} p_{32} - p_{31} > 168 \\ p_{52} - p_{51} = 21 \end{cases} \quad \text{.....(161)}$$

- ***Erythema marginatum and Minor Symptoms***
  ms =Minor Symptoms

$$Occurs(em, p_{31}, p_{32}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{32} = p_{62} \wedge p_{32} - p_{31} > 168, where \begin{cases} p_{32} - p_{31} > 168 \\ p_{62} - p_{61} = 77 \end{cases} \quad \text{.....(162)}$$

D. Temporal relation between Chorea, Subcutaneous Nodules and Minor Symptoms

- ***Chorea and Subcutaneous Nodules***

  sn =Subcutaneous Nodules

$$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{41} = p_{51} \wedge p_{52} - p_{42} = 14 \wedge p_{42} - p_{51} = 7, where \begin{cases} p_{42} - p_{41} = 7 \\ p_{52} - p_{51} = 21 \end{cases} \quad \text{.....(163)}$$

OR

$$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(sn, p_{51}, p_{52}) \wedge p_{51} - p_{41} = 147 \wedge p_{52} - p_{42} = 161 \wedge p_{51} - p_{42} = 140, where \begin{cases} p_{42} - p_{41} = 7 \\ p_{52} - p_{51} = 21 \end{cases} \quad \text{.....(164)}$$

- ***Chorea and Minor Symptoms***

  ms =Minor Symptoms

$$Occurs(chorea, p_{41}, p_{42}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{61} - p_{41} = 91 \wedge p_{62} - p_{42} = 161 \wedge p_{61} - p_{42} = 84, where \begin{cases} p_{42} - p_{41} = 7 \\ p_{62} - p_{61} = 77 \end{cases} \quad \text{.....(165)}$$

E. Temporal relation between Subcutaneous Nodules and Minor Symptoms

- **Subcutaneous Nodules and Minor Symptoms**

  sn =Subcutaneous Nodules; ms=Minor Symptoms

$$Occurs(sn, p_{51}, p_{52}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{61} - p_{51} = 91 \wedge p_{62} - p_{52} = 147 \wedge p_{61} - p_{52} = 70, where \begin{cases} p_{52} - p_{51} = 21 \\ p_{62} - p_{61} = 77 \end{cases} \quad \text{.....(166)}$$

OR

$$Occurs(sn, p_{51}, p_{52}) \wedge Occurs(ms, p_{61}, p_{62}) \wedge p_{51} - p_{61} = 56 \wedge p_{52} = p_{62} \wedge p_{52} - p_{61} = 77, where \begin{cases} p_{52} - p_{51} = 21 \\ p_{62} - p_{61} = 77 \end{cases} \quad \text{.....(167)}$$

The above equations are applied for analysing the relationship between symptoms and ARF. The Temporal Template was prepared based on equations 29-167.

4.7.8. Temporal Rule

A point-based time patterns of symptoms was created. Temporal rule and temporal reasoning will interpret each patient's symptoms and how to precisely relate that with

ARF. Based on Table 4.6 and equations 29-167, the systems can be identified through the evident strength of ARF symptoms and how they are related with ARF. Example of the temporal rule is given below:

IF *GAS Infection present* AND *Arthritis is present* AND time period is *between 14 – 35 days*
THEN RELATION between ARF and Arthritis is ***ABSOLUTELY POSITIVE***.

IF *GAS Infection present* AND *Arthritis is present* AND time period is (*between 0 – 14 days OR between 35 – 49 days*)
THEN RELATION between ARF and Arthritis is ***VERY POSITIVE***.

IF *GAS Infection present* AND *Arthritis is present* AND time period is *between 49– 63 days*
THEN RELATION between ARF and Arthritis is ***RELATIVELY POSITIVE***.

IF *GAS Infection present* AND *Arthritis is present* AND time period is *between 63 – 168 days* THEN A RELATION between ARF and Arthritis is ***SUSPECTED***.

4.7.9. Temporal Reasoning

Development of an effective DSS in medicine demands a good reasoning mechanism, which captures the duration of symptoms (how long the symptoms last), the order in which symptoms are presented and ultimate analysis of the relationship between symptoms and disease. Therefore, Temporal Reasoning (TR) is the study of time theory and its associated reasoning process, which is applied in clinical decision support systems. Temporal reasoning processes reasons about time and relations between symptoms and helps make decisions based on the Temporal Knowledge foundation. Therefore, TR is used to determine and analyse the relationship between symptoms and produce the Temporal Template, which provides the linguistic information revealing how closely related a particular symptom is with ARF. The process of Temporal Reasoning is described in the flowchart presented in Figure 4.22.

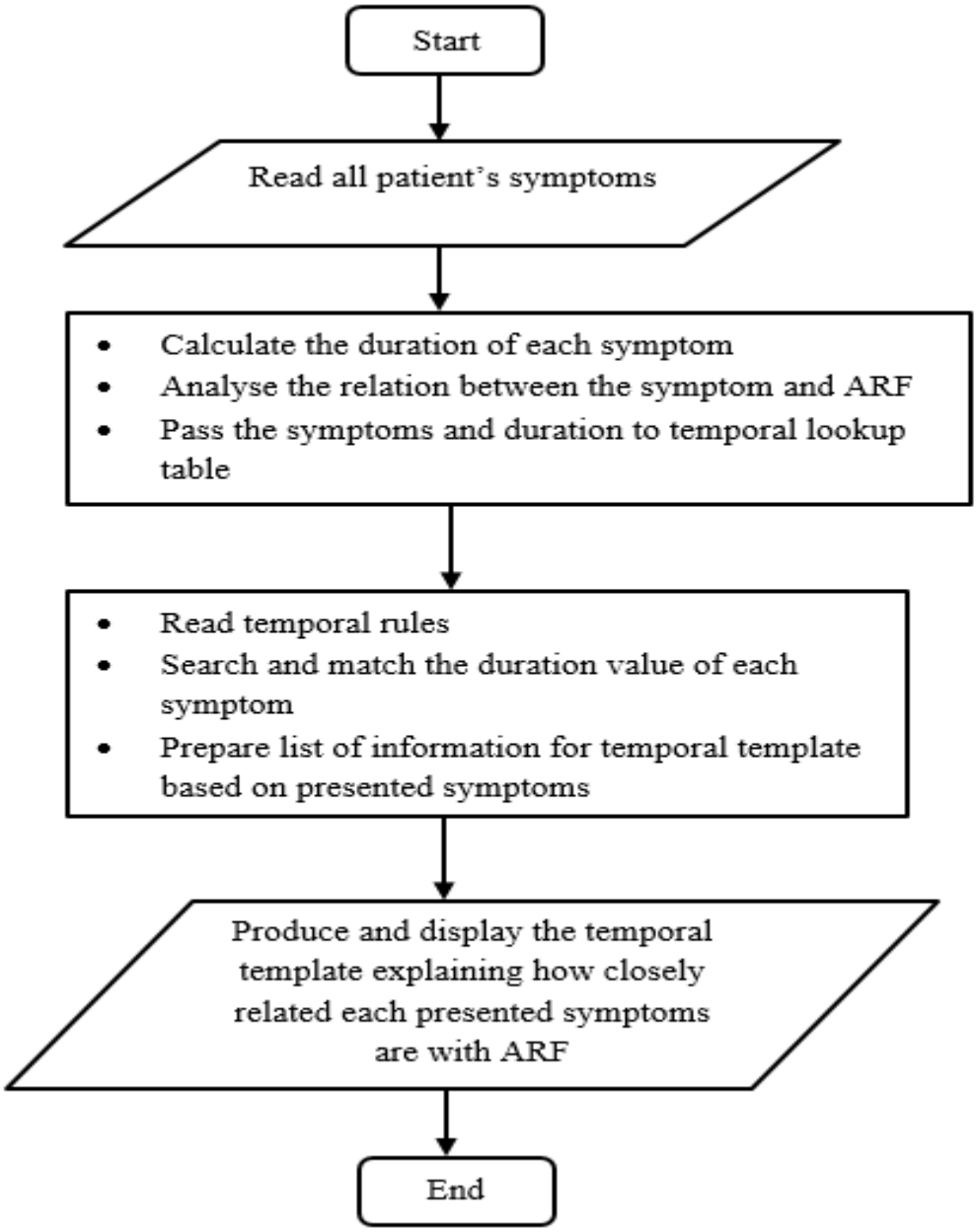


Figure 4.22: Temporal Reasoning Process

4.7.10. Temporal Template

Temporal Template is designed in linguistic variables for instance "Absolutely Positive for ARF", "Very Positive for ARF", "Relatively Positive for ARF" and "Suspected for ARF". These linguistic variables have been selected based on the NHF's expert guidelines with a view to provide a specific relationship name between ARF and particular symptoms. In addition, the Temporal Template facilitates them to reason their validity by providing a specific Crisp value for each particular symptom.

4.8. The Fuzzy Model

Fuzzy Logic is used to deal with situations of uncertainty in data by analysing the process of human reasoning. The fact that we are dealing with some situations of uncertainty in doctors' belief values for the severity of ARF signs and symptoms, leads us to employ Fuzzy Logic to refine their belief values as part of the diagnostic process. This section has been divided into three parts. The first highlights the fuzzy membership function and input/output parameter; the second explains the diagnosis of arthritis pain and the last part discusses the role of the Fuzzy Model in diagnosing ARF.

4.8.1. Fuzzy Membership Functions and Input/output Parameters

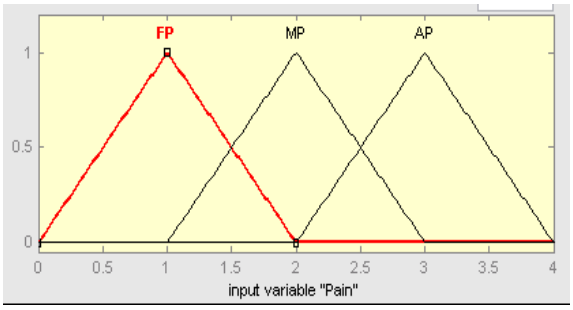
Determining the input parameter for any object that does not reflect any accurate measurement value is difficult. For example diagnosis of rheumatic fever's arthritis pain, hotness, swelling, redness, weakness in hand, weakness in feet etc. are important signs and symptoms but these symptoms do not reflect any accurate measurement value of severity. The impact of these symptoms will be determined by an expert based upon his/her knowledge and experience. The question of which input parameters and partitions will be best suited for such cases and their symptoms will arise inevitably. It is made complicated, as there are no feasible technical methods for choosing precise input values and their partitions in these circumstances. Therefore, the selection of numbers might be random and partitions of inputs can be fixed or manually adjustable or it will be more practical to determine them through expert knowledge or by observing the set of fuzzy rules. Different people have different ways for determining the distribution of the fuzzy set partition and selection of membership. So that the selection of the membership function and input methods depend on the nature of the application domain (Chen M. S. and Wang S. W., 1999). Throughout the literature review, it was perceived that the triangular and the trapezoidal membership functions are applied in a variety of applications because they reflect good results for most application domains (Kaya M. and Alhajj R, 2003). Nevertheless, it is still difficult to indicate the exact membership functions for specific applications because every application's domain has different objects and the level of uncertainty may therefore differ from one to another. It is clearly essential to be able to understand the nature of problems and ascertain availability of adequate data before selecting the membership functions and determining the input/output parameters.

Genetic Algorithms, Artificial Neural Networks, Evolutionary Programming and Statistical Approaches are available for automatic selection of the membership functions and are being applied in various medical diagnosis processes. Whilst it is agreed that usually these methods are suitable and possible to apply when huge volumes of related data sets are available, unfortunately, as pointed out by Bernadette *et al.*, (2007), these methods do have the serious limitation that they are unable to provide adequate explanation of results (Bernadette *et al*., 2007).

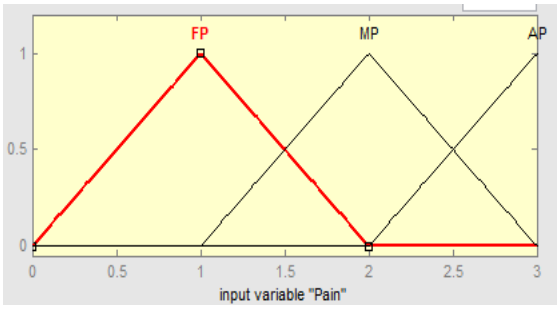
Another fundamental constraint at the moment is that Nepal does not have a comprehensive computerized health informatics system. A patient's essential medical information such as physical examination reports, present symptoms, laboratory reports and prescriptions, has to be recorded by hand. This situation therefore imposes severe constraints so that in the absence of computerised automatic methods some symptoms of ARF cannot be determined in ways that reflect calculated measurements and numerical values. In a manual environment, symptoms will be expressed in linguistic terms based on the doctor's personal perceptions only.

In the context of Nepal, it is evident that the best practice would be to formulate fuzzy rules for diagnosis of ARF. These could then be applied using a variety of membership functions with different input/output parameters based on expert knowledge and experience and evaluate each of them with predefined fuzzy set rules. The best membership functions could then be selected to provide the best match against the established fuzzy rules. We proposed to adjust manual methods in order to determine the input/output parameters and membership functions based on a predefined set of fuzzy rules. We then tested different membership functions and changed the output parameter values until a suitable result was achieved. We applied this method to diagnoses of arthritis pain and evaluated a system for use in the Matlab Fuzzy Toolbox (Pandey S. *et al*., 2014).

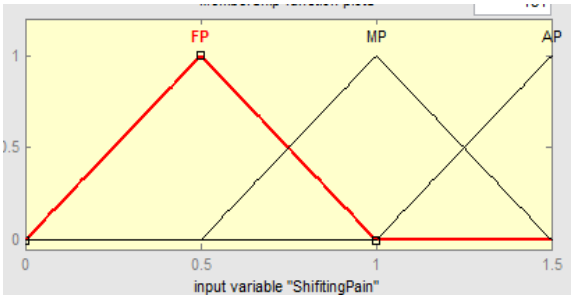
The membership functions shape with different input coverage is presented in Figure 4.23.



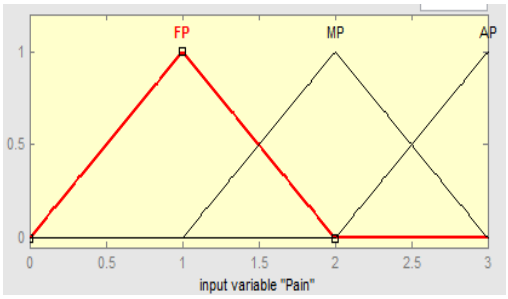
(1) Traingular (input parameter : 0-4)



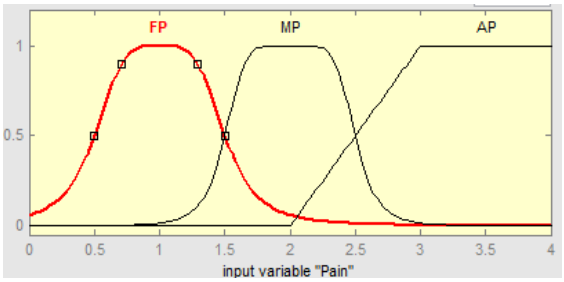
(2) Triangular (input parameter : 0-3)



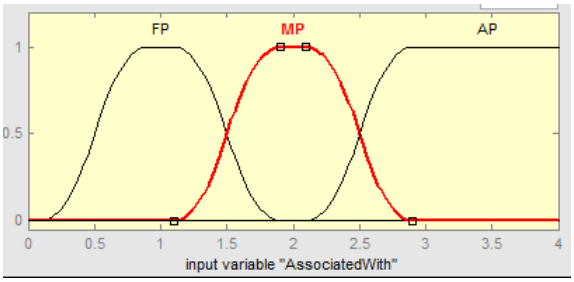
(3) Traingular (input parameter : 0-1.5)



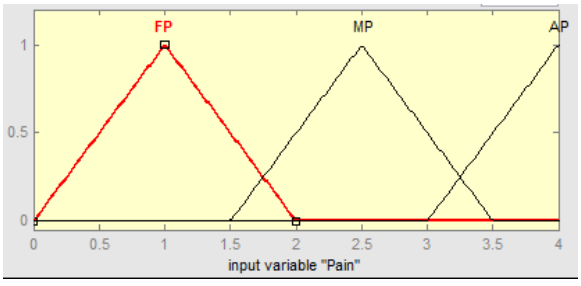
(4) Traingular + Trapezoidal (0-4)



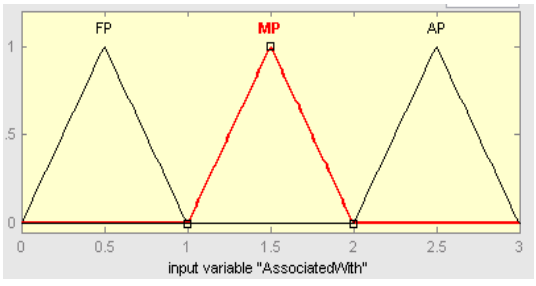
(5) Bell Shape + Trapezoidal (0.5-4)



(6) Π-shaped (0-4)



(7) Trangular, Overlape changes

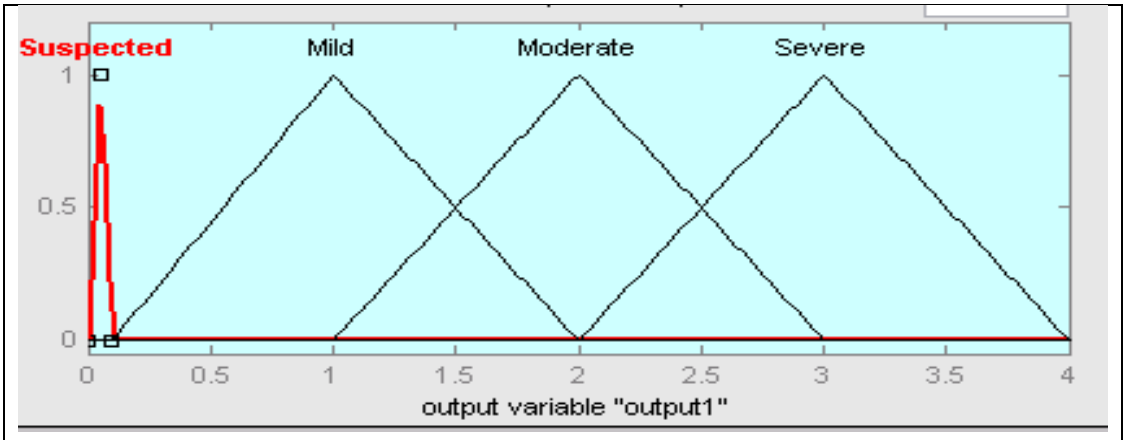


(8) Traingular, no overlap

Figure 4.23: Membership Functions Shape with Different Input Coverage

The different sets of input number and membership functions do not cause any serious differences in output as shown Table 4.7. Table 4.7 demonstrates the output parameter and distribution of the result between different input parameters with the same output parameters (Pandey S *et al.*, 2014).

Table 4.7: Result Between Different Input Parameters with the Same Output Parameters


Suspected : [0 0.5 0.1], Mild : [0.1 1 2], Moderate : [1 2 3], Severe : [2 3 4]
Tested with : (1) Triangular (input parameter : 0-4) **Result** Input value: [4; 4; 4] according to fuzzy rules, it is SEVERE case. Output : **2** (Moderate) – Not match with fuzzy rule
Tested with (2) Triangular (0-3) **Result** Input value: [3; 3; 3] according to fuzzy rules, it is SEVERE case. Output: **2.87** (75% Severe, 25% Moderate) match the fuzzy rule. Input value: [1; 1; 1;] according to fuzzy rules it is MILD case. Output: 0.986 (98% Mild match fuzzy rules).
Tested with (3) Triangular (0-1.5) **Result** Input value: [1.5; 1.5; 1.5] according to fuzzy rules, it is SEVERE case. Output: **2.87** (about 75% Severe, 25% Moderate) match the fuzzy rule. Input value: [0.5; 0.5; 0.5;] according to fuzzy rules it is MILD case. Output: 0.986 (98% Mild match the fuzzy rules).

The comparison between the same input parameter and different output parameter (Triangular) is illustrated in Figure 4.24 and the comparison between same input parameters and different output parameters (Triangular) is shown in Table 4.8 (Pandey S *et al.*, 2014).

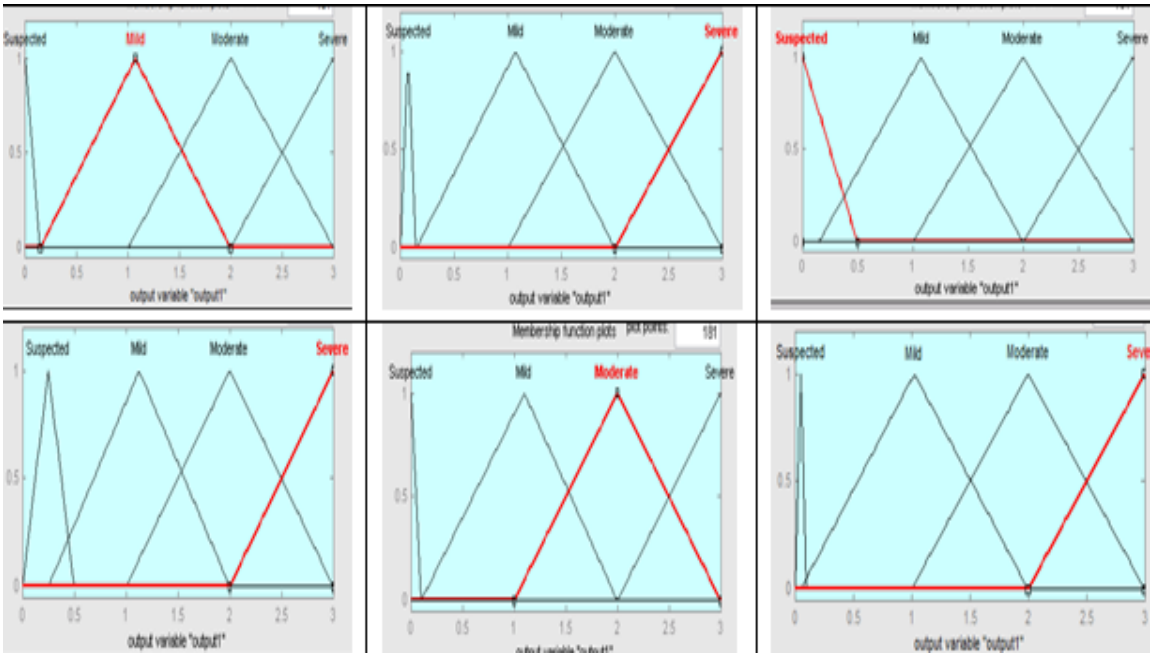


Figure 4.24: Different Output Shapes

Table 4.8: Comparison of the Result of Same Input and Different Output Parameter

A= Suspected, B=Mild, C=Moderate, D=Severe and Input parameter 0-4

Output Parameter	Mild	Moderate	Severe	Mild+Mode
Input parameter ---------→	[1 1 1]	[2 2 2]	[3 3 3]	[1.5 1.5 1.5]
A=[0 0 0.15], B=[0.15 1.075 2], C=[1 2 3], D=[2 3 3]	0.983	1.84	2.28	1.49
A=[0 0.75 0.15], B=[0.15 1.075 2], C=[1 2 3], D=[2 3 3]	1	1.87	2.36	1.5
A=[0 0 0.5], B=[0.15 1.075 2], C=[1 2 3], D=[2 3 3]	0.89	1.61	1.82	1.4
A=[0 0.25 0.5], B=[0.25 1.125 2], C=[1 2 3], D=[2 3 3]	0.944	1.65	1.88	1.44
A=[0 0 0.1], B=[0.1 1.1 2], C=[1 2 3], D=[2 3 3]	0.999	1.88	2.37	1.49
A=[0 0.05 0.1], B=[0.05 1.025 2], C=[1 2 3], D=[2 3 3]	0.981	1.91	2.45	1.48
A=[0 0.05 0.1], B=[0.05 1.025 2], C=[1 2 3], D=[2 3 4 4]	0.098	1.91	3.14	1.48

Figure 4.25 and Table 4.9 show comparison of results with the same input parameters and different output parameters in triangular and trapezoidal membership functions (Pandey, S. *et al.*, 2014).

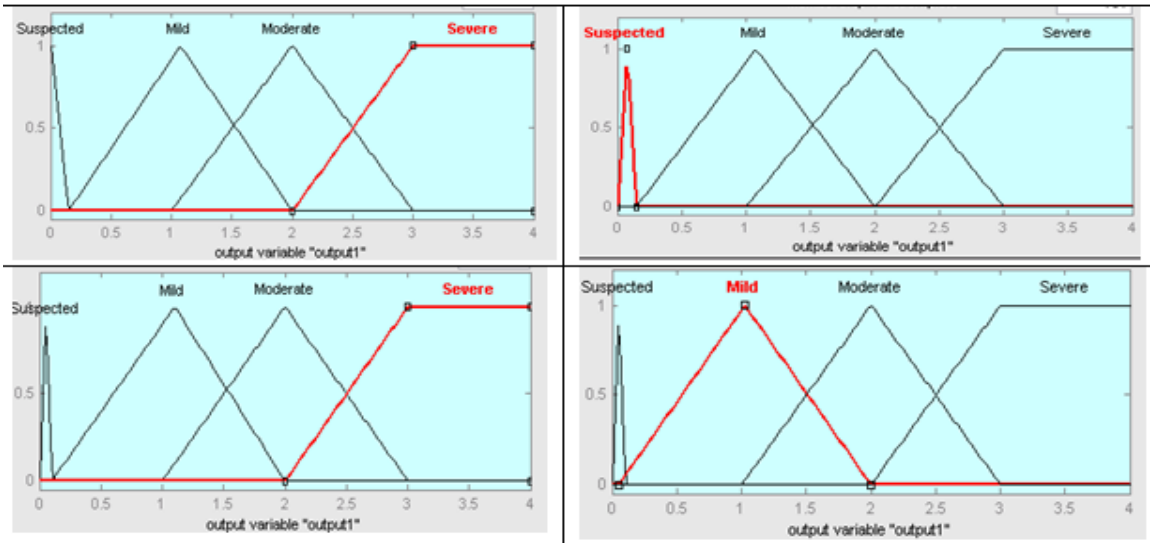


Figure 4.25: Output Shapes: Triangular and Trapezoidal

Table 4.9: Comparison of the Result of Different Shapes (Traingular and Trapezoidal)

A= Suspected, B=Mild, C=Moderate, D=Severe and Input parameter (0-4)

Output Parameter	Mild	Moderate	Severe	Mild+Mode
Input parameter ----------→	[1 1 1]	[2 2 2]	[3 3 3]	[1.5 1.5 1.5]
A=[0 0 0.15], B=[0.15 1.075 2], C=[1 2 3], D=[2 3 4 4]	0.977	1.83	3.04	1.49
A=[0 0.75 0.15], B=[0.15 1.075 2], C=[1 2 3], D=[2 3 4 4]	1	1.87	3.08	1.5
A=[0 0.50 0.1], B=[0.1 1.1 2], C=[1 2 3],D=[2 3 4 4]	1.02	1.91	3.14	1.51
A=[0 0.05 0.1], B=[0.05 1.025 2], C=[1 2 3],D=[2 3 4 4]	0.98	1.91	3.14	1.48

The comparison with a same input parameter and different output parameter is shown in Figure 4.26 and comparison result of same input parameter and different output parameter (Π-shaped) is given in Table 4.10 (Pandey, S. *et.al*, 2014).

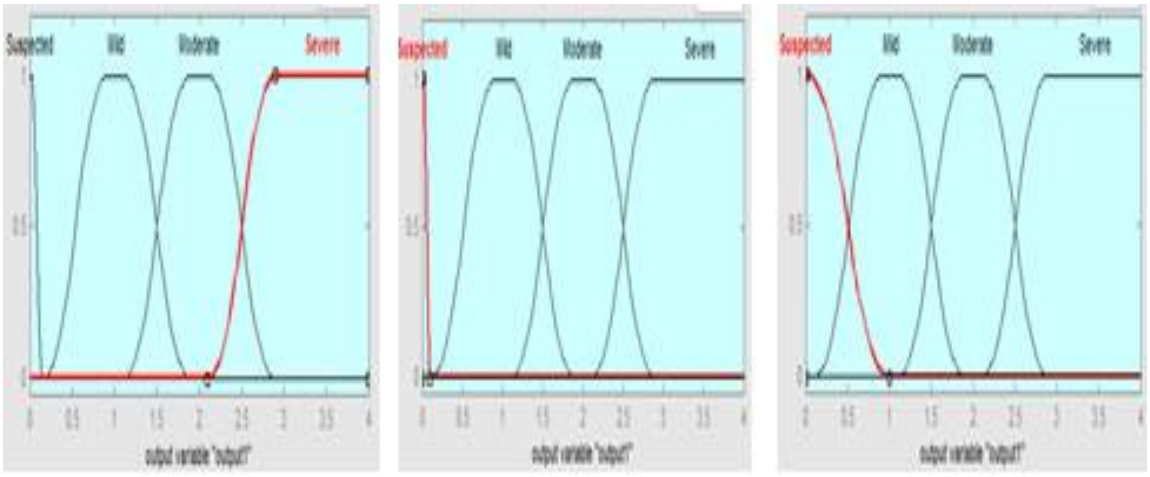


Figure 4.26: Output Π-Shaped

Table 4.10: Comparison of Results with Π-Shaped

A= Suspected, B=Mild, C=Moderate, D=Severe and Input parameter (0-4)

Output Parameter	Mild	Moderate	Severe	Mild+Mode
Input parameter ---------→	[1 1 1]	[2 2 2]	[3 3 3]	[1.5 1.5 1.5]
A=[0 0 0.015 0.15], B= [0.15 0.925 1.1 1.9], C= [1.1 1.9 2.1 2.9], D= [2.1 2.9 4 4]	0.925	1.82	3.05	1.44
A= [0 0 0.01 0.1], B= [0.1 0.925 1.1 1.9], C= [1.1 1.9 2.1 2.9], D= [2.1 2.9 4 4]	0.936	1.86	3.1	1.45
A= [0 0 0.01 1], B= [0.1 0.925 1.1 1.9], C= [1.1 1.9 2.1 2.9], D= [2.1 2.9 4 4]	0.778	1.41	2.49	1.31

In the membership function, overlapping is important and has great strength as a fuzzy controller. Overlap provides strength to the fuzzy controller because within a given input at least one rules will be fired (Bernadette *et al*., 2007). In the membership function if there is no overlap than it reduces the system to **Boolean logic**. When the overlap exits between two membership functions then they should not have the same point of maximum truth and the sum of truth for any point within the overlap must be less than or equal to one. Regarding setting the completeness level, some authors (Kosko B. 1992) suggest a minimum completeness level =0.25 and others (Mizumoto M. 1988) suggest an average completeness level=0.50. This depends fundamentally upon the indicated set of fuzzy rules and application domains. Increasing the completeness creates redundancy and decreasing the completeness captures a value for a lower level of truth. The membership function with different overlaps is demonstrated in Figure 4.27 (Pandey S *et al*., 2014).

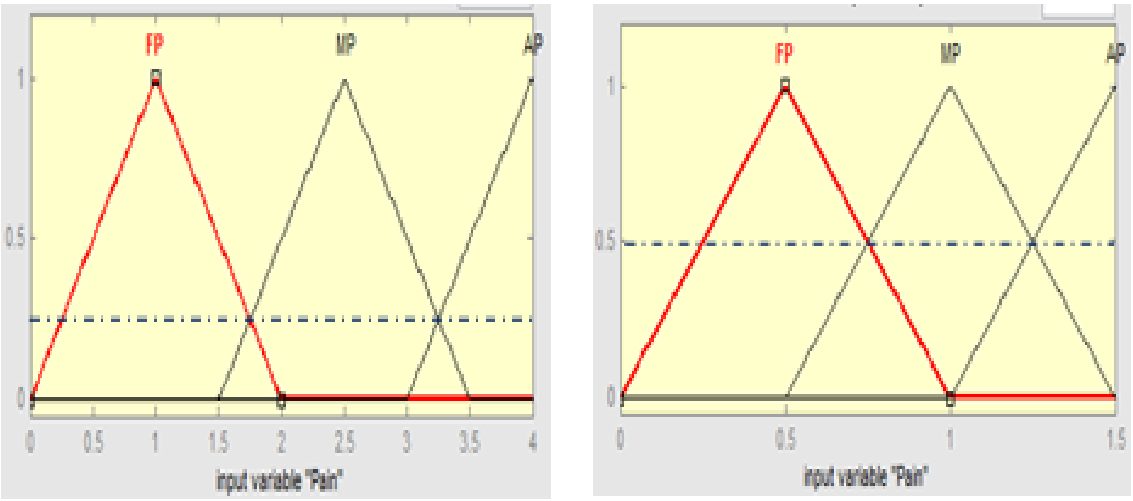


Figure 4.27: Different Overlaps (0.25) and (0.5)

The comparison with the same input parameter (overlap change) and a different output parameter (Triangular + Trapezoidal), are shown in Figure 4.28 and Table 4.11 (Pandey, S. *et.al*, 2014).

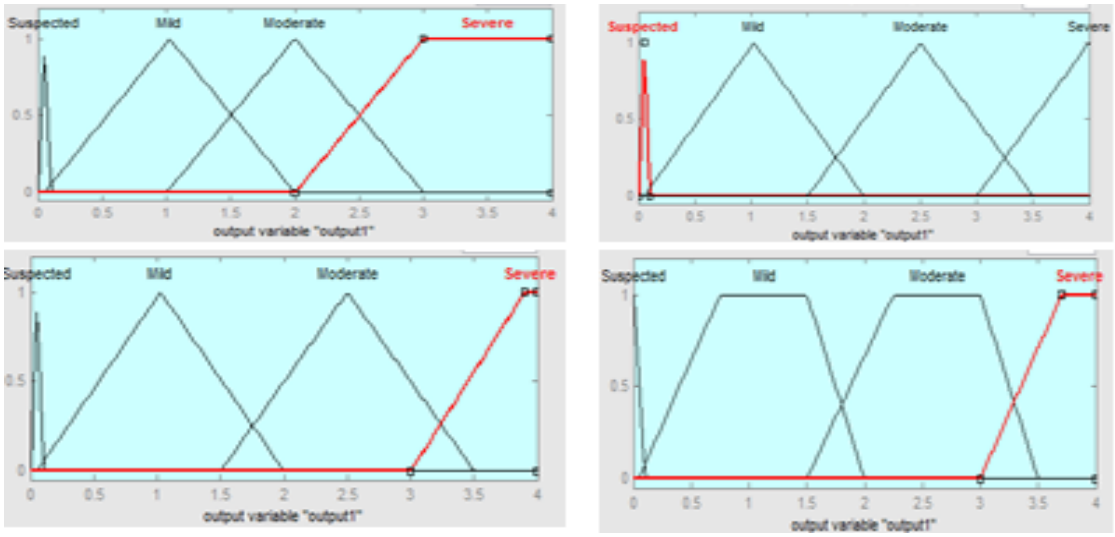


Figure 4.28 :Output Shapes: Triangular and Trapezoidal

Table 4.11: Comparison of Result with Different Overlaps

A= Suspected, B=Mild, C=Moderate, D=Severe and Input parameter (0-4)

Output Parameter	Mild	Moderate	Severe	Mild+Mode
Input parameter ----------→	[1 1 1]	[2 2 2]	[3 3 3]	[1.5 1.5 1.5]
A= [0 0.05 0.1], B= [0.05 1.025 2], C= [1 2 3], D= [2 3 4 4]	0.98	1.91	1.91	0.981
A= [0 0.05 0.1], B= [0.05 1.025 2], C= [1.5 2.5 3.5], D=[3 4 4]	0.98	2.39	2.39	0.981
A =[0 0.05 0.1], B= [0.05 1.025 2], C= [1.5 2.5 3.5], D=[3 3.9 4 4]	0.98	2.39	2.39	0.981
A =[0 0 0.1], B= [0.05 0.75 1.5 2], C= [1.5 2.25 3 3.5], D=[3 3.7 4 4]	1.02	2.39	2.39	0.994

In Nepal (2011), based on NHF data, 75% of cases diagnosed with ARF included arthritis as one of the major symptoms observed. This is much higher compared with cases where other major symptoms have been observed as part of the patients' symptoms. It is for this reason that doctors tend to place greater emphasis on accurate diagnosis of the severity of arthritis and its associated factors such as hotness, redness, swelling, movement restriction in the large joints, compared with other symptoms, using this as an important step in the diagnosis of ARF. Ascertaining the severity of arthritis or indeed any pain in general is marred by uncertainty. This area of assessment would normally differ from one individual to another. In Nepal, rural health workers or inexperienced doctors are often struggling to determine whether particular arthritis pains and other factors related to arthritis are associated with rheumatic fever or not. What is required is that community

rural health workers and inexperienced doctors have a system that allows them to explain the severity of the pain in their diagnosis process. Clearly, there is a degree of uncertainty in this process, for which we have attempted to use Fuzzy Logic to refine and confirm belief in the accuracy of the model. We wanted to make sure whether Fuzzy Logic can be applied for diagnosis of ARF or not. We determined that if applying Fuzzy Logic initially for diagnosis of arthritis pain and subsequently evaluating the system does provide a positive result, then it can be applied in the ARF Diagnosis Process.

4.8.2. Diagnosis of Arthritis Pain for ARF

We have discussed and described how Fuzzy Logic could be applied for the development of a CDSS application that could be used for diagnosing arthritis pain (arthritis pain for rheumatic fever patients only) in four different stages: 1) Fairly Mild; 2) Mild; 3) Moderate and 4) Severe. This system helps to measure the level of arthritis pain in different stages, which helps determine whether the existing arthritis pain is associated with ARF or not. In this system, Mild, Moderate and Severe stages of pain are related to ARF whereas the Mild stage is not related.

4.8.2.1. Membership Functions for Arthritis Pain Diagnosis

The signs and symptoms of arthritis are determined by linguistic variables (e.g. pain, hotness, swelling, movement restriction etc.) with fuzzy intervals and linguistic labels (fairly positive, moderately positive, and absolutely positive). Three input variables and one output variable are designed to diagnose the stage of arthritis pain for rheumatic fever. Three input variables and one output variable were designed to diagnose the stage of arthritis pain for rheumatic fever cases. The linguistic variable consists of the name of the variable (u), the term set of the variable (T(μ) and the universe of discourse (μ) for which the fuzzy sets will be defined as shown in Tables 4.12 and 4.13) (Pandey S. *et al*., 2015).

Table 4.12: Input Variables, Ranges and Fuzzy Sets

Input Variables	Ranges	Fuzzy Sets
All Arthritis-related signs and symptoms: Pain in ankles, knees, elbows, wrists; pain associated with hotness, swelling, movement restriction, redness and migratory/shifting pain.	0 0-2 1-3 2-4	None Fairly Positive Moderately Positive Absolutely Positive

Table 4.13: Output Variables

Output Variables	Ranges	Fuzzy Sets
Arthritis pain stages	<1	Fairly Mild
	0-2	Mild Stage
	1-3	Moderate Stage
	2-4	Severe Stage

a. Fairly Positive

$$\mu_{fp^{(x)}=}\begin{cases} 0 & if x \le 0 \\ \frac{x-0}{1-0} if & 0 \le x \le 1 \\ \frac{2-x}{2-1} if & 1 \le x \le 2 \\ 0 & if \quad 2 \le x \end{cases} \quad \text{..... (168)}$$

b. Moderately Positive

$$\mu_{mp^{(x)}=}\begin{cases} 0 & if x \le 1 \\ \frac{x-1}{2-1} if & 1 \le x \le 3 \\ \frac{3-x}{3-1} if & 2 \le x \le 3 \\ 0 & if \quad 3 \le x \end{cases} \quad \text{..... (169)}$$

c. Absolutely Positive

$$\mu_{ap^{(x)}=}\begin{cases} 0 & if x \le 2 \\ \frac{x-2}{3-2} if & 2 \le x \le 3 \\ 1 & if \quad 3 \le x \le 4 \\ 0 & if \quad 4 \le x \end{cases} \quad \text{..... (170)}$$

If a membership degree does not totally participate in one of the linguistic variables, then NOT methods will be applied for getting the membership degree of the nearest linguistic variable.

4.8.2.2. Determining the Input Value of Arthritis Pain

In determined circumstances if the input value of arthritis pain and pain associated with hotness, swelling, redness, movement restriction, the equations 171 and 172, were applied to find the maximum value (0-4) then that is given by doctors or rural health workers for arthritis-related pain symptoms in the ankle, , elbow, wrist or knee, (Pandey S. *et al.*, 2015).

$$\mu_{ar\_pain}(x) = max\{\mu_{ank\_pain}(x), \mu_{elb\_pain}(x), \mu_{kne\_pain}(x), \mu_{writ\_pain}(x), \} \text{.....(171)}$$

$$\mu_{pain\_associated}(x) = max\{\mu_{swelling}(x), \mu_{hotness}(x), \mu_{redness}(x), \mu_{mov\_rest}(x), \} \text{ ... ...(172)}$$

If a membership degree does not totally participate in one of the linguistic variables then NOT methods will be applied for getting the membership degree of the nearest linguistic variable.

4.8.2.3. Fuzzy Inference System for Arthritis-related Pain

Fuzzy triangular and trapezoidal membership functions are applied to determine the degree of symptoms to ascertain the doctor's belief in a symptom's severity. The fuzzy inference mechanism maps the entire set of rules with membership degrees and fuzzy logical operators can be used to evaluate the strength of firing rules. The output of each rule is aggregated and the Mamdani's Centre of Gravity (CoG) methods are applied for the defuzzification process. Our proposed diagnostic tool allows doctors to log symptoms describing arthritis pain using numerical values, 0–4, that are estimates of the severity of pain that a patient feels. These values are used as input parameters to the fuzzy system and apply the membership function, trapezoidal and triangular, to obtain the degree of belief. The membership function for arthritis-related pains is shown in Table 4.14 and Figure 4.29. Similarly, membership function output is shown in Table 4.15 and Figure 4.30. Fuzzy inference uses rules in the KBS to determine whether the symptoms logged describe arthritis as being Fairly Mild, Mild, Moderate or Severe (Pandey S. *et al*., 2015).

Table 4.14: Membership Function for Arthritis Pain

Linguistic Label	Fuzzy Interval	Membership Type	Input variable (parameter)
Fairly Positive	0 to 2	Triangular	[0 1 2]
Moderately Positive	1 to 3	Triangular	[1 2 3]
Absolutely Positive	2 to 4	Trapezoidal	[2 3 4 4]

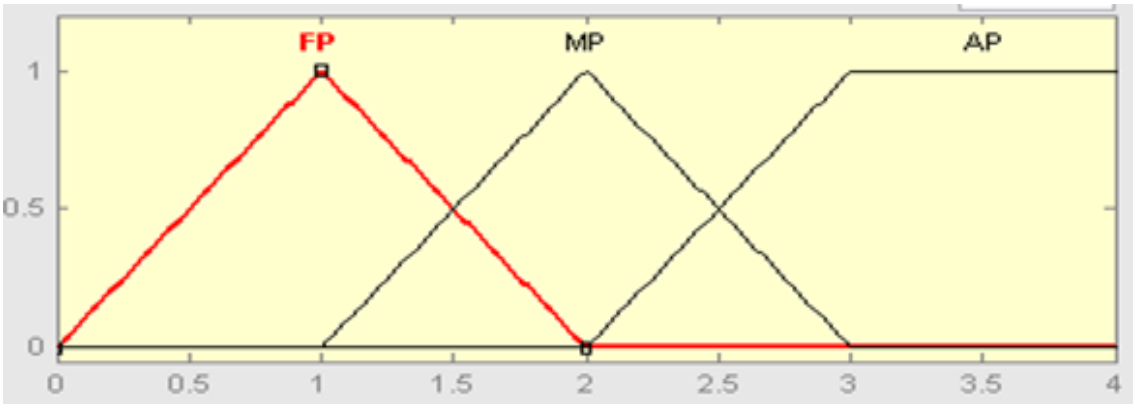


Figure 4.29: Input Variable of Arthritis Signs and Symptoms

Table 4.15: Membership Functions of Outputs

Linguistic Label	Fuzzy Interval	Membership Type	Output
Fairly Mild	<0.1	Triangular	[0.00 0.05 0.1]
Mild	0.5 to 2	Triangular	[0.05 1.025 2]
Moderate	1 to 3	Triangular	[1 2 3]
Severe	2 to 4	Trapezoidal	[2 3 4 4]

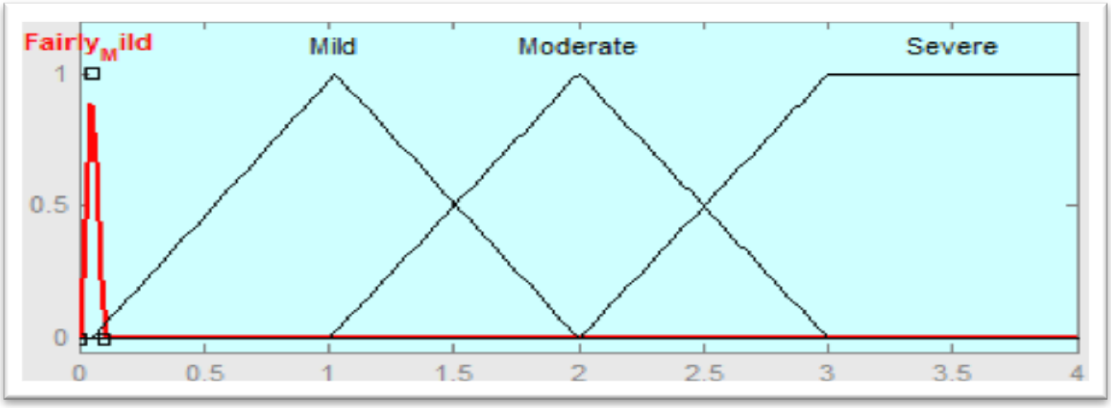


Figure 4.30 : Membership Function for Fuzzy Outputs

4.8.2.4. Fuzzy Rule of Arthritis Pain Diagnosis

In the fuzzy approach, the decision support system and the decision-making processes are undertaken by the fuzzy inference engine using the fuzzy rules. Basically, fuzzy rules are the connections between input and output fuzzy values. The detailed descriptions of rules and algorithms for arthritis related pain diagnosis of ARF, system process architecture and detailed fuzzy rules are found in (Pandey S. *et al*., 2015). The fuzzy rule method was determined using support provided by experts from Nepal. Some samples of fuzzy rules are shown in Table 4.16.

Table 4.16: Sample of Rules for Arthritis Diagnosis

Rule No	Rule descriptions
Rule 1 :	**IF** arthritis pain is ***AP*** **AND** pain associated with is ***AP*** **AND** migratory pain is ***AP*** **THEN** diagnosis arthritis pain=”Severe”.
Rule 7 :	**IF** arthritis pain is ***AP*** **AND** pain associated with is ***MP*** **AND** migratory pain is ***FP*** **THEN** diagnosis arthritis pain=”Moderate”.
Rule 24:	**IF** arthritis pain is ***FP*****AND** pain associated with is ***MP*** **AND** migratory pain is ***FP*** **THEN** diagnosis arthritis pain=”Mild”.
Rule 36:	**IF** arthritis pain is ***FP*** **AND** pain associated with is ***AP*** **AND** migratory pain is ***NONE*** **THEN** diagnosis is that arthritis pain=”Not RF”.

The rule viewer for arthritis pain for the ARF inference system and plots of an output surface map for the system are based on the rules given in Figures 4.31 and 4.32 (Pandey S. *et al.*, 2015).

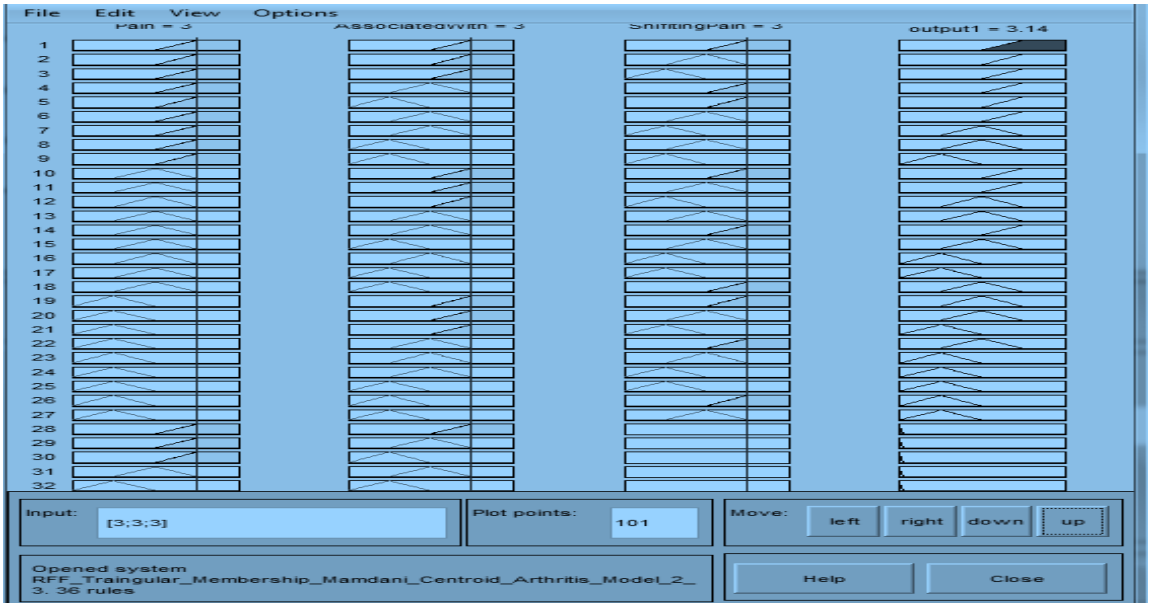


Figure 4.31 : Rule Viwer for Arthritis Pain for ARF Inference Systems.

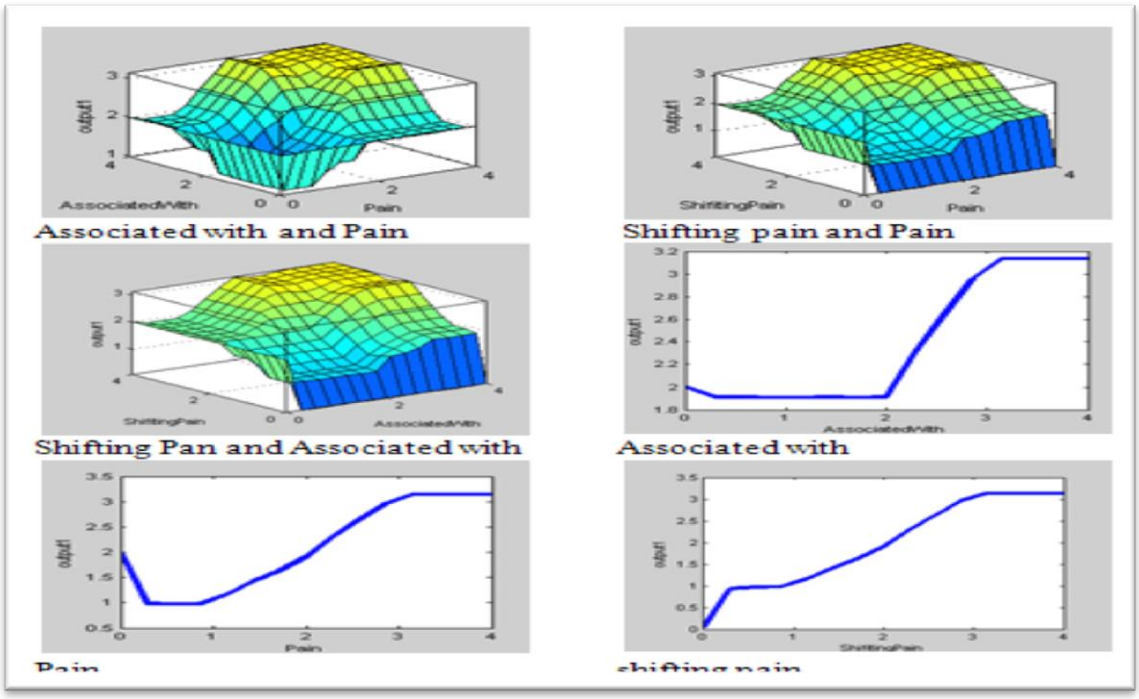


Figure 4.32: Plot of an Output Surface Map for the System Based on the Fuzzy Rules.

The system we developed for the diagnosis of arthritis pain in different stages was implemented in Matlab. Our experiment's results are based on the fuzzy rule that was designed based on expertise and guidelines obtained from the NHF. The system experiments were done by selecting different range random values 0-4 and evaluating the

performance of the system with the predefined set of fuzzy rules. If the output value crosses over two output membership functions, then the maximum number will be taken for the final result. The validation result shows that the designed fuzzy approach system is accurate and the fuzzy inference system is reliable especially for helping the rural health worker or health assistant to make a diagnosis easily. More details can be found on Pandey S. *et al*., (2015).

4.9. Fuzzy Model for Diagnosis of ARF

Fuzzy Logic can be used to deal with situations of uncertainty in data by analysing the process of human reasoning. The central issue is the fact that we are dealing with some situations of uncertainty in doctors' belief values regarding perception of the severity of arthritis pain covering presence of swelling, hotness, movement restriction, redness, pain migratory on the large joints, small joints pain, weakness in hand and feet, twitchy and jerking movement etc. These are some of the important symptoms of ARF. Unfortunately, a doctor's perception does not provide immediately any accurate numerical measurement value. This weakness steered us towards employing Fuzzy Logic in order to refine their belief values as a formal part of an improved and more efficient diagnostic process for ARF. The architecture of Fuzzy Logic for our model is provided in Figure 4.33, which shows how Fuzzy Logic can be incorporated within the model (Pandey S. *et al*., 2015).

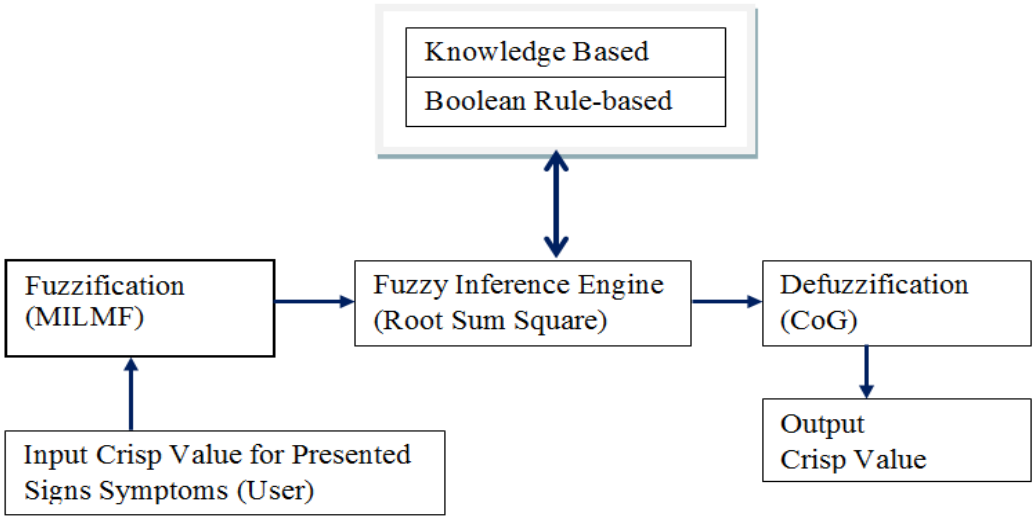


Figure 4.33: A Fuzzy System for ARF Diagnosis

This model of architecture of a Fuzzy Logic System takes a Crisp value that is given by users of ARF symptoms and follows the rest of the processes of fuzzification, fuzzy inference and defuzzification. The defuzzification process shows the output in a Crisp

value. Understanding usage of the process of a Fuzzy Model for diagnosis of ARF can be followed by examination of the flowchart diagram illustrated in Figure 4.34.

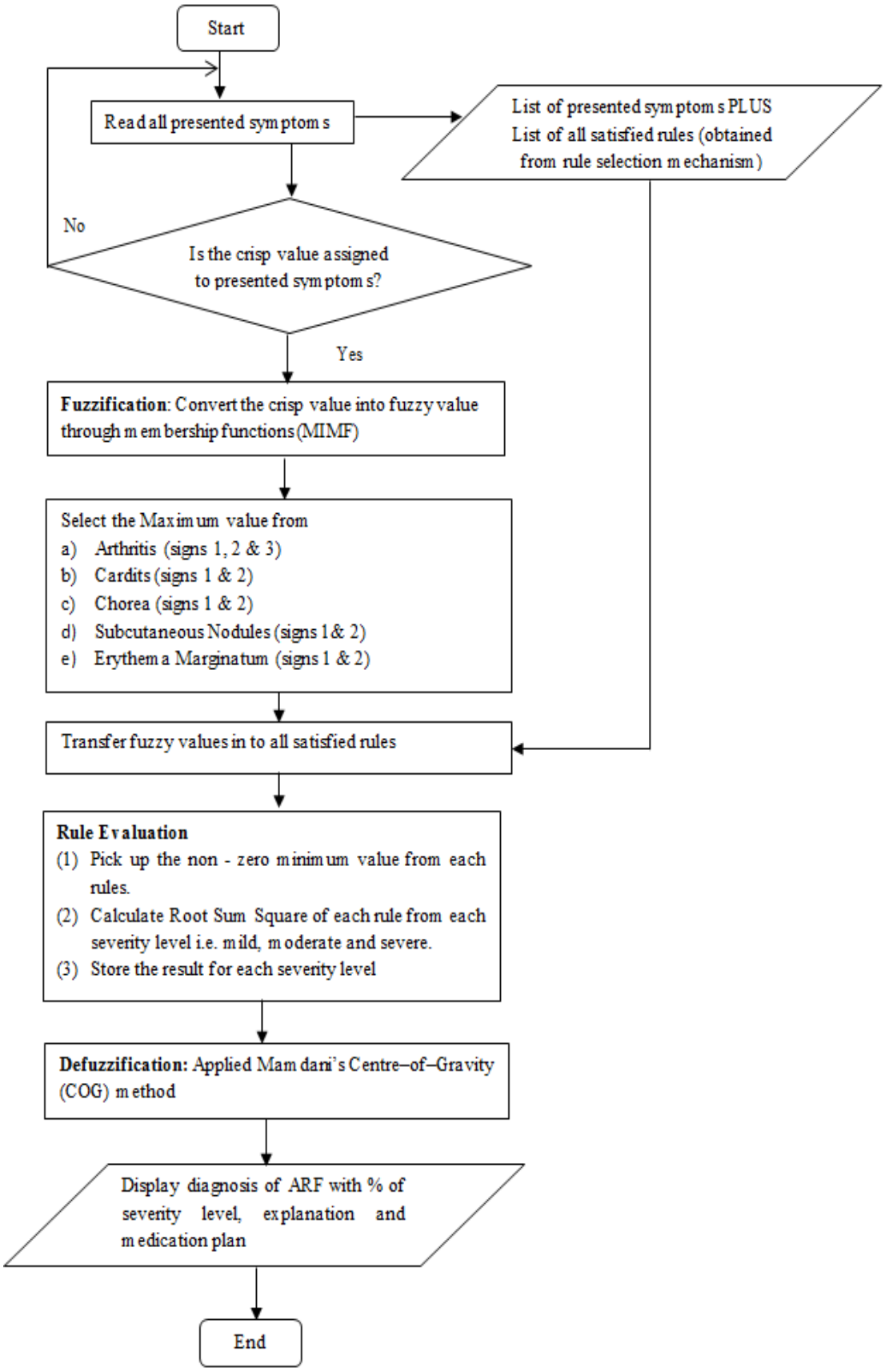


Figure 4.34: Fuzzy Process for ARF Diagnosis

4.9.1. Fuzzy Inference

The fuzzy logic inference model consists of four components: 1) fuzzification; 2) fuzzy inference engine; 3) fuzzy rules and 4) defuzzification. In addition, Mamdani-Type, Takagi-Sugenokang (TKS) and Singleton-Type are available for determining the fuzzy reasoning mechanism (Pandey S. *et al*., 2014). The fuzzy operators: min., max., product and probabilistic sums are being used for a variety of applications. Based on the literature review, it was identified that the most commonly used fuzzy inference technique is the Mamdani method. The processes of Mamdani-style fuzzy inference are: 1) fuzzification of the input variables; 2) evaluation of fuzzy rules; 3) aggregation of the rule output; and 4) defuzzification. The processes are shown in Figure 4.35.

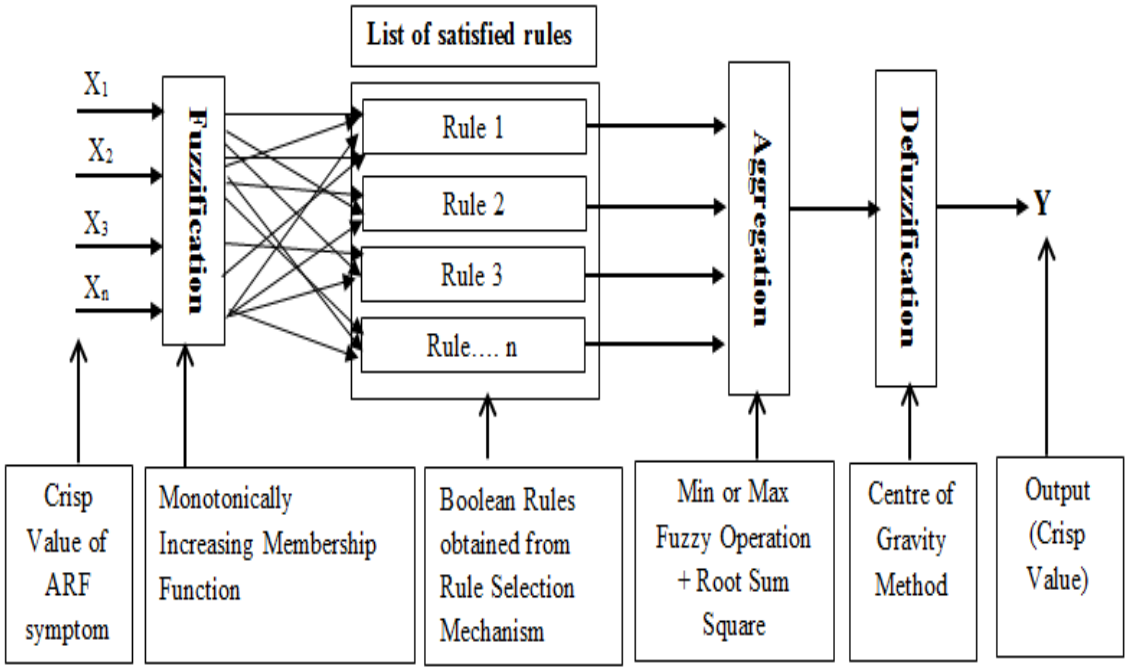


Figure 4.35 : Fuzzy Inference of an ARF Diagnosis System

The fuzzification process takes as input, crisp values, representing doctors' beliefs in the severity of ARF symptoms in an observed patient. These values are then used in a fuzzy membership function (using monotonically increasing membership functions), which convert them into values representing degrees of belief. The fuzzy inference engine is a reasoning process, which will map the degree of belief into an output using a chosen membership function. These values are then used in conjunction with suitable logical operators. The result is the subject of defuzzification, which is the process of translating Fuzzy Logic results into Crisp values, which can be used as final outputs for the system. The maximum fuzzy operation is applied to obtain the maximum Crisp Value from

Arthritis, Carditis and Chorea sysmptoms. The diagram below shows the ARF symptoms and the fuzzy process or diagnosis of ARF. The process is shown in Figure 4.36.

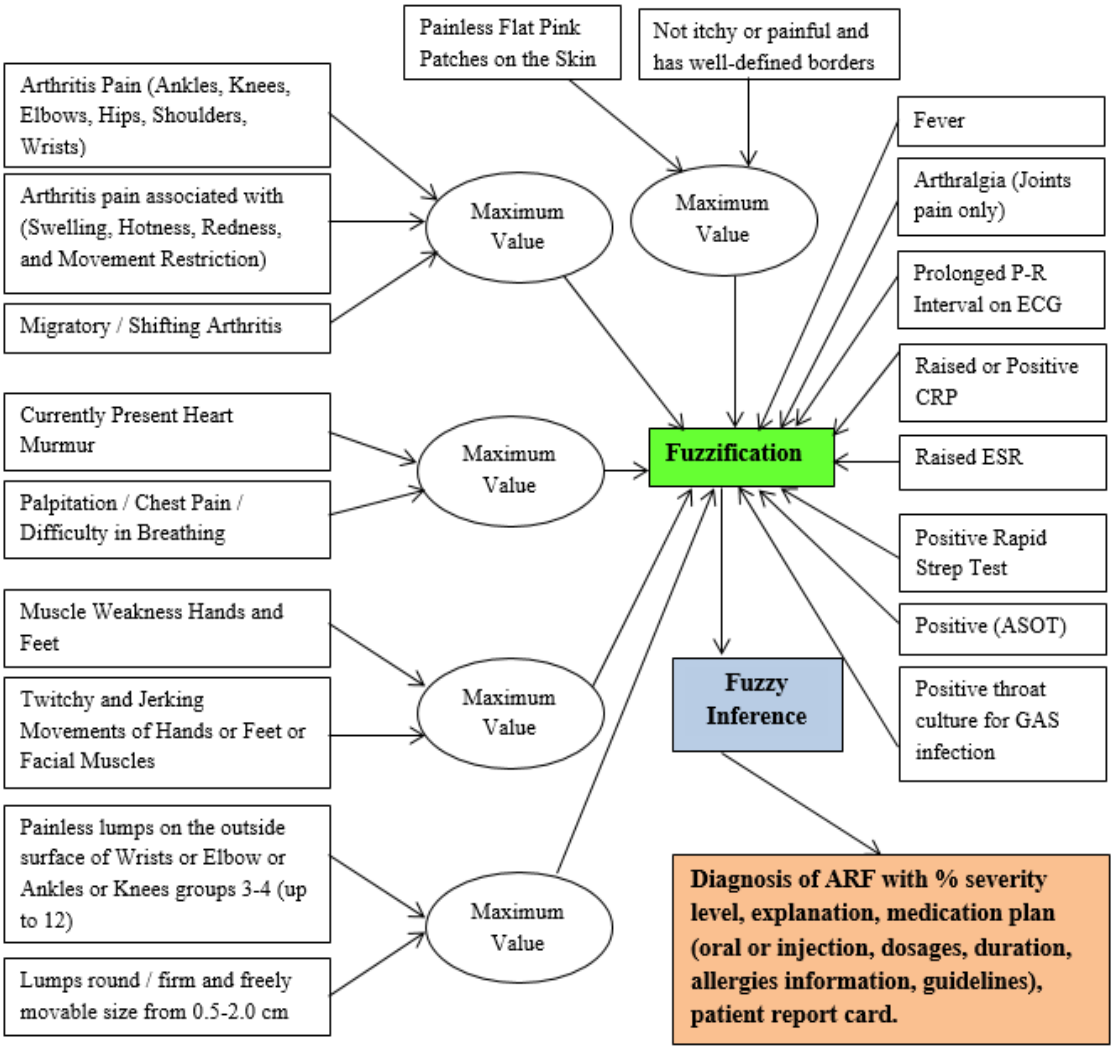


Figure 4.36 : ARF's Symptoms and a Fuzzy Process

4.9.2. Fuzzification

In the Fuzzy System, membership functions will be used during the fuzzification and defuzzifications processes. Membership functions map the Crisp input values or non-fuzzy input values to fuzzy linguistic terms and vice versa. Different types of membership functions are available i.e. Piece-wise linear, Gaussian, Sigmoid, Singleton, Triangular, Trapezoidal, Z-shaped etc. (Pandey S. *et al*., 2014). Due to the lack of proper guidelines, methods and theory, it is hard to choose a specific membership function suited to any particular problem (Medasani S *et al*., 1998) as it is dependent upon the nature of the problem and individual practitioner's experiences. The involvement and implication of uncertainty level, types of data and the availability of data may well differ from one

problem to another problem. This is the case in Nepal, where electronic data sets are not available so that automatic membership selection methods namely: Genetic Algorithms, Artificial Neural Network, Evolutionary Programming Approach, very often are not applied under prevailing circumstances., (Pandey S. *et al*., 2014). Automatic selection methods often cannot provide, on their own, adequate explanations and therefore justification for some apparent results (Bernadette B. M. *et al*., 2007). Example of this are when symptoms of ARF cannot be measured in accurate numeric values notably during description of severe pain in ankle, swelling, hotness, redness, red patches on the skin etc. These symptoms will be observed and described by community health workers or inexperienced doctors based on the basis of a patient's narrative account. Then they could express the severity of the symptoms in linguistic terms describing them as severe pain, moderate pain or mild pain but this would be based entirely on his/her perception and relative experience.

We tested different membership functions and changed output parameter values until acceptable results were achieved. As a consequence, in our model we applied manually adjustable methods, monotonically increasing linear membership functions to convert a Crisp Value into a Fuzzy Value. The ranges of Fuzzy Values were determined by experts from the NHF. The monotonically increasing linear membership function and equation are given in Figure 4.37 (Pandey S. *et al*., 2015).

$$L(x;\alpha,\beta) = \begin{cases} 0 & x < \alpha \\ \dfrac{x-\alpha}{\beta-\alpha} & \alpha \le x \le \beta \\ 1 & x > \beta \end{cases}$$

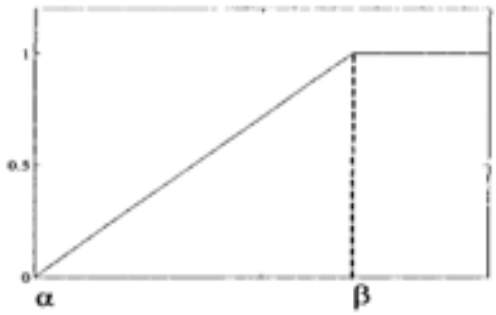


Figure 4.37: Monotonically Increasing Linear Membership Function and Equation

The symptoms of ARF are determined by linguistic variables: arthritis pain, movement restriction, heart murmur, weakness in hand, feet, chorea etc. incorporating fuzzy intervals and linguistic labels: Fairly Positive, Moderately Positive, and Absolutely Positive. Three input variables and one output variable were designed to diagnose the severity level of ARF. The linguistic variable consists of the name of the variable (u), the term set of the variable (T(μ) and universe of discourse (μ) with which the fuzzy sets will be defined (Pandey S. *et al*., 2015).

Example for Heart Murmur (μ),

T (Heart Murmur): fairly positive, moderately positive, and absolutely positive.
Heart_murmur(μ) = [0...3]

The input variables, value range and fuzzy set are shown in Table 4.17. Each linguistic variable has different parameters: Fairly Positive (0-1), Moderately Positive (1-2) and Absolutely Positive (2-3). Doctors or community rural health workers provide a numerical value (0-3) for sign and symptom that a patient exhibits. Where "x" is a Crisp Value given by doctors or rural health worker, this Crisp Value will be converted into a Fuzzy Value by the following membership function equation:

$$\mu_{ARF_{Symptoms}}(x)\begin{cases} 0 & if\ x \le 0 : None \\ \frac{x-0}{3-0} & if\ \ 0 \le x \le 1 : Fairly\ Positive \\ \frac{x-0}{3-0} & if\ \ 1 \le x \le 2 : Moderately\ Positive \\ \frac{x-0}{3-0} & if\ \ 2 \le x \le 3 : Absolutely\ \ Positive \\ 1 & if\ x = 3\ \ : Absolutely\ Positive \end{cases} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots (173)$$

Table 4.17: Input Variables, Ranges and Fuzzy Sets

Input Variables	Ranges	Fuzzy Sets
All ARF signs and symptoms that presented in above table 3.11	0 0-1 1-2 2-3	None Fairly Positive Moderately Positive Absolutely Positive

Fuzzy monotonically increasing the linear membership function is applied to determine the degree of symptoms and to ascertain the doctor's belief of the symptoms' levels of severity. The fuzzy inference mechanism will map the entire set of rules with membership degrees and fuzzy logical operators that will be used to evaluate the strength of firing rules. Then the output of each rule is aggregated and the Mamdani's Centre of Gravity (CoG) methods are applied for the defuzzification process. Our diagnostic tool allows doctors to log symptoms describing all ARF symptoms using numerical values (0-3) that are estimates of the severity of symptoms reportedly felt by a patient. These values will be used as input parameters to the fuzzy system and apply the membership function to obtain the degree of belief. The fuzzy inference uses rules in the rule-based to determine

whether the symptoms logged accurately describe ARF as being a mild, moderate or severe case.

Root Sum Square (RSS) is applied for obtaining the values from the firing rules. Thus,

$Rv_{i.....}Rv_n$ = Value of firing Rules.

Ov_i.....Ov_n = Output value of RSS.

$Ov_i = \sqrt{Rv_i^2}$.....(174)

4.9.3. The Rule Evaluation Process

We used the Boolean rules instead of fuzzy rules because their membership function does not have an overlapping input parameter. During the rule evaluation process, the Crisp Value of each symptom was transferred into list of satisfied rules (rules obtained from the Rule Selection Mechanism, which is discussed in the KBS/Boolean Rule Model (Chapter 3, subsection 4.6.5). A fuzzy rule consists of IF<*Condition*> AND/OR/NOT <*Consequences*>, where the condition is a fuzzy logic expression and the consequence is the fuzzy output value. Fuzzy rules are formed in order to control output variables. Basically, if rules have multiple antecedents then fuzzy operators AND or OR are applied to attain a single number or truth value. The AND fuzzy operation is applied to evaluate the conjunction of the rule antecedents for example: $\mu_A \cap B^{(x)} = \min[\mu_A(x), \mu_B(x)]$. The OR fuzzy operation is applied to evaluate the disjunction of the rule antecedents for example $\mu_A \cup B^{(x)} = \max[\mu_A(x), \mu_B(x)]$. In this ARF model the AND fuzzy operation is used. The AND, OR and NOT can be used in the following way:

$\mu(cond_1 AND\ cond_2 AND \ldots cond_n = MIN(\mu(cond_1), \mu(cond_2), \mu(cond_n))$.....(175)

$\mu(cond_1 OR cond_2 OR \ldots cond_n = MAX(\mu(cond_1), \mu(cond_2), \mu(cond_n))$.....(176)

$\mu(NOT\ cond_1) = 1.0 - \mu(cond_1)$.....(177)

The implication of a rule is described by following the flow diagram in Figure 4.38

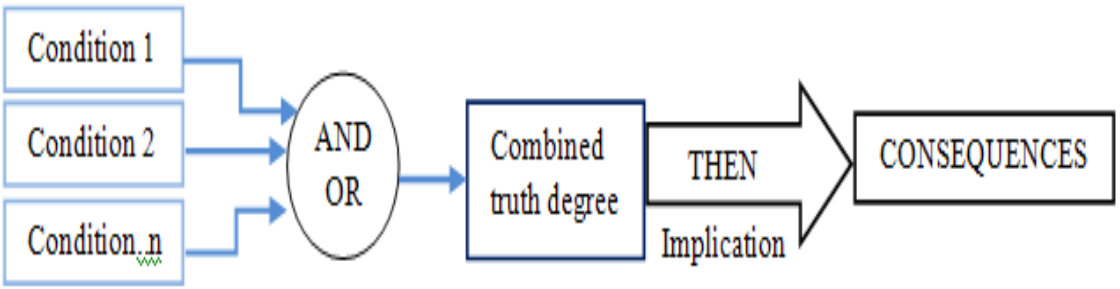


Figure 4.38: Rule Implication.

4.9.4. The Defuzzification Method

The defuzzification method translates the output from the fuzzy inference engine into a Crisp output. The defuzzification process uses a variety of methods but the two most popular are: Centre of Area (COA), and the Mean of Maxima (MOM) (Yager R. *et al*., (1994), Mendel J. M., (1995)). The output of the defuzzification process is a single number or Crisp value. In the COG that we applied, the relevant equation is set out below (Pandey S, *et al*., 2015).

$$\text{COG (Y)} = \frac{\sum \mu_y(x_i)x_i}{\sum \mu_y(x_i)} \quad \text{.....(178)}$$

Where,

$\mu_y(x_i) =$ Membership value in the membership function.

x_i = centre value of membership function.

4.10. Chapter Summary

Diagnosis of ARF should be carried out promptly to protect patients' further heart damage. Under prevailing conditions in Nepal, doctors often find this complicated and difficult. Therefore, our model described in this chapter is designed helps to identify ARF at an early stage. In our ARF diagnosis process, the practitioner needs to know about the basic information on which a diagnosis has been made as this is essential for him/her to know if the diagnosis made was based on the right grounds. To achieve this, users need to understand all aspects of the program, in effect the finally developed application.

In the medical diagnosis process KBS is a powerhouse consisting of expert knowledge embracing all relevant knowledge gathered from practical experiences and theoretical understanding of a particular domain and its facts and rules. Once to hand, these will prove to be positive assets for solving any particular problem supported by valid justifications. Therefore, for the clinical decision support system KBS it is an irreplaceable and supportive tool. It is especially significant for designing and developing a CDSS system appropriate for use by inexperienced end users. Temporal logic represents symptom-to-symptom relations and the symptoms and diseases relations for the specific diseases. Thus, temporal information is a valuable asset, which can be used to provide clear-cut, unambiguous justification for making particular diagnoses. In essence, fuzzy logic can be used to deal with uncertain or imprecise data, by analysing the process of human reasoning.

Initially we propose a knowledge-based model where we capture the required information for the diagnosis of ARF. Then we present a diagnosis model that is divided into four stages and required signs and symptoms separately defined for each stage. To achieve this we designed a rule for the diagnosis of ARF at different stages and severity levels in accordance with the KBS. A Rule Pattern Mechanism was designed in order to fire appropriate rules. A Rule Selection Mechanism was added to be able select the required rules from all severity levels that might be encountered in ARF. If presented signs and symptom do not match patterns within the rule-based systems, then the New Rule Formation process produced to enable a rule in the rule-based system, which experts can accept, reject or modify as required.

Later we designed a Temporal Model to show the relationship between the symptoms and ARF. Then we analysed the ARF symptoms and the usual development progress timeframe. The resulting temporal rule-based system was introduced to explain the relationship the symptoms with ARF using linguistic measures of perceived severity: absolutely positive, very positive, relatively positive and suspected. Then we applied fuzzy logic to handle the uncertainty factor as well as to facilitate making a final decision over an ARF case. A Fuzzy Model is designed by applying the knowledge from the ARF's expert support mechanism namely: set up the input parameter; selection relevant linguistic variables and set the fuzzy value ranges. In this way, the final diagnosis of ARF reveals the percentage of severity level of the ARF in the given case backed by a full explanation and justification a medication plan whether oral or injection; appropriate dosages, duration, allergy information and other necessary clinical guidelines. The chapter focussed on description of a diagnosis process for ARF, which we consider appropriate for the Nepalese environment and lifestyle. In Chapter 5, we discuss development of applications and usage of a proposed Hybrid Approach.

Chapter 5: Research Design and Development

"If the facts don't fit the theory, change the facts" – Albert Einstein.

5.1. Introduction

This chapter describes our research analysis, the design and development process and prototypes of the Acute Rheumatic Fever (ARF) Diagnosis System Application. The design architecture, algorithm of all processes, domain knowledge modelling, source of knowledge, collection of data, prototype designing, inference engine, user interface, database, technology etc. are examined. The prototype in design and development was based on the three-layer architecture, which is also discussed in this chapter. **Our main aim in this chapter is to prove our concept and determine whether the Hybrid Approach can be applied usefully for the diagnosis of ARF within the Nepalese setting or not.**

The chapter is organised as follows: Section 5.2 design and development of ARF prototypes; Section 5.4 concerns application development architecture and functionalities; Section 5.6 the ARF application development platform; Section 5.7 the User Interface; Section 5.8 the KBS/Boolean Rule Model development process; Section 5.9 the Temporal Model development process; Section 5.10 the Fuzzy Model and diagnosis process; Section 5.11 medication and treatment processes and finally Section 5.12 summarises the whole chapter.

5.2. Design and Development of the ARF Prototype

The methodology used for designing and developing our ARF diagnosis model was discussed in Chapter 4. The design and development of any clinical decision support system is a very time consuming process as it requires keeping a balance between the users and application requiring excellent programming skills to apply to the proposed Hybrid Approach. This ability is essential for developing an ARF application, designing, and maintenance of the knowledge-based system.

During the literature review, various system development methodologies were identified which are readily available and that could be applied to the development of a system, such as a structured system analysis and design; a waterfall model; rapid application development; dynamic system development; object-oriented programming; agile methodology; extreme programming; spiral development; iterative and incremental

development etc. In our research, a Rapid Application Development Method (RAD) eventually was selected for the development of an ARF Diagnosis Application. The ARF Diagnosis Application was developed on the basis of modules. Each module had a process with particular functionalities and responsibilities for completion of assigned jobs. For example in the "KBS/Boolean Rule Model" there are four different processes (Chapter 2, Section 4.6) but it was decided to use the "Search and Match Case" as most appropriate for identifying the various stages of ARF. The ARF diagnosis development process was adopted from Efrain Turban and Jay E. Aronson as shown in Figure 5.1 (Efrain T. and Jay E. A., 2001).

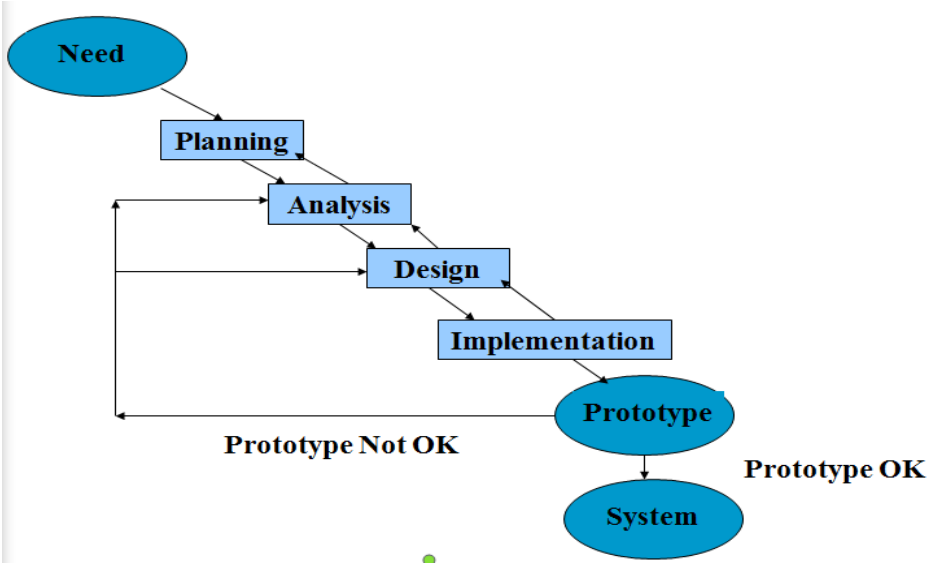


Figure 5.1:The Process of Prototype Development

In the development of a prototype, the analysis, design and implementation phases can be performed concurrently and can switch back to any phase as many times as required. The reasons for applying the prototype development method were: 1) during the ARF's application development process, NHF experts were involved in every phase of development; 2) NHF experts can easily understand what their application looks like and functionalities of its application in a Nepalese setting; 3) NHF experts quickly provided the feedback; 4) ARF's diagnosis application was developed quickly; 5) it was easy to modify the application; 6) the users' reaction time was short; 7) NHF experts and users can understand the application's process, user interface, functionalities of each component of the application as well as application information, data pattern, etc. The following points were considered in the development stage:

- Selection of development tools and their environment (tools and environment are discussed below).

- Design and create the ARF architecture for the diagnosis application.
- Selection, design and development of the database schema (back-end) to create and store Boolean rule-based, Temporal Lookup Table, temporal rules, patient data, and the application users' information etc.
- Design and develop components suitable for the user interfaces based on the community rural health workers' and NHF expert guidelines.
- Design and prepare help/guideline files (the detailed information of ARF's symptoms and treatments (including image, video, audio, questions and answer booklet, slides etc. in Nepali and English languages) based on the NHF expert inputs.
- Design and develop all model processes and sub-processes according to the application development architecture and proposed Hybrid Approach.
- Design and create user documents the user manual and technical documentation.

5.3. The ARF's Application Development Process

The development process of the application was design, development, testing, validation and implementation. The testing, validation and implementation are discussed in the next Chapter 6, Experiment and Evaluation. The summary diagram of the development process is presented Figure 5.2 with the main tasks listed.

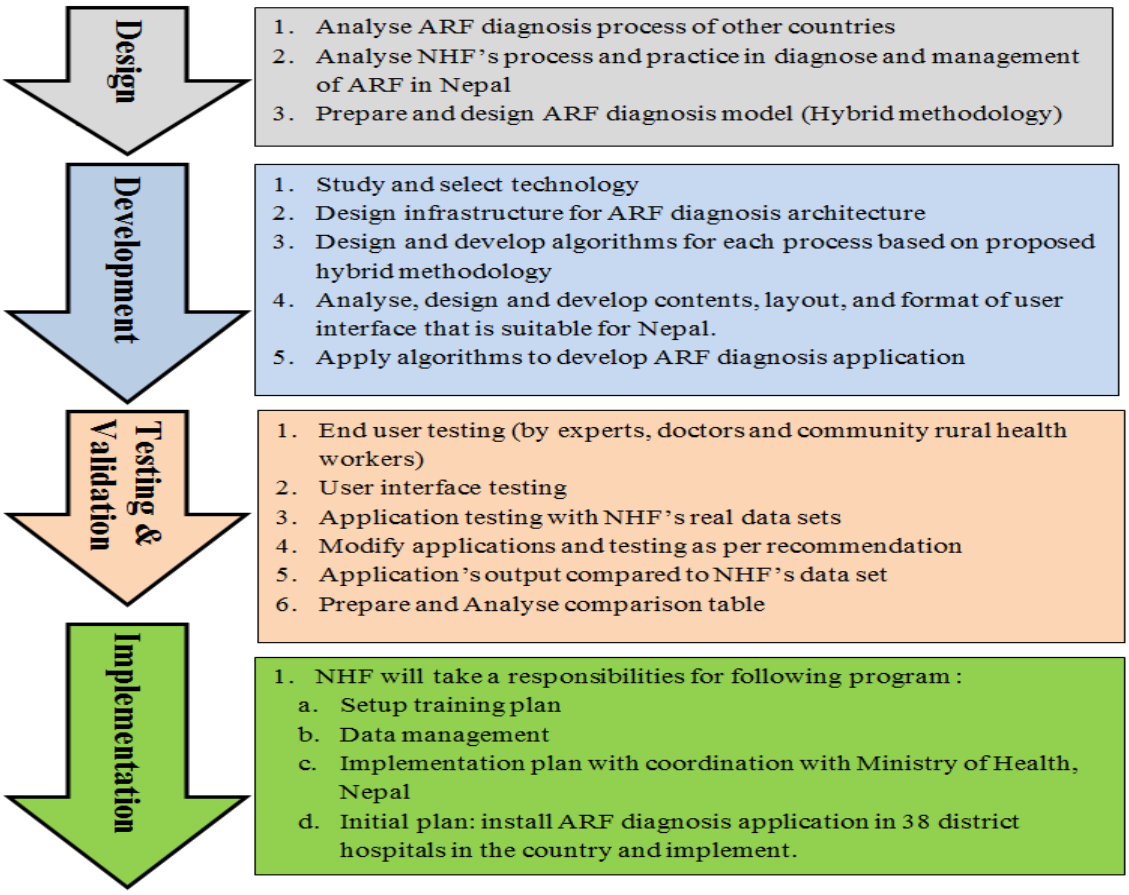


Figure 5.2: Summary of the ARF Application Development Process

5.4. ARF Application Architecture and Functionalities

Figure 5.3 demonstrates how the application design architecture and functionalities used a simplified interface to enable experts or knowledge workers to incrementally add new rules, modify existing ones and delete those that were deemed obsolete. These rules were formulated in such a way that all possible cases of ARF were considered. The New Rule Formation (NRF) process can be invoked automatically if a rule has not been found on the database. The NRF generates a new rule based on the KBS and stores it on the database. Later, experts can observe and verify newly added rules. In addition, experts can modify the rule if required.

Only valid users can access the application. After successful login, the user (community rural health workers, inexperienced doctors mainly) can register the patients and once the registration process has been completed another window will appear showing the list of signs and symptoms of ARF so that further process can start. The following system architecture (in Figure 5.3) for ARF and it shows the functionalities and detailed process of the ARF Diagnosis Application. Detailed discussion of the process is given below in Figure 3.

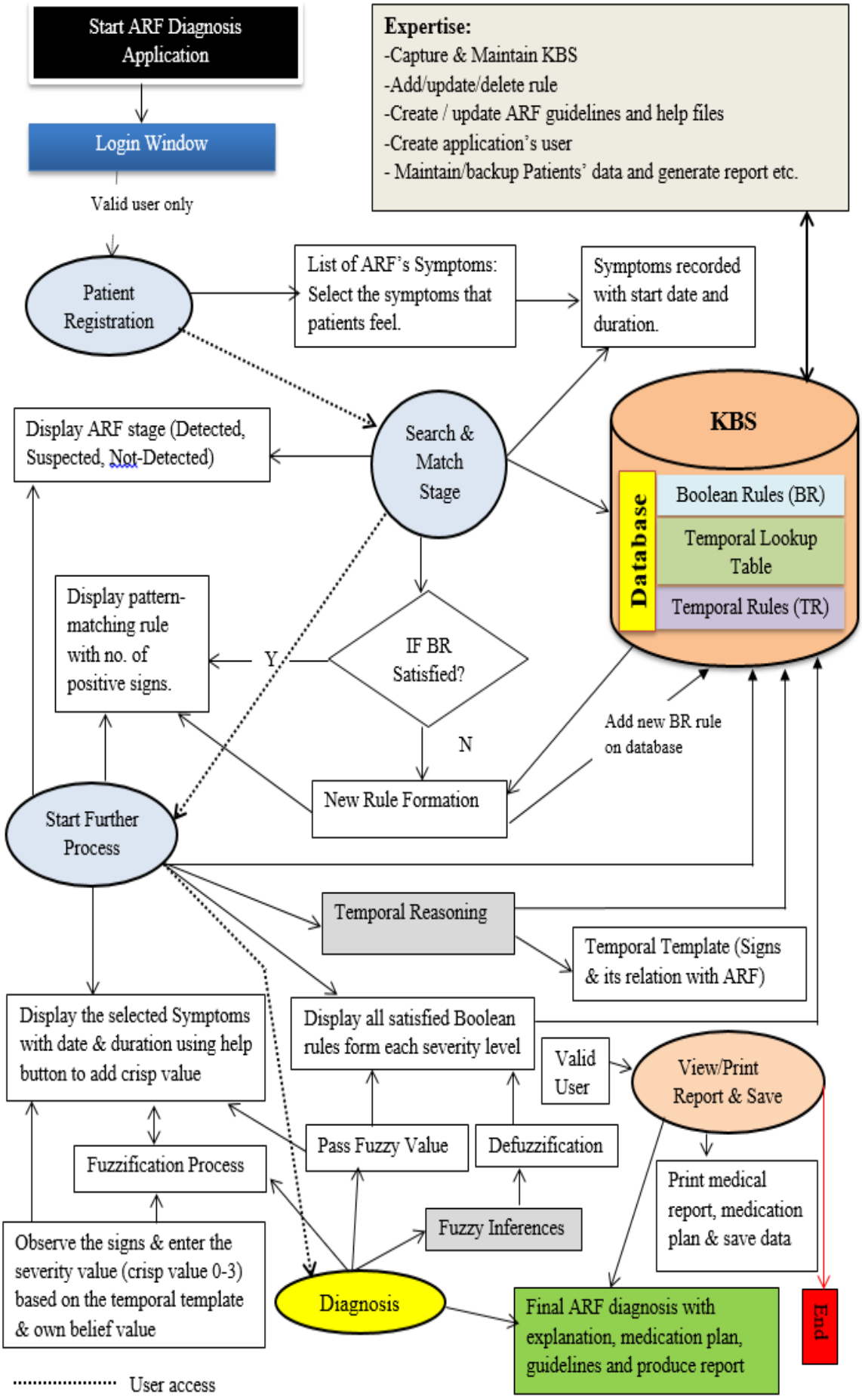


Figure 5.3: The ARF Application Architecture and Functions

The ARF Diagnosis Application's process is as follows:

5.4.1. User login

This process will check a user's authentication or check if he/she is an authorized user. Only valid users can access the application.

5.4.2. Patient Registration Process

The new patient's personal information is recorded on the database and he/she is issued a patient identification number.

5.4.3. Search and Match Process

The functionalities of this process are: 1) identify and display ARF stages; 2) descriptive explanation of ARF symptoms (capture the symptoms start date, duration and time sequence of symptoms during the explanation of symptoms by patients, or doctor/community rural health workers could ask questions about each symptom's start date and duration and place in order; 3) check the start date and duration of each presented symptom; display the message if date and duration have not recorded; 4) Rule Pattern Matching 5) New Rule Formation; 6) Rule Selection Mechanism and 7) clear screen, add/remove symptoms. The algorithms of 1, 4, 5 and 6 are described in the KBS/Boolean Model section below.

5.4.4. Start a Further Process

The functions of this process are: 1) Temporal Lookup Table; 2) temporal reasoning: a temporal reasoning process which is responsible for preparing the Temporal Template based upon the presented symptoms, temporal information and temporal rule. Temporal rules were created based upon the Temporal Lookup Table. The Temporal Template provides precise information about a particular symptom and its relationship with ARF in linguistic terms. Essentially: Absolutely Positive for ARF; Very Positive for ARF; Relatively Positive for ARF and Suspected for ARF. The fuzzification process itself: this process is responsible for generating a fuzzy value for each recorded symptom based on a severity value (Crisp value 0-3) given by doctors or community rural health workers. The monotonically increasing linear membership function is applied for the fuzzification process. The algorithm is described below in the Fuzzy Model section below.

5.4.5. Diagnosis and Medication

This process is responsible for converting a fuzzy value into a satisfied Boolean rule and performing the fuzzy reasoning process. The Root Sum Square and Center of Gravity Area methods are applied for the fuzzy inference and defuzzification process respectively. The final diagnosis of ARF will be made by providing the explanation/justification of diagnosis, severity level of ARF in percentage, medication plan (oral or injection treatment, dosages, duration, allergies information etc.), and patient report. The processes of fuzzy reasoning, diagnosis and medication plan are described below in the Fuzzy Model section.

5.4.6. Save Data and Report and Print

This process will insert the records on the patient database and print out the patient's medication report. A sample of the patient report card is given in the next Chapter 6, Experiment and Evaluation and Fuzzy Model section.

5.5. Domain Knowledge Modelling

The development of a suitable and usable clinical decision support application requires sufficient information about particular problems, where rules can be formed and applied easily. This knowledge is the backbone of a CDSS and for effective use of the CDSS knowledge base; it must have as much sufficient, complete and reliable information as possible. Thus, it can be seen that knowledge acquisition and presentation are important tasks and essential for the development of a knowledge-oriented CDSS.

In the development of ARF diagnosis, understanding the ARF symptoms along with diagnosis and treatment procedures were underlined as key points. Once the domain specific Knowledge has been captured then it has to be transferred into computer as interpretable information using the proposed knowledge representation method. We have captured all required knowledge from various sources concentrating on WHO, Jones' Criteria, World WHF, NHS Choice (UK), internet, books, journals and guidelines from Australia and New Zealand's guidelines as well as immensely helpful guidelines from the NHF's experts. Based on this knowledge formulated a set of rules: Boolean rule, temporal rule, identification of ARF stage, severity of ARF etc. in order to develop methods for diagnosing ARF in Nepal.

We recognised that there are many useful computerised knowledge acquisition tools: Unified Medical Language System (UMLS) as developed by Achour *et al*., (2001). KRITON, which is a Hybrid method that combines AI and cognitive science methods for an automatic knowledge acquisition tool for use by experts, discussed by Diederich J. *et al*., (1987). NHF has the experts and ARF diagnosis guidelines, treatment practice and procedure that were made available for our use so that we did not need to use any computerised knowledge acquisition tool for our own work. We used and formulated all required rules according to NHF guidelines. I visited Nepal three times (2011, 2014, and 2015) to understand the ARF situation, to develop a new ARF Diagnosis Application and evaluation application. We had meetings and focus group discussions with NHF experts regarding creation and validation of rules for an innovative diagnosis and medication plan for ARF. We also communicated frequently via email and phone for additional information to enhance our research and development programme.

The research programme has already been introduced in Chapters 3 and 4, discussing the symptoms of ARF, diagnosis criteria, the other countries where there are existing procedures for diagnosis of ARF and our proposed new method for diagnosis of ARF. In the following sections, we focus on development of each component of the Hybrid Process.

5.6. The ARF Application Development Platform

The ARF application development environment was Visual Studio 2012 .NET framework, on Windows X operating system. The programming language we used was C#, SQL. The Relational Database Management System (RDBMS) was MS Access 2010. Other software used was MS word, MS Excel, Acrobat Reader which was used for design and development of the ARF Diagnosis Application.

The .NET framework is not a language; it is a software platform where languages are neutral. Multi-language support, cross-platform interoperability, reuse of code, automatic resource management, safety and security, debugging and error handling etc. are a few of the many capabilities of the .NET Framework. The .NET framework is a development environment that supports different programming languages and libraries to work together for the development of a Web-based and Windows-based application within the Microsoft environment (Microsoft 1 & 2).

The .NET Framework's main three components in the class library are ADO.NET, ASP.NET and Windows Forms which developers use for the development of robust Web-based and Windows-based applications. ADO.NET and XML provide various functionalities that are used for data access. The XML Web Services allow applications to communicate and share data over the internet, enabling the .NET framework to provide tools and libraries that permit the programmer to develop applications faster and more easily. The .NET Framework architecture was adopted from Microsoft and presented in Appendix 5.1.

The .NET Framework is well suited to quick application developments because it has various built-in classes that can be applied easily and there is a helpful reuse code in the application development process. Similarly, applications in any .NET compatible language can readily interact with each other.

5.6.1. Hardware / Software Requirements

The requirements of hardware and operating system for the .NET Framework 4.5 are shown in Tables 5.1 and 5.2 (Microsoft 3).

Table 5.1: Hardware Requirements

Hardware Requirements	*Version 4 full*	*Version 4 client*	*Version 3.5*	*Version 3.0*
Processor				
Minimum	1 GHz	1 GHz	400 MHz	400 GHz
Recommended	1 GHz	1 GHz	1 GHz	-
RAM				
Minimum	512 MB	512 MB	96 MB	96 MB
Recommended	512 MB	512 MB	256 MB	256 MB
Disk Space (minimum)				
32-bit	850 MB	600 MB	280 MB	280 MB
64-bit	2 GB	1.5 GB	610 MB	610 MB

Other requirements: Monitor, Sound box, Printer, Scanner, external hard drive or any other storage device, Office Products, Acrobat Reader, Windows Vista or Windows 7 Operating System (OS).

Table 5.2: Operating System Requirements

Operating System	*Supported editions*	*Preinstalled with the OS*	*Installable separately*
Windows 10	32-bit & 64-bit	The .NET Framework 4.6	--
Windows 8.1	32-bit, 64-bit and ARM	The .NET Framework 4.5.1	The .NET Framework 4.5.2 The .NET Framework 4.6
Windows 8	32-bit, 64-bit & ARM	The .NET Framework 4.5	The .NET Framework 4.5.1 The .NET Framework 4.5.2 The .NET Framework 4.6
Windows 7 SP1	32-bit & 64-bit	--	The .NET Framework 4 The .NET Framework 4.5.1 The .NET Framework 4.5.2 The .NET Framework 4.6
Windows Vista SP2	32-bit & 64-bit	--	The .NET Framework 4 The .NET Framework 4.5.1 The .NET Framework 4.5.2 The .NET Framework 4.6
Windows XP	32-bit & 64-bit		The .Net Framework 4

5.6.2. C# Programing Language

C# is a modern object oriented programming language derived from C and C++. It was designed specifically for the .NET platform as a language that would enable programmers to migrate easily to .NET. Microsoft introduced C# along with its .NET strategy in 2000. C# is a sophisticated, well-designed and popular object-oriented programming language. C# has various useful features such as advanced code editor, suitable user interface designers, debugger, etc. that enable programmers to construct different types of secure and robust applications which run on the .NET Framework. C# can be applied to design and create Windows client applications, notably XML Web Services, distributed components, client server applications and other database applications. The relationship of C# and .NET framework is adopted from Microsoft and presented in Appendix 5.2.

C# is suited to many of our needs and is being applied for the development of various kinds of applications: computer games, operating systems and compliers, Web-based applications, laboratory and medical information systems, any other industry-based applications. C# is a European Computer Manufacturers Association (ECMS) and International Standard Organization (ISO) standard. It is a powerful multi-paradigm programming language.

The reason for using the .NET Framework and C# programing language to develop our ARF Diagnosis Application was to prove conclusively my own concepts by developing a workable prototype. The .NET Framework and C# have good facilities and tools, such as various classes of library and integrated development environments, which provide the means for rapid application development. Another reason for choosing C# was its ease of use thereby helping to create the user interface and suitable for use by novice computer users. Ultimately, the whole of our ARF Diagnosis Application coding was done using C# and SQL.

5.6.3. The ARF Diagnosis Application's Architecture Layer

This application was developed by applying a three-layer concept. The three-tier architecture enables increased performance, easy maintainable code, flexibility and reusability. The application was deployed using C#, window forms on the front-end and MS Access as back-end. The front-end consists of a variety of forms: login, patient registration, check-up, patient history, diagnosis, medication, report, help/guidelines etc. The components of the layered architecture are given in Figure 5.4.

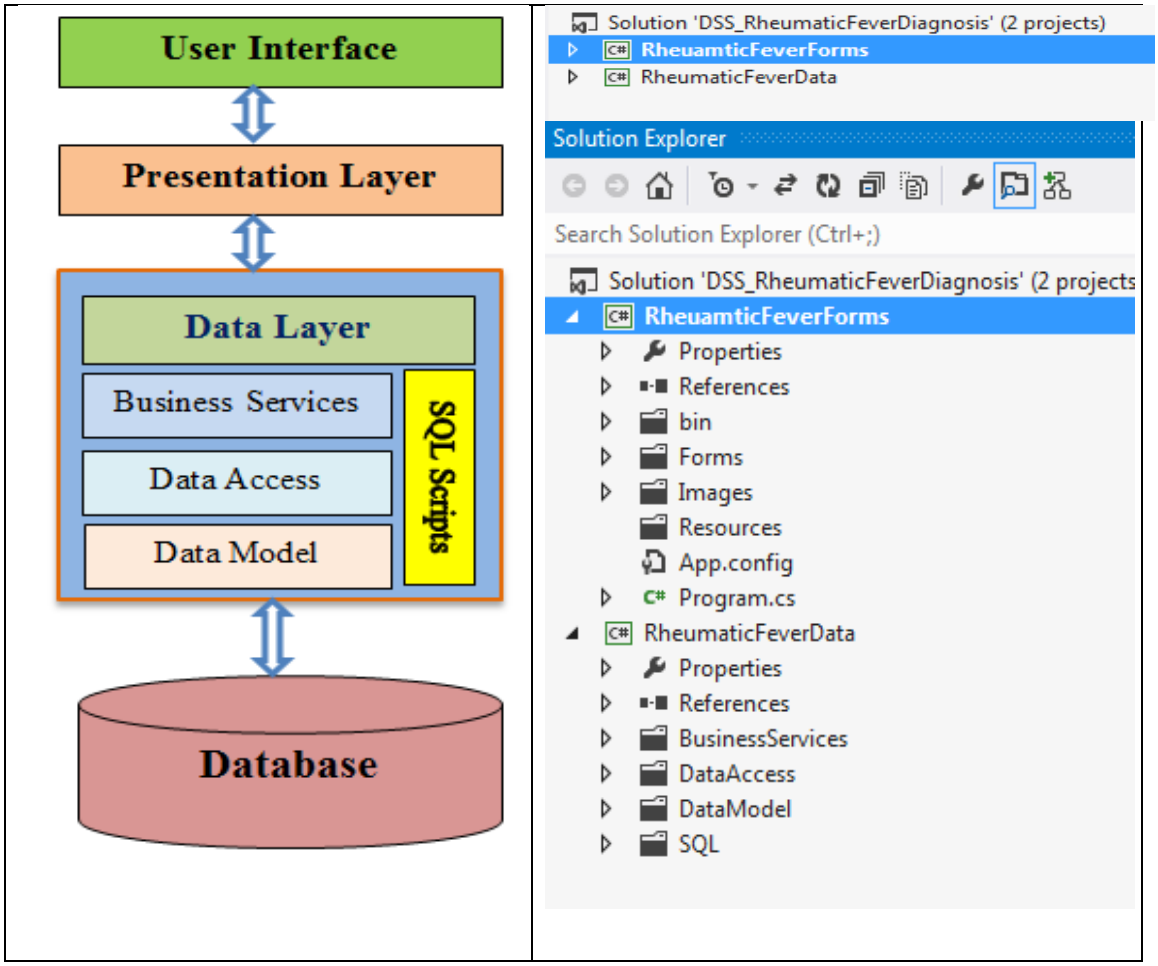


Figure 5.4: The ARF's Architecture Layers

The ARF Diagnosis Application was developed using the following software environments:

- Development environment: Visual Studio.NET 2012.
- Framework: .NET Framework 4.5.
- User Interface: Windows Forms.
- Programming language: C#.NET .
- Data Access: ADO.NET.
- Database: MS Access 2010.
- Others: Windows operating system, acrobat reader, MS office product, outlook.

5.6.3.1. The Presentation Layer / Graphical User Interface (GUI)

The presentation layer consists of the components of the user's input and information display. This layer manages the user's interaction with the ARF application. Therefore, the presentation layer is comprises screens of various programs or forms that are associated with suitable GUI components. Each GUI's components have code-behind them, which handles the assigned instruction appropriately. This layer delivers the information to the user and to the application. The user interface's components have visual elements that display information, guidelines, result and so forth to the user as well as being able to accept instructions from the user. The presentation layer is responsible for the implementation of any of the user's instructions.

Design of the user interface or presentation layer is dependent upon the user's particular requirements. In development of our research, we used Windows Forms that are part of the .NET framework, and we found that it was well suited to this application.

5.6.3.2. Business Layer /Services

This layer implements the functionalities of the ARF application including capturing the relevant business logic. The business logic is concerned with the retrieval, processing and management of data. It also ensures the consistency and validity of data. User interface components collect the given information and instructions according to the user's input and transforms them into the business layer, then the application will use this information to perform any requisite business process.

5.6.3.3. Data Layer

This layer has other sub-components: business service methods, data access logic, and data model that all require Structured Query Language (SQL) coding for ARF Diagnosis Application. Business service is a method that is used to communicate data access. This service is called the "data access method". It delivers results into the presentation layer. The data model consists of a set of entities (or table) where records are stored. The SQL code is a set of statements that is used to manipulate the data.

Data Access is defined as the data access task, which enables access to data stored on the database through a SQL code.

5.6.4. The ARF Application's Components

The ARF's application is developed and implemented in the three-layer architecture, which was mentioned previously. The components of ARF were developed based on the algorithm approach. The main components of the application are given below:

1. Inference Engine: The inference engine is responsible for:

1) Interaction between user's inputs and applications: search rules, match rules, insert patient record, modify record, view help file etc.
2) Inference engine matches the rules; if a rule has not been found on the database then it will automatically add the rules on the rule-base.
3) Invoke Rule Selection Mechanism and display all satisfied rules.
4) Produce the Temporal Template through temporal reasoning.
5) Automatic diagnosis (fuzzy processing) of an ARF case, medication plan; produce patient report.
6) A Knowledge-based system for organizing and maintaining all Boolean rules, temporal rules and Temporal Template.

3. **Knowledge-based**: Organized and managed ARF symptoms, ARF diagnosis procedure, medical planning, supporting information, Boolean rules, Temporal Lookup Table/Rules and Temporal Template.

3. Data Set: We used NHF's survey dataset and based on this dataset we designed and developed the database system for the development of the ARF application. Examples are: understanding the entity; the relationship between entities; identifying attributes; integrity constraints etc. Another benefit of using of this dataset was to make an evaluation of the application based on a real datasets. Detailed information about the datasets and variables are discussed in the Database section below.

5.6.5. Database

We established a project Database using a collection of relevant inputs and for management we used a database management system (DBMS) as the software for management and control as well as formal access to the main database. Three phases: 1) conceptual; 2) logical and 3) physical database design, were applied in order to design the database system itself (Connolly T. M. and Begg C.E., 2010). DBMS is software that manages. It defines, creates, maintains and controls access to the database.

Various DBMSs are available including Oracle, SQL Server, MS SQL, Sybase, MS access etc. During development of our research, we applied MS Access as a relational database with standalone architecture. The reason for this choice was that in Nepal, almost all hospital computers have Microsoft Access databases and most of the users (those who are dealing with ARF cases in particular) are familiar with MS Access database systems. Another reason is that the structure of ARF applications is not large so MS Access is sufficient to manage the rules and patients' data. The designed entities and their descriptions are given in the next section.

5.6.5.1. Patient Entity

A patient data table is used to store a patient's personal information including, the presented ARF symptoms, physical examinations, laboratory reports and diagnosis information together with any related medication plans. Table 5.3 shows the structure of patient entity.

Table 5.3 : The Structure of Patient's Entity

Attributes	Data type	Descriptions	Constraints
PatientID	Integer	Patient Personal Identification Number	Primary Key
PatientName	Text	Patient's full name	Not null
Age	Integer	Age of patient	Not null
Sex	Text	Sex of Patient	{male, female, other}
Address	text	Address of patient	Not null
District	Text	District	
ContactPerson	String	Patient's relatives' information e.g. father, mother etc.	Not null
Mobile	Text	Contact number mobile	Not null
Home	Text	Home telephone number	
Email	Text	Contact email address	
SignsList	Memo	Present symptoms,	Not null
StartDate	Memo	Present symptom's start date	Not null
Duration	Memo	Present symptoms' duration	Not null
SeverityLevel	Text	Presents symptom's severity	{AP,MP,FP}
Height	Text	Patient's height	
Weight	Text	Patient's weight	
BP	Text	Patient's Blood Pressure	
Temperature	Text	Patient's current fever or history	
LaboratoryReport	Memo	Patient laboratory test report	
OtherObserveration	Memo	Other signs observed by doctors or community rural health workers	
Diagnosis	Text	Diagnosis of ARF	Not null
ARFSeverity	Text	Severity level of ARF	
InjectionRequired	Integer	No of injection	
Medication	Memo	Medication details	
Summary	Memo	Diagnosis detail, doctors summary and treatment information	Not null
DiagnosisBy	String	Doctors / community health workers name	Not null
DiagnosisDate	Date	Diagnosis Date	Not null

Note: FP (fairly positive), MP (moderately positive), AP (absolutely positive)

5.6.5.2. Rule Entity

A Rule Data Table will be used to store the rule base information. Tables 5.4 and 5.5 show the structure of a Rule Data Table.

Table 5.4: Structure of Rule Entity

Attributes	Data type	Descriptions	Constraints
ruleno	Integer,	rule identification number	Primary key
arthritis	Text	P : present, A : Absent	No null
carditis	Text	P : present, A : Absent	No null
chorea	Text	P : present, A : Absent	No null
sn	Text	P : present, A : Absent	No null
em	Text	P : present, A : Absent	No null
fever	Text	P : present, A : Absent	No null
arthralgia	Text	P : present, A : Absent	No null
ecg	Text	P : present, A : Absent	No null
crp	Text	P : present, A : Absent	No null
esr	Text	P : present, A : Absent	No null
throat infection	Text	P : present, A : Absent	No null
asot	Text	P : present, A : Absent	No null
gas	Text	P : present, A : Absent	No null
rule output	Text	Severity level of ARF	{Severe, Moderate, Mild or Suspected}
explanation	Memo	Explanation of rule	Not null
t_p_signs	Integer	No of total positive signs	Not null

Table 5.5 : The Structure of Rules

Rule No.	Antecedent Part													Consequent Part		
	Arthritis	Carditis	Chorea	SN	EM	Fever	Arthralgia	ECG	CRP	ESR	Throat	ASOT	GAS	Rule Output	Explanation	T_P_Signs

T_P-Signs = number of total positive signs.

5.6.5.3. Temporal Entity

A Temporal Data Table was created in order to construct a temporal knowledge base. It is used to store temporal information. Table 5.6 illustrates the structure of temporal entity.

Table 5.6: Structure for Temporal Entity

Attributes	Data type	Descriptions	Constraints
TID	Integer	Temporal identification number	Not null
Symptoms	String	Description of symptoms	Not null
AP_Start	Number	Start day for absolutely positive	Not null
AP_Stop	Number	Stop day for absolutely positive	Not null
VP_Start	Number	Start day for very positive	Not null
VP_Stop	Number	Stop day for very positive	Not null
RP_Start	Number	Start day for relatively positive	Not null
RP_Stop	Number	Stop day for relatively positive	Not null
Sus_Start	Number	Start day for suspected	Not null
Sus_Stop	Number	Stop day for suspected	Not null

5.6.5.4. Doctor entity

A Doctor Data Table will be used to store doctors' and system users' personal information including, the access level of application: user, administrator, expert and so forth. Table 5.7 shows the structure of doctor entity.

Table 5.7 Structure for a Doctor's and User's Entity

Attributes	Data type	Descriptions	Constraints
UserID	Integer	User identification number	Primary key
FirstName	Text	First Name	Not null
LastName	Text	Last Name	Not null
Sex	Text	Doctor's gender	{M,F,O}
MaritalStatus	Text	Doctor's Marital Status	
Address	Text	Address	Not null
District	Text	Address	
ContactHome	text	Contact home number	
ContactMobile	text	Contact mobile number	
EmailAddress	text	Email address	
Qualifications	text	Highest Qualification	Not null
Training	Memo	Training information	
Specialisation	text	Specialization	
WorkExperience	text	No of year	Not null

Hospital	text	Working Hospital / Clinical Name	
Position	text	Job Position	Not Null
MedicalNo	text	Medical Registration Number	
ReferenceName	Memo	Reference person name or later from Lecturer, workplace	Not null
User Name	text	Name of doctors	Not null
Password	text	Password	Not null
User Level	text	Admin user, user, Both	Not null
RegisDate	date		Not null

M=male, F=Female, O=other

5.7. User Interface

User Interface is also known as Human Computer Interaction (HCI), which incorporates social science, cognitive science and information technology. During our research, we noticed that the common principles of user interface design are: simplicity, consistency, visibility, familiarity, recoverability, navigation, user guidance, affordance, effectiveness, safety, security, user diversity, command language, natural language and menu selection etc. The user interface is how users interact with a system or it can be the method of communication between an ARF Diagnosis Application and its user. The design guidelines of user interface are a) know the user; b) minimize memorization; c) optimize operation and d) engineers for errors, as proposed by Hansen in 1971. Further information on good interface design and software design guides are found in Mayhew and Shneiderman, (1992).

A good user interface needs to match the skills, experience and expectations of the users. Therefore, during the ARF designing process we needed to understand the target users because the user might have short term memory (this is human nature), users can make mistakes, users are different (physical capabilities, mental limitation) and what they like can be very different. We also needed to understand the choice of interaction and layout such as a navigation method, colour, font, font size, picture, background colour, text, audio, video, other related information and other similar features.

During the design of the user interface process, we had to focus on how to design and develop a robust user interface that would suit the Nepalese setting, life style and context. The user interface had to be appropriate capture of patient's symptoms, representation of user's queries, analysis, process clinical tasks (diagnosis of ARF) and produce the result, in effect ARF medication, in an efficient way. We developed the application in the user-centred design approach to handle questions such as what do they like, what do they not like etc. These were analysed by questions, answers, and various other interview methods.

During the application development process, users could look at and appreciate the interface and those were able to provide feedback with suggestions, without any appreciable delay. We held several focus group discussions with NHF experts regarding scope and design of the user interface. As a result, it was concluded that the user interface had to be suited specifically for the Nepalese setting, lifestyle, environment and guidelines, with help files prepared and introduced in the Nepalese language. Discussions were held to address issues related to content, layout, format of each form and means for reporting on the ARF application. Similarly, images, sound, video and other supporting information such as help and guidelines in English and Nepali. The input form design, size, button, colour, message box, warning information etc. were considered in depth as key components of the ARF interface development process. In addition, matters relating to accessibility, usability and user friendless were thoroughly considered during research for the design of the user interface. According to the International Standards Organization (ISO), it was emphasised that *"The usability of a computer product is the extent to which the product can be used by specified users to achieve specified goals with effectiveness, efficiency and satisfaction in a specified context of use"*, (ISO 9241, 11: 1994). According to Nielsen (1993), usability means IT that applications should have "*learnability", be* easy to learn*; "efficiency" and "memorability" that is to say* easy to remember the process and steps of application must be *"error free"* and offer *"satisfaction"*.

We recognised that in the ARF Diagnosis Application, the user interface must be very easy to use because the Nepalese users in rural areas are generally not familiar with computer-based applications. We therefore designed a user interface that was as simple as possible and that included explanatory functionalities, proper guidelines for analysing symptoms, appropriate and less navigation options and minimum forms to access for the diagnosis processing. The ARF Diagnosis Application have various types of input and output forms for example: user logon, patient's registration, view patient's history/report, diagnosis, patient's report, view/update rules etc. Only registered users can use the

application. NHF experts are permitted to update, modify, delete, and add rules etc. In effect, experts are the people responsible for managing and updating all the rules and help/guideline information.

Input Process and Output

The input process and output of each model are described below with a related algorithm. The diagram of input, process and output is provided in Figure 5.5.

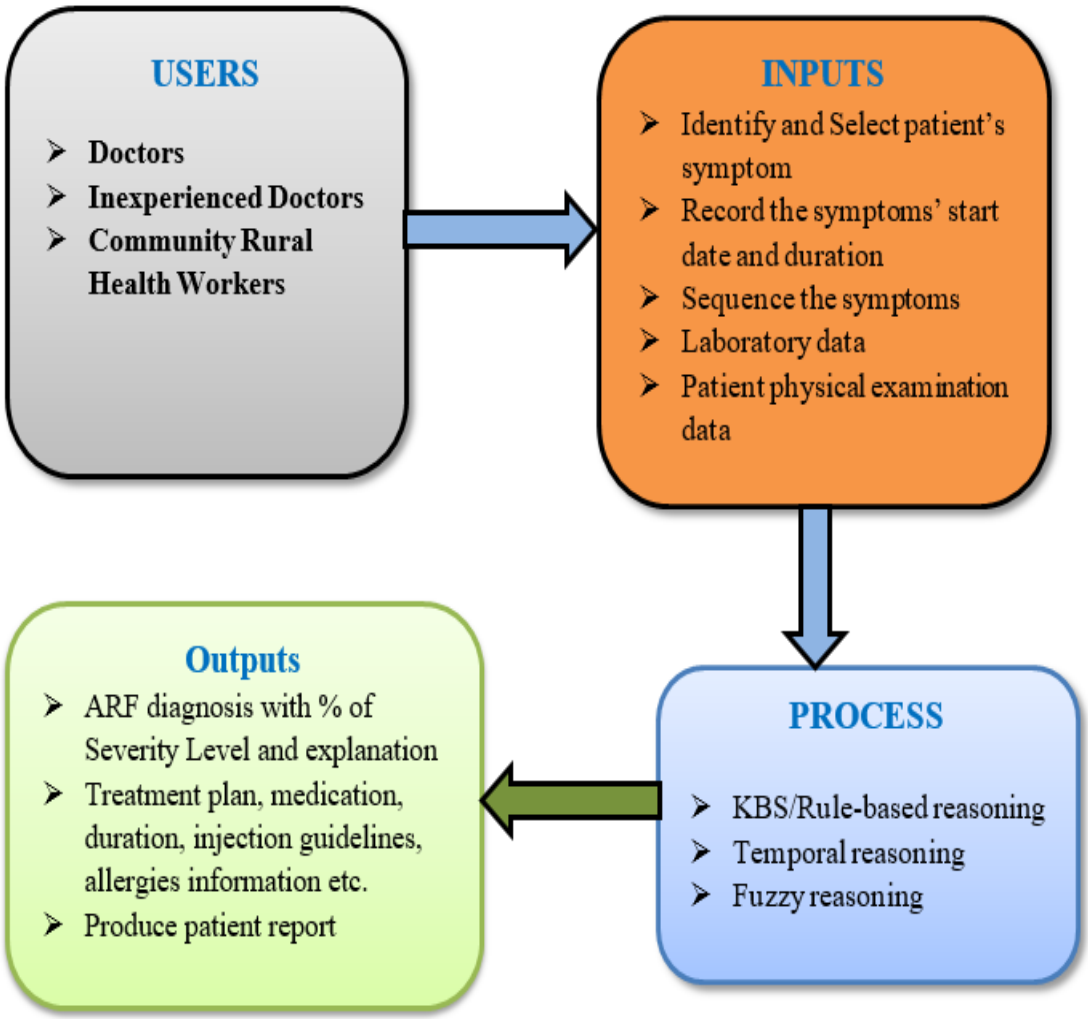


Figure 4.5 :Input Process and Output

5.8. KBS/Boolean Rule Model: the Development Process

Search and Match Process

The Search and Match process is responsible for the following computations:

1. Identify ARF stage: A Matrix Decision Table is applied to identify the ARF stages, which are discussed further in the Research Methodology, Chapter 4. Identification of the ARF stages in the ARF development process is described by the algorithm set out in Table 5.8.

Table 5.8: Identify ARF stages

Steps	***Development Process***
Step 1:	**START** Process
Step 2:	Define array and store all selected signs and symptoms.
Step 3:	Create three memory variables to keep the number of major, minor and essential, symptoms from array (which is defined in *Step 2*)
Step 4:	Read all symptoms from array.
Step 5:	Check, whether all symptoms are read from array?
Step 6:	IF *NO*- checks and matches the signs with KBS (ARF manifestation) and identify the satisfied sign then increment value by 1 in appropriate memory variable for example major += 1 or minor += 1 or essential += 1.
Step 7:	Go to Step 4 until the *Step 5* has not been answered *YES*
Step 8:	If *Step 5 YES Then*.
Step 9:	Read the value from three variables (major, minor & essential) and apply Decision Matrix Table, to prepare the identification stage of ARF.
Step 10:	Display ARF stage either in *Detected* or *Suspected* or *Not-Detected.*
Step 11:	**END** Process.

2. **Rule Pattern Matching (RPM):** the RPM process engages automatically, after identifying the correct ARF stage. The RPM will search and identify the exact rule that matches between the pattern and fact: observed signs and symptoms. The pattern of the rule matches the facts in the working memory then the activation of the rule will be fired. The development process of RPM is explained by the algorithm shown in Table 5.9.

Table 5.9: Rule Pattern Matching Algorithm

Steps	***Development Process***
Step 1:	**START** Process
Step 2:	Identify the patient's presented /selected symptoms.
Step 3:	Indicate all presented symptoms by "*P"* and transfer and store them into "*Sign List"* class.

Step 4:	Open and read the Rule-based System and match the pattern with *Signs List* class.
Step 5:	Check, whether rules have been read and match pattern with the *Signs List's* Class?
Step 6:	IF *NO*- go to *Step 4.*
Step 7:	IF *YES* then verify or check, Rule Pattern Matching is found?
Step 8:	If *YES* then.
Step 9:	Select and display the matching rules with no. of positive symptoms, explanation and level of severity of ARF.
Step 10:	IF *NO* then activate "New Rule Formation Process".
Step 11:	**END** Process.

3. **New Rule Formation (NRF)**: NRP process is automatically invoked, if the Rule has not been found in the rule-based system it creates a new rule in the rule-based system. The Decision Tree is then applied to generate the Rule. The detailed description of a Decision Tree is provided in Research Methodology, Chapter 4. The development process of NRF is defined by following an algorithm shown in Table 5.10.

Table 5.10: A New Rule Formation Algorithm

Steps	***Development Process***
Step 1:	**START** Process.
Step 2:	IF Rule Pattern Matching Process is not successful then.
Step 3:	New Rule Formation Process will be activated.
Step 4:	Read all symptoms from *Sign List* class.
Step 5:	Apply and match case with decision tree, which is discussed in Research Methodology, Chapter 4.
Step 6:	Identify the severity level of ARF based on the Decision Tree.
Step 7:	Display a windows form showing the presented symptoms, output (severity level of ARF), number of positive symptoms, explanation and providing the options of *ADDITION* or *CANCELLATION rule*.
Step 8:	If *ADDITION* store rule in the Rule-based System and go to *step 10.*
Step 9:	If *CANCELLATION* – STOP program and go to *step 10*
Step 10:	**END** Process.

4. **Rule Selection Mechanism:** The RSM is responsible for searching for and selecting rules appropriate for every level of a complaint: severe, moderate, mild and suspected based on a given total number of positive signs. The algorithm provided in Table 5.11 describes the development process of RSM.

Table 5.11: Rule Selection Mechanism Algorithm

Steps	***Development Process.***
Step 1:	**START** Process.
Step 2:	IF Rule Pattern Matching Process is successful then.
Step 3:	Read the value - number of positive symptoms from satisfied rule.
Step 4:	Transfer the value into an appropriate severity level (Severe, Moderate, Mild).
Step 5:	Select all the rules that matches the value with each severity level.
Step 6:	Combine rules from each severity level and store them into a memory.
Step 7:	Retrieve/display rules from memory during the temporal and fuzzy processes.
Step 8:	**END** Process.

5.9. Temporal Model's Development Process

This is a user's (doctor or community rural health worker) reasoning task, which means that when a patient gives an explanation of the symptoms, the starting date of each symptom is captured, its duration and its appearing order (which symptom was presented first and others listed in order). The user could then ask question for example: when did your symptoms start and for how long did they last (date and duration of symptom); what appears to make your symptoms worse or better; severity of symptoms, medical history, allergies, family history etc. After completing this task, the user has to summarise the information by identifying the main complaint; its severity level, start date, duration, order of appearance of symptoms etc. From these data, the user could assess the information by observing the Temporal Template for further fuzzy processes. If users have already seen such types of case then it will help them to make a more reliable diagnosis. The development process is defined by following the temporal algorithm shown in Table 5.12.

Table 5.12: Temporal Algorithm

Steps	***Development Process***
Step 1:	**START** Process.
Step 2:	Select all patient's symptoms.
Step 3:	Put questions to a patient: when did symptoms start and for how long did it last (date and duration of symptom).
Step 4:	Read the symptoms and capture the symptoms' start dates and duration from *Step 3.*
Step 5:	Complete the record of the start date and duration for all presented symptoms.
Step 5:	Prepare temporal array and store all the symptoms in temporal order with start dates and durations.
Step 6:	If not completed then go to *Step 3.*
Step 7:	**END** Process.

Temporal Reasoning

Temporal reasoning prepares a Temporal Template that describes the symptoms and their relationship with ARF using linguistic form: absolutely positive, very positive, relatively positive or suspected. The temporal reasoning process is described by following the algorithm shown in Table 5.13 and an example of output is shown in accompanying Figure 5.6.

Table 5.13: Temporal Reasoning Algorithm for Temporal Template

Steps	***Development Process***
Step 1:	**START** Process.
Step 2:	Read the temporal array (symptoms are in temporal order with start date and duration)
Step 3:	Transfer the temporal array's data into temporal rule-based.
Step 4:	**Temporal reasoning process** analyses the relation between symptoms and ARF.
Step 5:	Read and match the pattern with temporal rules.
Step 6:	Check, whether rules have been read and match patterns with temporal rules.
Step 7:	IF *NO*- go to *Step 2.*
Step 8:	Prepare table and display the Temporal Template by explaining how closely related particular symptoms are to ARF.
Step 9:	**END** Process.

Examples of a Temporal Template are illustrated in the screenshot in Figure 5.6 below and in Chapter 6, Experiment and Evaluation.

5.10. The Fuzzy Model's Development Process

The development process of a Fuzzy Model is defined in the algorithm shown in Table 5.14.

Table 5.14: A Fuzzy Model Development Process Algorithm

Steps	***Development Process***
Step 1:	**START** Process.
Step 2:	Read all presented symptoms.
Step 3:	User provide the Crisp value into symptoms.
Step 4:	Check: all Crisp value is provided, if NOT, go to Step 2.
Step 5:	Convert the Crisp value into fuzzy value.
Step 6:	Calculate the maximum value for Arthritis**:** arthritis pain, arthritis pain associated with hotness, swelling, redness, migratory / shifting arthritis.
Step 7:	Calculate the maximum value for Carditis**:** Heart Murmur, Chest Pain / Difficulty in Breathing/ Palpitation.
Step 8:	Calculate the maximum value for Chorea**:** Twitchy and Jerking Movements of Hands, Feet, Facial Muscles, Tongue and Muscle Weakness Hands and Feet.
Step 9:	Calculate the maximum value for Subcutaneous Nodules: painless lumps on the outside surface, lumps round/firm size 0.5-2.0.
Step 10:	Calculate the maximum value for Erythema Mrginatum: painless flat pink patches on the skin, not itchy or painful and has well defined borders.
Step 11:	Prepare array to store all symptoms list with fuzzy values.
Step 12:	Transfer the fuzzy values into a Satisfied Rule Table.
Step 13:	Calculate the non-zero minimum value from the Rule Table and store the value.
Step 14:	Calculate the root sum square of each rule derived for each severity level.
Step 15:	Store the value of each severity level.
Step 16:	Use centre of gravity method to defuzzification (convert fuzzy values into Crisp values).
Step 17:	Open new window and display the diagnosis of ARF with % of severity level incorporating a medication plan, guidelines, patient report card and other information.
Step 18:	**END** Process

The development process is also shown with a screenshot demonstrating the User Interface. Figure 5.6 shows a table of satisfied rules; a Temporal Template and information that are used to provide Crisp values presented in signs and symptoms.

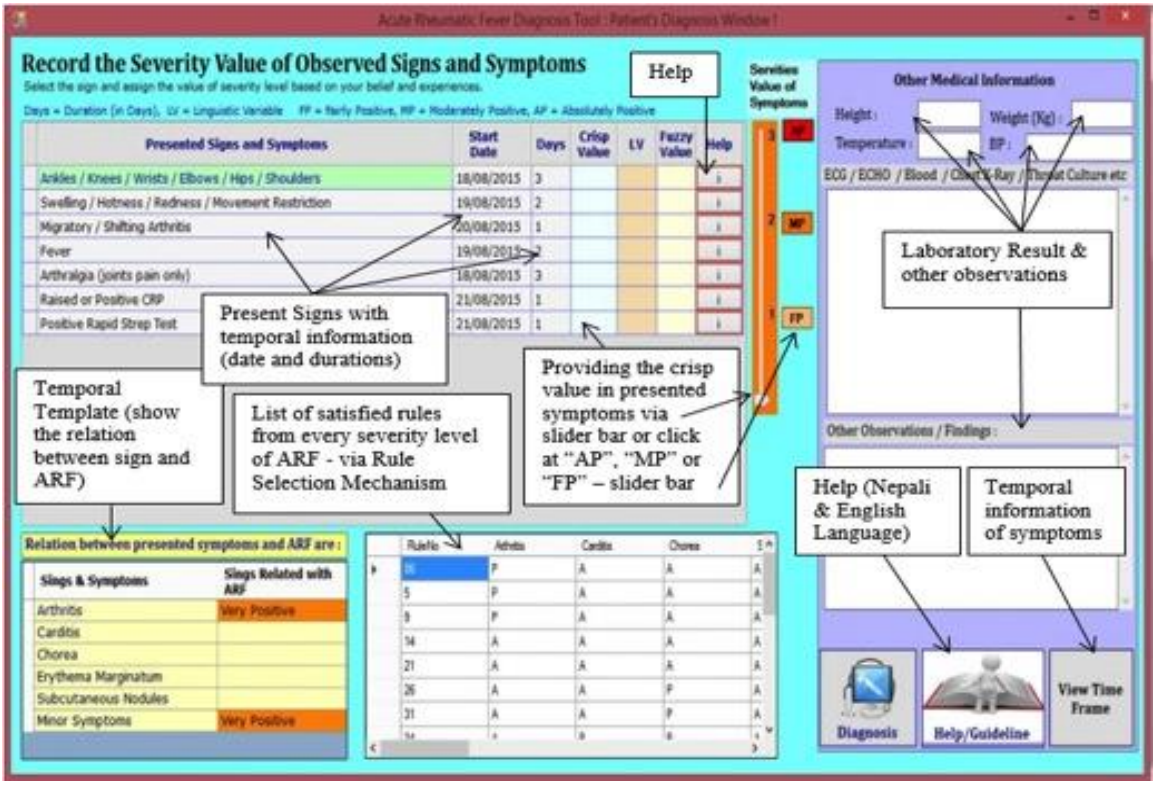


Figure 5.6: Temporal Template, Satisfied Rules, Fuzzy Process

The C# code for finding the maximum value derived from arthritis, carditis, chorea, subcutaneous nodules, Erythema marginatum are shown in Figure 5.7

```
double[] arth = { myAr1, myAr2, myAr3 };
_Arthritis = arth.Max();
_Arthritis = System.Math.Round(_Arthritis, 2);

_Carditis = System.Math.Max(myCarditis1, myCarditis2);
_Carditis = System.Math.Round(_Carditis, 2);

_Chorea = System.Math.Max(myChorea1, myChorea2);
_Chorea = System.Math.Round(_Chorea, 2);

_SN = System.Math.Max(mySn1, mySn2);
_SN = System.Math.Round(_SN, 2);

_EM = System.Math.Max(myEm1, myEm2);
_EM = System.Math.Round(_EM, 2);
```

Figure 5.7 : Sample of Code to Identify Maximum Values

The C# code to find out non-Zero minimum fuzzy value from the Rule Table is given in Figure 5.8.

```
var ty=0;
Double[] myVal = { s1, s2, s3, s4, s5, s6, s7, s8, s9, s10, s11, s12, s13 };
var minVal = myVal.Where(x => x > ty).Cast<Double?>().Min();
```

Figure 5.8 :Sample of Code of Findout Non-Zero Minimum Fuzzy Value

The C# code of Root Sum Square and defuzzification is shown following Figure 5.9 below:

```
if (dgvRuleView.Rows[i].Cells[14].Value.ToString() == "Mild")
{
    Double myMildVal = 0;
    myMildVal = Convert.ToDouble(dgvRuleView.Rows[i].Cells[15].Value.ToString());
    mild = mild + (myMildVal * myMildVal);
}

if (dgvRuleView.Rows[i].Cells[14].Value.ToString() == "Moderate")
{
    Double myModVal = 0;
    myModVal = Convert.ToDouble(dgvRuleView.Rows[i].Cells[15].Value.ToString());
    moderate = moderate + (myModVal * myModVal);
}

if (dgvRuleView.Rows[i].Cells[14].Value.ToString() == "Severe")
{
    Double mySevVal = 0;
    mySevVal=Convert.ToDouble(dgvRuleView.Rows[i].Cells[15].Value.ToString());
    severe = severe + (mySevVal * mySevVal);
}

  if (mild != 0)
  {
     squareMild=Math.Sqrt(mild);
  }

  if (moderate !=0)
  {
      squareModerate=Math.Sqrt(moderate);
  }

  if (severe !=0)
  {
      squareSevere=Math.Sqrt(severe);
  }

   resultValue = ((squareMild * 0.215) + (squareModerate * 0.505) + (squareSevere * 0.84)) / (squareMild + squareModerate + squareSevere);
   myans = resultValue * 100;

SignsList._SeverityPercentage = myans.ToString();
```

Figure 5.9 : Code of Fuzzy Processing

5.11. The Medication and Treatment Process

The Medication Treatment Process was prescribed based on the NHF's expert guidelines. We developed an algorithm for a patient's medication plan as shown in the example algorithm set out in Table 5.15.

Table 5.15: Medication Planning Algorithm

Steps	***Development Process***
Step 1:	**START** Process.
Step 2:	Has patient's ARF has been confirmed indicating a severity level.
Step 3:	IF yes, then identify the treatment plan: ORAL Treatment or Injection or Surgical Case.
Step 4:	Identify the patient's age.
Step 5:	Patient: Age > 30 OR Age < 30.
Step 6:	Injection Treatment: Injection information with dosage, apply method, no. of injection, guidelines.
Step 7:	Oral Treatment: Medication name, application method, times, duration.
Step 8:	Other medication: if any other medication, apply method, times and duration.
Step 9:	Monitoring patient progress.
Step 10:	Complete treatment / refer hospital.
Step 11:	**END** Process.

The screenshot of a Medication Plan and patient Medical Report are considered in Chapter 6, Experiments and Evaluation.

5.12. Chapter Summary

This chapter discusses the detailed design and development process of ARF's diagnosis Application. The chapter also explains how a proposed Hybrid Approach was applied in the application development phase. It defines how Three-layer architecture was employed in development and design of the ARF treatment application. It reports on the proposed knowledge-based/Boolean rule model development process, Temporal Model development process, Fuzzy Model development process, diagnosis and medication process and records how they were discussed and developed supported by examples of algorithms and coding. In summary, C# programing language in .NET framework was used for development of the application and MS Access database was used to design and

implement the Temporal Lookup Table, KBS/rules and patient data etc. This development covered ARF's stage reasoning process, Rule Pattern Matching, representing and reasoning processes, managing uncertain clinical data via Fuzzy Logic and the relationship between the signs and ARF. It was shown how the application diagnoses ARF cases by defining severity levels with a percentage at the same time as generating justifications for diagnosis and consequential medication treatment plan. Development process for the Application explained the requirement for sufficient support and help files in Nepali and English. The ARF Diagnosis Application was designed and developed in the Nepalese setting and was therefore prepared so that it would be suited to the Nepalese environment and lifestyle. The chapter closes by confirming how the proposed Application would provide effective support for community rural health workers for diagnosis of ARF in Nepal. Chapter 6 discusses Experimentation and Evaluation of our ARF Diagnosis Application in Nepal.

Chapter 6: Experiment and Evaluation

"Effective evaluation is not an "event" that occurs at the end of a project, but is an ongoing process which helps decision makers better understand the project; how it is impacting participants, partner agencies and the community; and how it is being influenced / impacted by both internal and external factors."(W.K. Kellogg, 2004)

6.1. Introduction

This chapter describes experimentation and evaluation of our ARF Diagnosis Application. It also describes overall performance of our ARF Diagnosis Application where focus is on evaluation of the proposed Hybrid Approach. It covers our experiments and evaluation of all the components of the Hybrid Approach, performance evaluation of the ARF application and testing of the knowledge base. It describes user requirements, usability of the application impacts; technical issues, sensitivity analyses and performance evaluations are discussed. It elaborates on how questionnaires, primary observations, statistical methods and confusion matrices were used to evaluate the ARF diagnosis and treatment application.

My main aim, set out in this chapter, was to review and evaluate a developed ARF diagnosis decision support system and its ability to provide effective diagnosis and management of ARF in Nepal. The objectives of my experiments and evaluation were to test and validate the four key areas of the proposed Application as given below:

1. The developed ARF Diagnosis Application meets the pre-defined NHF requirements or not. These were: i) does it suit the Nepalese environment and lifestyle; 2) does it incorporate NHF procedures and practice for the diagnosis and management of ARF in Nepal; 3) is it a reliable method for the diagnosis of ARF cases in the Nepalese setting or not.

2. Evaluate whether the proposed Hybrid Approach and its components are appropriate for the development of an ARF Diagnosis Application for Nepal or not. Evaluate the inference engines, which are responsible for the diagnosis of ARF using methods for identifying severity levels and the proposed means for justification of recommendations of medication and related treatment plans.

3. For the proposed ARF Diagnosis Application's usability, evaluate whether the application can be used by community rural health workers and inexperienced doctors and check how ARF Diagnosis Applications can handle ARF ambiguities.

4. Analyse the ARF Diagnosis Application's impact on the quality of decision-making and examine the application's impact on users: how the user feel about the application's performance; the quality of the Temporal Template; explanation and justification of diagnosis and recommended medication, structures and format of supporting information and the user interface.

The chapter is organised as follows: Section 6.3 ARF diagnosis application verification and validation; Section 6.4 experimentation and evaluation of our proposed ARF application; Section 6.5 experimentation and evaluation of the proposed Hybrid Approach; Section 6.6 ARF Diagnosis Application comparisons and result; Section 6.9 sensitivity analysis and performance evaluation and finally Section 6.10 summarises the chapter.

6.2. The ARF Diagnosis Application

A computer is not a doctor but is able to store information indefinitely, contrasting with doctors without such systems who can get tired, forget facts or knowledge and often have difficulty in retaining information over long periods. Having the ability to store information on a computer and with the means for programming / configuring them appropriately to facilitate diagnosis in the clinical domain, was proved to be an effective tool which can help decision-making and above all can provide significant benefits for the work of healthcare professionals in Nepal. Our research aimed to measure the impact of our new ARF Diagnosis Application, to see how it can provide tangible support for rural health workers in the diagnosis of ARF and management of treatment plans.

Underpinning our processes, it was recognised that CDSSs have been shown to be effective tools for helping users make effective decisions in various domains especially healthcare (Dorr *et al*., 2007). However, we were able to establish that, "Approximately 90%" of all computerized medical expert systems have not been evaluated in clinical environments (Lundsgaarde H., 1987). The ARF Diagnosis Application we developed was tested, evaluated and finally accepted by the NHF for use in their diagnosis of ARF.

Evaluation of the application involved looking closely at all the components, processes, and outputs to determine whether the application is the best approach for a particular user's needs. Application testing is a process to execute the program and then identify potential errors. Initially, several methods were developed in the field by using various expert systems for software testing, (Meyer, 2008). The testing methods for the Decision Support System (DSS) classified into two categories: 1) static and 2) dynamic following Preece (1994). In the static method, the DSS system's knowledge base was review manually by experts, so that no DSS application was required for this testing method. The static method can also be called a verification system because it checks whether or not the DSS meets the requirements as specified by particular users (Preece, 1998). The dynamic method requires use of the DSS system in order to test the functionality of a system. Dynamic methods can also be viewed as a validation procedure because it checks whether the DSS satisfies the user's actual requirement or not (Preece, 1998). These two methods were applied for evaluating our new ARF Diagnosis Application.

The NHF's members include doctors, rural health workers, healthcare assistants and Information Technology (IT) staff, all of whom consistently participated with us at the early stages of design, development and evaluation phase to help us eventually to complete the ARF Diagnosis Application phase. On account of this, they had a good understanding of our ARF Diagnosis Application's functionalities. They actively participated in the development phase incorporating selection of technology, design of application components, the process of ARF diagnosis, report formatting, medication plans, designing of the user interface etc. All participants accepted the model we had proposed. Users also collaborated with us during the testing and evaluation processes.

Our ARF Diagnosis Application has capacity for different levels of user authority. Doctors can create a new user, add/view/update/delete rules, and view/update/delete Temporal Lookup Table, Temporal Template, modify and update help and support information (text files, images, etc.). Administrators can create a new user, data backup, management of ARF information and data, integrate data, compile data and transfer it into a spreadsheet such as MS Excel and produce various reports etc.

The director, Dr. Prakash Raj Regmi, of RF/RHD, president of NHF and other doctors actively participated in the design, development, testing and evaluation phase of our ARF Diagnosis Application. The proposed Hybrid Approach was tested and evaluated further by NHF experts and we modified the application according to their feedback. This

process was continued until we were all satisfied with the application's output. During the evaluation process, community rural health workers and doctors also made use of the application and were thereby able to evaluate thoroughly the User Interface.

NHF's registry data were applied to facilitate the evaluation and their experts' guidelines were applied for design and development of the following tasks:

1. New Rule Formation via use of Decision Tree methods - to create a new rule.
2. The Decision Matrix to identify the stage of ARF.
3. The Boolean rule to identify the level of ARF severity.
4. The Temporal Lookup Table and temporal rule for development of Temporal Templates.
5. Fuzzy process and reasoning for diagnosis of ARF including the % of severity level of ARF, explanation and justification of diagnosis, offered medication etc.

In this way, the ARF Diagnosis Application was tested and NHF experts evaluated all the above mentioned tasks 1-5. This is a list of participants who actively assisted us: the Director of RF/RHD prevention and control program and the President of NHF, Dr. Prakash Raj Regmi; 2 physicians, 2 cardiologists, 2 program administrators, 2 community rural health workers, 1 internal evaluator and 1 external evaluator (IT expert) and other NHF executive committee members. The experiment, evaluation and modification of the ARF Diagnosis Application task was done for a period of 8 weeks at Bir Hospital, Kathmandu, Nepal and the NHF head office, Lalitpur, Nepal. The community rural health workers, doctors experimented with and tested the ARF Diagnosis Application over a period of 7 days, with a total of 28 hours at NHF head office.

The NHF experts observed each module, process output and provided feedback with suggestions including modification, addition, deletion, improvement etc. The NHF experts also labelled each model's functionality as either "Accept and Approve" or "Not Approve". Our ARF Diagnosis Application was tested and evaluated with real NHF registry data sets consisting of 676 records. These, reflected 98% matching. Finally, I can report that on **August 23, 2015, a first ARF Diagnosis Application was formally launched in Nepal as a trial version** (Nepal: Himalayan Time (2015)).

6.2.1. Problems encountered

The IT external evaluator did not have prior knowledge of ARF symptoms, diagnosis processes and implementation plan. Therefore, the external evaluator specifically tested

the Application's User Interface and provided us with verbal feedback. The external evaluator's feedback and suggestions were then integrated into the Application. Unfortunately, lack of sufficient knowledge of the ARF diagnosis process meant that the external evaluator could not provide any technical information regarding implementation of the Application. However, this was not a killer constraint, so that the evaluator was able to highlight some helpful existing techniques for us to install and implement in our Application. Proposed techniques included training for users, parallel, direct or phase-wise application installation options, data management and backup policy, remote connection and support, application backup and restore policy in particular.

Most of the doctors who were surveyed were satisfied with performance of our ARF Diagnosis Application. They stated in consensus that, "***It is a very useful and appropriate tool for the diagnosis of ARF cases in Nepal".***

6.3. ARF Diagnosis Application Verification and Validation

Verification and Validation starts with a check on requirements for continuing through application design coding and testing. Verification is more about checking functional and non-functional requirements than to examining the Application's specification. It also addressed and confirmed that the Application met potential customers' expectations. The verification and validation process was designed to check whether the Application was 'fit for use' or not (Boehm, 1979).

The main purpose/immediate objective of the ARF Diagnosis Application verification was to examine all the application's components: the diagnosis model; knowledge base (source of knowledge, knowledge acquisition, representation and validation), Boolean rules, user interface, database, application architecture and process etc. and whether it met the NHF's defined requirements or not. The verification therefore dealt with making sure that the components of software met the user specified requirements (CMMISM, 2000). Inspection and tests were used for the software verification. Black box and white testing methods were applied for the software validation tasks (Ian S., 2001). Source code complier was also used for inspection of the Application. White box (code based or structure testing) and black box testing (specification based testing or functional testing) were both applied for testing the Application. In the white box testing all the codes of the Application were tested. Black box testing of all input and output was carried out and matched with the specifications. The ARF diagnosis process, sub process, function, algorithms, coding were developed based on the NHF's requirements and tested

thoroughly to determine whether each activity met our defined requirements or not. A questionnaire was designed and distributed at the end of each day during the performance evaluation of our ARF Diagnosis Application. The results are described in the following sections.

6.4. Experiment and Evaluation of the ARF Application

"Evaluation is a means to assess the quality, value, effects and impacts of information technology and applications in the health care environment, to improve health information applications and to enable the emergence of an evidence-based health informatics profession and practice" (Ammenwerth *et al*., 2004). ISO 9126 is the software product evaluation standard derived from the International Organisation for Standardisation (ISO). This international standard defines six characteristics to be considered: 1) functionality; 2) reliability; 3) usability; 4) efficiency; 5) maintainability and 6) portability. Having regard to testing and evaluation of our ARF Diagnosis Application, our research ensured that due attention was paid to factors relating to the functionality, usability, accuracy and efficiency of the Application. These are explained in this section.

The experiment and evaluation of our ARF Diagnosis Application took place in the head office of NHF, Lalitpur, Nepal. The following points were set up for the experiment and evaluation:

- Set up the evaluation criteria.
- Evaluation of functionality, usability, accuracy, efficiency and performance of the ARF Application.
- Test the requirements of the Application (which are discussed in the Introduction, Chapter 1).
- Test the Hybrid Approach (discussed in Research Methodology, Chapter 4).
- Integration testing (test each model's process of the Hybrid Approach).
- Testing of the User Interface.
- User acceptance testing and impact of the Application.
- Validity of the ARF Diagnosis Application using NHF real data sets.
- Application sensitivity analysis.

6.4.1. Setup Evaluation Criteria

The setup of evaluation criteria for the ARF Diagnosis Application is shown in Table 6. Interview, questionnaire and observation methods were used to complete the tasks.

Table 6.1: ARF Diagnosis Application Evaluation Criteria

Evaluation		Criteria
Application's user-friendless	ARF Diagnosis Application	Application design, input/output, format, layout, font, size, colour, title, messages, report format etc.
		Ease to use and learn.
		Sequence of functionalities.
		Material and contents on the input/output forms and reports, enjoy ability using of application.
Application's Components efficiency	Selection of ARF Symptoms and temporal information (providing date, duration)	Simplicity of form, ease to use, clearly understand the symptoms, ease to provide temporal information and completeness.
	Identification of ARF stage	Quality and accuracy.
	Rule Pattern Matching and ARF's severity level	Quality and accuracy of Rule Pattern Matching.
	New Rule Formation (NRF)	Quality and accuracy, effectiveness and usability of NRF.
	Temporal Template	Quality and accuracy, relevant and clear.
	Rule Selection Mechanism and Fuzzy processing	Quality and relevance to displaying the rules, effectiveness, ease to understand and process to provide the Crisp value into presented symptoms.
	Diagnosis of ARF	Quality of ARF diagnosis and its explanation. Accuracy level of ARF diagnosis and its effectiveness.
	Application Sensitivity Analysis	Quality, accuracy and role of each model (KBS/Rule base Model, Temporal and Fuzzy Model) for ARF diagnosis process.
	Treatment and medication planning	Quality and accuracy of medication, option of treatment and medication plan, easy to understand/modify the treatment information.
	Patient's Report Card	Quality and accuracy of patient report card, format and layout; easy to understand report card, efficiency of report card.
	Supporting/Help files	Ease of use, sufficient for particular symptom, contents, image, video are easy to understand, it is in Nepali and English, effectiveness of documents .
	Patient's Information Retrieval	Quality and accuracy, clarity and completeness of retrieval information.
Overall ARF Diagnosis Application's performance		

6.4.2. Experiment and Validation of the Knowledge-based process

The source of Knowledge for the development of our ARF Diagnosis Application was mainly WHO, WHF, journals, books most importantly NHF's information and expert's guidelines. NHS choice (UK) and the Australian and New Zealand guidelines and information were also investigated and integrated as far as possible during the ARF's Application design phase. The captured ARF Knowledge can be considered therefore procedural knowledge since the captured knowledge was often in the form of instructions on how to diagnose ARF cases. The ARF Knowledge base includes systematic sequences of how to identify ARF stages and how to identify the severity level of the identified ARF stages. Similarly, these processes also integrate with the explanation of certain procedures of how to use the Knowledge and how to make decisions on a particular case. The manual (interview, observation the current process, analyses of NHF's survey form data; tracking the manual reasoning process etc.) and semi-automatic (create a spread sheet file and transfer the NHF's survey form's data into spread sheet and analysis it in various ways) were methods used to acquire subject-specific knowledge for our work.

6.4.3. Protocol Analysis

NHF experts' suggestions and guidelines and were recorded in order to understand thoroughly the steps and information needed to engage in the diagnosis of ARF. These covered methods relating to the ARF diagnosis process, stages of ARF, severity level of ARF, rule formation, medication, Temporal Template etc. These are discussed in the Research Methodology, Chapter 4.

6.4.4. NHF RF/RHD Control Registry Datasets

NHF staff maintain an "*RF_RHD_Control_Registry*" spreadsheet (MS Excel) file where they only record medication information for specific RF/RHD diagnosed cases. The dataset of the registry table is shown in Table 6.2.

Table 6.2: RF/RHD Control Registry

S.N.	Data
1.	S.N. (Patient Number)
2.	Hospital No. (Lalitpur heart clinic, Kanti Bal Hospital, Man Mohan Cardiac Centre, Bir Hospital, Patan Hospital, Shahid Gangalal National Health Centre).
3.	Date of Entry
4.	Name of the patient, Age, Sex, Address, Telephone no.
5.	Diagnosis
6.	No. of Injection, 6L / 12L (Lakah: measurement).
7.	Reoccurrence of RF
8.	Allergy.
9.	Death, Cause of Death
10.	Remarks.

In the Control Registry dataset, NHF staff collects ARF/RHD case information from different hospitals and 1,859 patients' records were found and analysed using the registry file. Based on the registry data, we noted that there were 1,220 cases that were diagnosed with RHD disease and 75 cases with RF disease. A total of 1,295 cases records recorded as having ARF/RHD diseases for which medication records were included. We found that there was no diagnosis information at the Shahid Gangalal National Health Centre where patients' names only appear in the registry. We also found that Control Registry data sets were not managed properly, with data not completely captured and all lacking registry updates.

In the control registry file, records often were not complete so that patients' medical information did not show data on physical examination, presented symptoms, laboratory results etc. However, we did note that the NHF had about 1,000 ARF/RHD survey forms, where they had collected basic case information, symptoms and temporal information. The survey form benefitted by having text in both Nepali and English. The survey forms are distributed at schools where they are fill-up by either parents or teachers. Rural health workers collected the completed forms from the school and took them to the closest doctors. If any suspected case was identified, they then contacted them for further treatment processing. The NHF organized the children-screening program in schools as frequently as possible in various part of the country, especially where there are NHF district offices. Data from patients were gathered and recorded on the survey forms during

the screening process where relevant key questions are put to respondents. Once these are analysed the doctor or community rural health worker judges whether a case is detected, suspected or not detected. All detected case patients are advised to visit the nearest hospital for the further treatment as soon as feasible.

The NHF was found not to have any computerized system to record and correlate these useful survey data, which are merely filed in paper-based formats. For this fundamental shortfall, I designed and created a file on MS Excel and entered 676 records from the NHF survey forms for experimentation and Diagnosis Application development. The format and some sample data in Excel are shown in Appendix 6.14. These data were further used to evaluate the development of our ARF Diagnosis Application.

6.5. Experiment and Evaluation of the Hybrid Approach

Information on the ARF Diagnosis System was tested and evaluated using NHF local guidelines and practices. Similarly, the Temporal Template information was tested in collaboration with NHF experts. The NHF's local procedures were tested using our new ARF Diagnosis Application, which indicated 100% accuracy. That confirmed that the developed application completely accords with the NHF own procedure for diagnosis of ARF. Further details are shown with figure in the section of identify of ARF stages below.

6.5.1. Experiment and Evaluation of the KBS/Boolean Rule Model

The search and match stage has four components: 1) identify the ARF stage; 2) Rule Pattern Matching; 3) New Rule Formation and 4) Rule Selection Mechanism. Each component was tested and evaluated by NHF experts and is described in the following section.

6.5.1.1. Identification of ARF Stages

The ARF Diagnosis Application tested using WHO guidelines plus the NHF's own diagnosis process. The Application was tested using NHF real survey datasets. Accurate identification of ARF stages is a vital task because based on this information user make initial decisions the status of ARF cases. The Decision Matrix Table was developed and applied in order to identify the various stages of ARF. The Decision Matrix Table is shown in Table 6.3. It was tested with NHF's datasets and the outputs are presented in Appendix 6.

Table 6.3: Applied Decision Matrix for Test of ARF Decisions

ARF Stage	S.N.	Major Signs	Minor Signs	Mandatory Signs	Output /screenshot
Detected ARF	1	≥1	≥2	≥1	achieved / Appendix: 6.1
	2	Chorea	=0	=0	achieved / Appendix: 6.2
	3	≥2	=0	≥1	achieved / Appendix: 6.3
	4	=5	=5	=3	achieved / Appendix: 6.4
	5	=0	$Arth_{13}$+ Fev_{12}+Crp_{15}	≥1	achieved / Appendix: 6.5
Suspected ARF	6	=1 ∧ ¬ *Chorea*	=1	≥1	achieved / Appendix: 6.6
	7	=0	$Arth_{13}$+ Fev_{12}	≥1	achieved / Appendix: 6.7
	8	=0	$Arth_{13}$+ Fev_{12} + Esr_{16}	≥1	achieved / Appendix: 6.8
	9	=0	$Arth_{13}$+ Fev_{12} + Ecg_{14}		achieved / Appendix: 6.8
	10	=0	$Arth_{13}$+ Fev_{12} + Ecg_{14} + Esr_{16}	≥1	achieved / Appendix: 6.8
Not-detected ARF	11	1 ∧ ¬*Chorea*	=0	≥1	achieved / Appendix: 6.9
	12	=0	≥1	=0	achieved / Appendix: 6.10
	13	=0	=0	≥1	achieved / Appendix: 6.11
	14	=0	(Art_{13} ∨ Ecg_{14} ∨ Crp_{15} ∨ Esr_{16}	≥1	achieved / Appendix: 6.12
	15	=0	(Fe_{12} ∨ Ecg_{14} ∨ Crp_{15} ∨ Esr_{16}	≥1	achieved / Appendix: 6.13

Based on the test results it was demonstrated that our Applied Decision Matrix was appropriate and suitable for identifying stages of ARF.

6.5.1.2. Rule Pattern Matching

The ARF Diagnosis Application rules were checked and tested by NHF experts. The Decision Tree method was used to create a rule to identify the severity level of detected ARF. In the rule-based system, the dataset of rules has two sections: 1) Antecedent part and 2) Consequent part. The ARF symptoms consisting in the Consequent part of the rule has two characters *P* (sign present) or *A* (sign absent or not present) are used to record symptoms. In the Consequent part, the rule outputs are: severe, moderate, mild or suspected case. Explanation of rules and total positive signs are recorded. If a Rule is not available on the rule-based system then New Rule Formation will be activated for the formation of a new Rule. The structures of samples of rules are shown in Table 6.4.

Table 6.4: The Sample of Rules

	Antecedent												Consequent		
RuleNo	Arthritis	Carditis	Chorea	SN	EM	Fever	Arthralgia	ECG	CRP	ESR	Throat Infection	ASOT	GAS	Rule Output	Explanation	T_P_Signs
1	P	A	A	A	A	P	P	P	P	P	P	P	P	Mild	Explanation	9
7	P	A	A	A	A	P	A	A	A	A	P	A	A	Suspected	Explanation	3
15	A	A	A	A	A	P	P	P	P	P	P	A	A	Mild	Explanation	6
18	A	A	A	A	A	P	P	A	A	A	P	A	A	Suspected	Explanation	3
20	A	A	A	A	A	P	P	A	A	A	A	P	A	Suspected	Explanation	3
33	A	A	P	A	A	A	P	A	A	A	A	A	P	Mild	Explanation	3
34	A	P	P	A	A	P	P	A	A	A	A	A	P	Severe	Explanation	5
35	A	P	P	A	A	P	P	P	A	A	A	A	P	Severe	Explanation	6
53	P	P	A	A	A	P	P	A	P	A	A	A	P	Severe	Explanation	6
54	P	A	P	A	A	P	P	A	P	A	A	A	P	Moderate	Explanation	6
55	P	A	P	A	A	P	P	A	P	P	A	A	P	Moderate	Explanation	7
56	P	A	P	A	A	P	P	P	P	P	A	A	P	Moderate	Explanation	8

A screenshot of Rule Pattern Matching is illustrated in Figure 6.1.

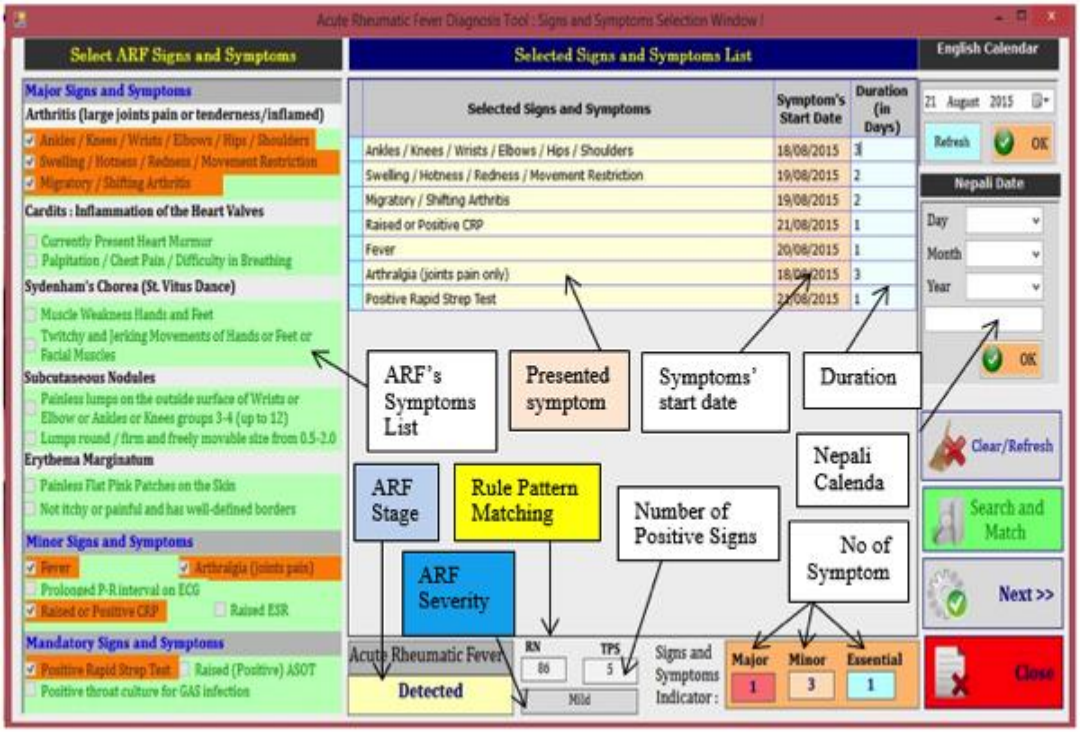


Figure 6.1: Screenshot of Rule Pattern Matching

In the rule-based system, for checking the rules three algorithms are proposed: 1) Integrity check (each rule check individually and its validity); 2) Rule Pair Check (check pair of rules separately) and 3) extension check (check all the possible paths in the rule of the knowledge base) for detecting logical anomalies (Preece and Shinghal, 1994). NHF's experts checked the New Rule Formation method and its integrity. The following areas were checked by NHF experts in order to test the accuracy of the rules:

- Knowledge base: checked and verified the source of knowledge, ARF diagnosis guidelines and procedures.

- Decision matrix table: checked and verified the decision matrix table and equations to identification of ARF stage.

- Decision Tree: checked and verified the output of a Decision Tree, which was used in the formation of a new rule for identification of level of ARF severity.

- Inference engine: checked and verified Boolean rule, Temporal Lookup Table, Temporal Template, reasoning mechanism and fuzzy process.

- The set of severe, moderate, mild and suspected cases rule checked thoroughly.

- Checked the inconsistency of rules since essential symptom is compulsory for make a diagnosis of ARF and *Carditis* must be present for a diagnosis of a severe case stage. *Arthritis pain must be migratory* to satisfy the Arthritis symptom.

- Check the completeness: guidelines and knowledge are sufficient to make a decision of case such as identification of stage of ARF, severity level, accuracy of New Rule Formation, Temporal Template, medication information etc.

6.5.1.3. ARF Severity Level

The ARF severity level (Severe, Moderate, Mild and Suspected cases) rule was developed using the Decision Tree method, discussed in Research Methodology, Chapter 4. The Severe and Moderate cases have only one type of rule condition. The Mild case has four different types of rule pattern and the Suspected case has five diverse types of rule condition. The sign and symptoms for different cases are shown in Figure 4.16 with equations 1-11 set out in the Research Methodology, Chapter 4. We tested each equation and severity level of ARF with NHF's dataset; an example of a Rule for the Severe level (Rule numbers 34, 35 and 53); Moderate (Rule numbers 54, 55 and 56); Mild (Rule numbers 1, 15 and 33), Suspected (Rule numbers 7, 18 and 20) are shown in Table 6.5 Some supporting screenshots of outputs are presented in Appendices 6.2, 6.3, 6.6 and 6.7.

6.5.1.4. Rule Selection Mechanism

The NHF experts (cardiologists and physician) experimented with and evaluated this process by selecting random data from their survey forms. They compared results of my ARF Diagnosis Application's (identify stage of ARF process) with their data. This reflected a significant positive result of 98% matching. Experts followed up by checking the consistency, accuracy and validating of rules that are produced by the Rule Selection Mechanism.

The Rule Selection Mechanism which was used read the total number of symptoms (which is produced by the Rule Pattern Matching process) and passes the number into each severity level (Severe, Moderate, Mild, Suspected cases) and selects a rule that matches the value (total number of symptoms). A sample of the evaluation is shown by screenshots in Figures 6.2 and 6.3.

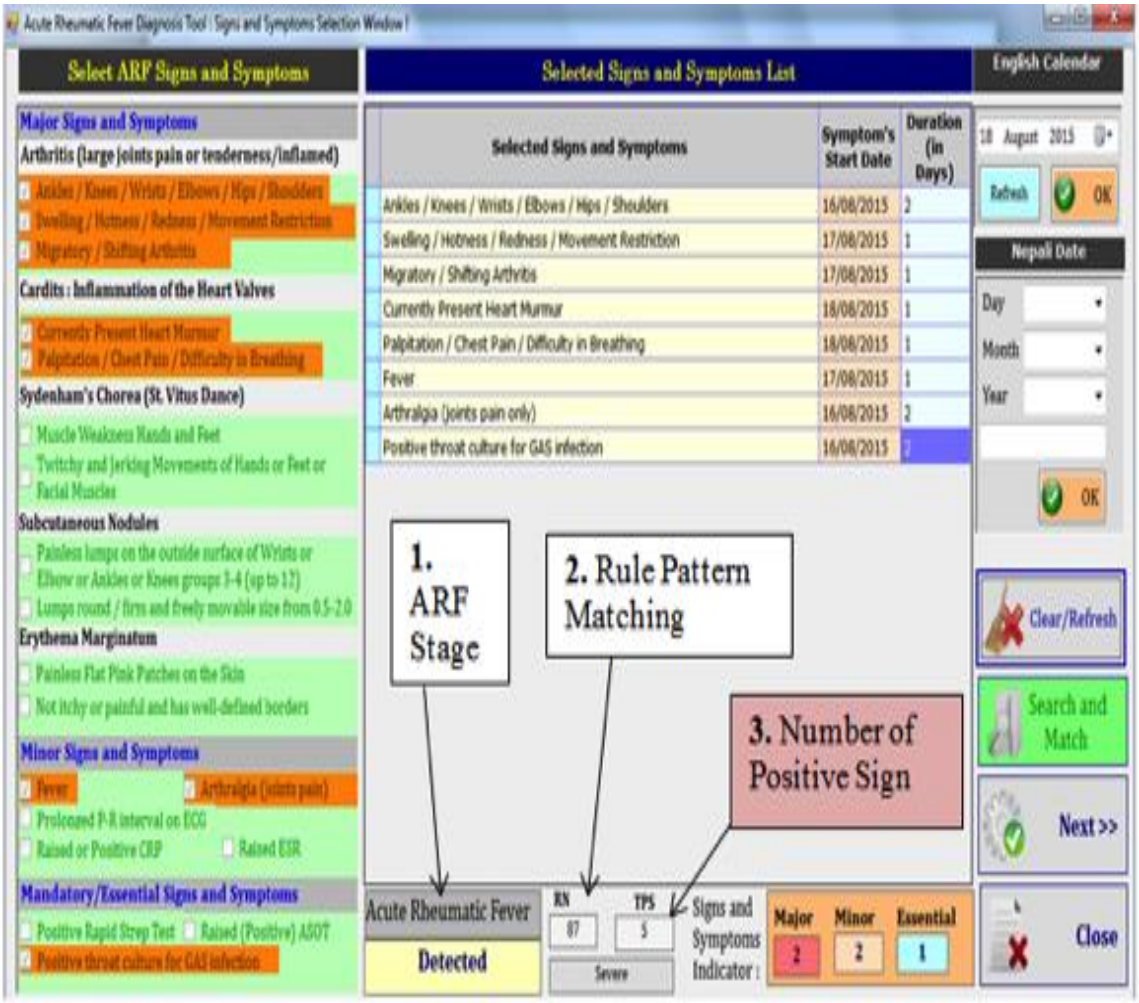


Figure 6.2: ARF Stage, Rule Pattern Matching and Number of Positive Signs

In Figure 6.2, 1 shows the identification of ARF stage detected; 2 shows the satisfied rule, with Rule number (87) and total positive signs (5) and in 3 this value (5) is used in the Rule Selection Mechanism to select the relevant rules derived from all severity levels.

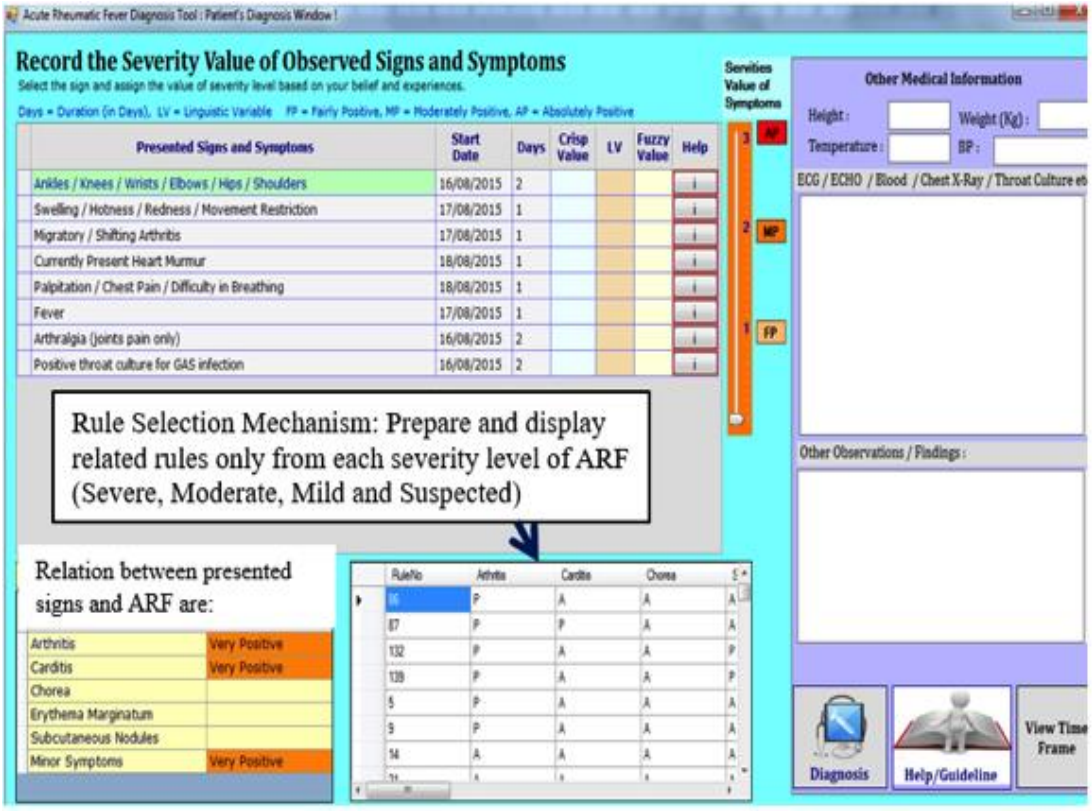


Figure 6.3: Displays the Relevant Rule derived from the Rule Selection Mechanism

6.5.1.5. New Rule Formation

A New Rule Formation (NRF) process was implemented to create a new Rule. The NRP was developed using the Decision Tree method, which is discussed in Research Methodology, Chapter 4. The NRF process and output were experimented with and evaluated by NHF experts. The experts also checked the consistency, accuracy and validity of the New Rule Formation process, which reflected a 100% match with the NHF's existing procedures. A screenshot is shown in Figure 6.4 for the output of NRF.

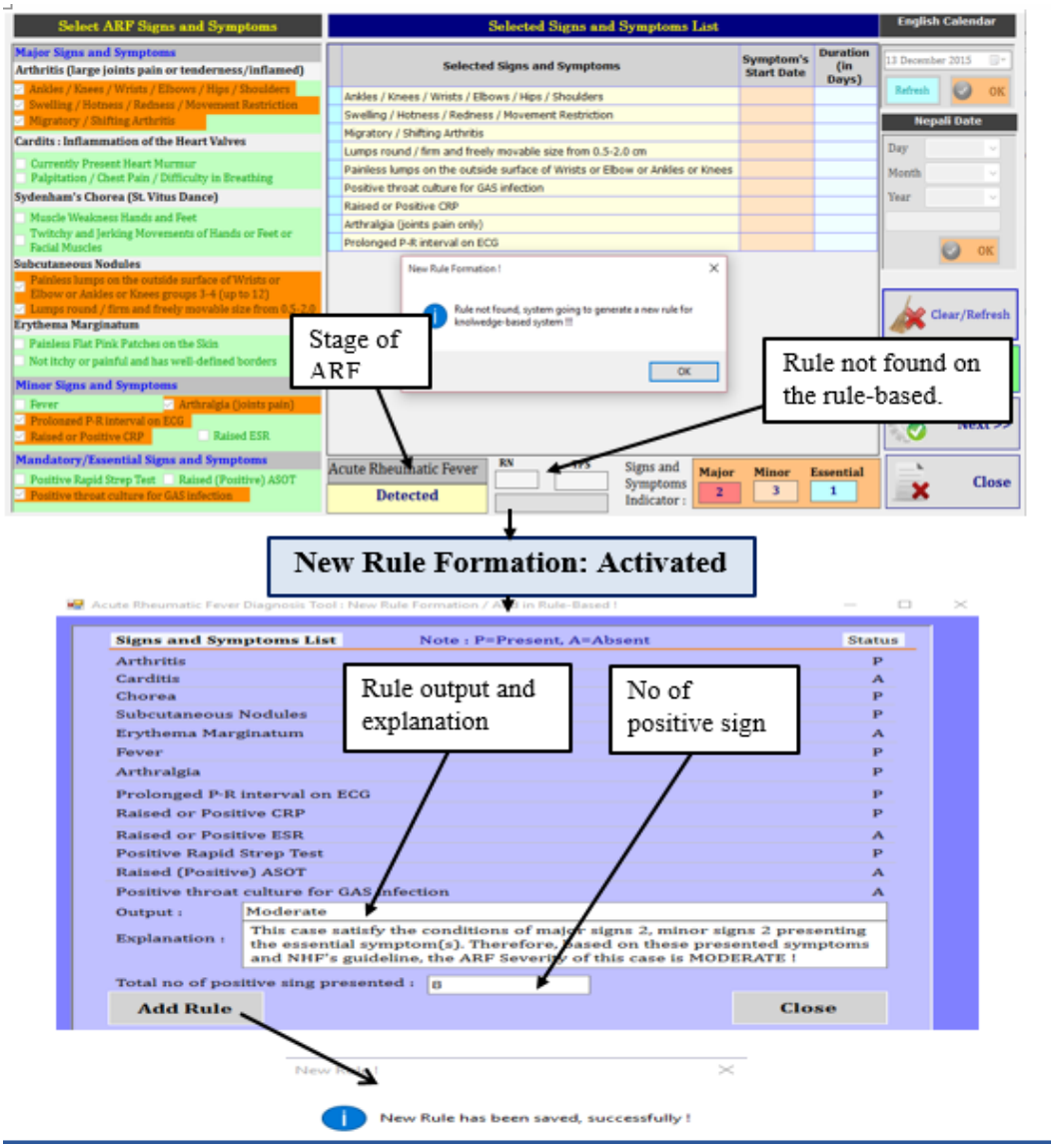


Figure 6.4 : Output of New Rule Formation

6.5.2. Experiment and Evaluation of Temporal Model

In the NHF's dataset, only a few data were recorded with temporal information but included patient check-up date, throat infection date and duration, the duration of fever and other symptoms. We applied these dataset to experiment and evaluate our Temporal Model, which reflected a promise output (quality and accuracy provided in subsection 6.7.1 below). In addition used random datasets (hypotheses) for the evaluation of temporal constraints and the Temporal Template (detail in sensitivity analysis given in Section 6.9.). The NHF experts examined the Temporal Lookup Table/Rules, Temporal Reasoning process that prepared the Temporal Template (the relations between symptoms and ARF). The experiments and evaluation of each temporal constraint are described in the next section.

6.5.2.1. Temporal Constraints for Absolutely Positive

The temporal constraints equations numbers 29-34, found in the Research Methodology, Chapter 4, were designed and used to illustrate the absolutely positive relationship between symptoms and ARF which were tested and their applications and outputs are presented in Figure 6.5.

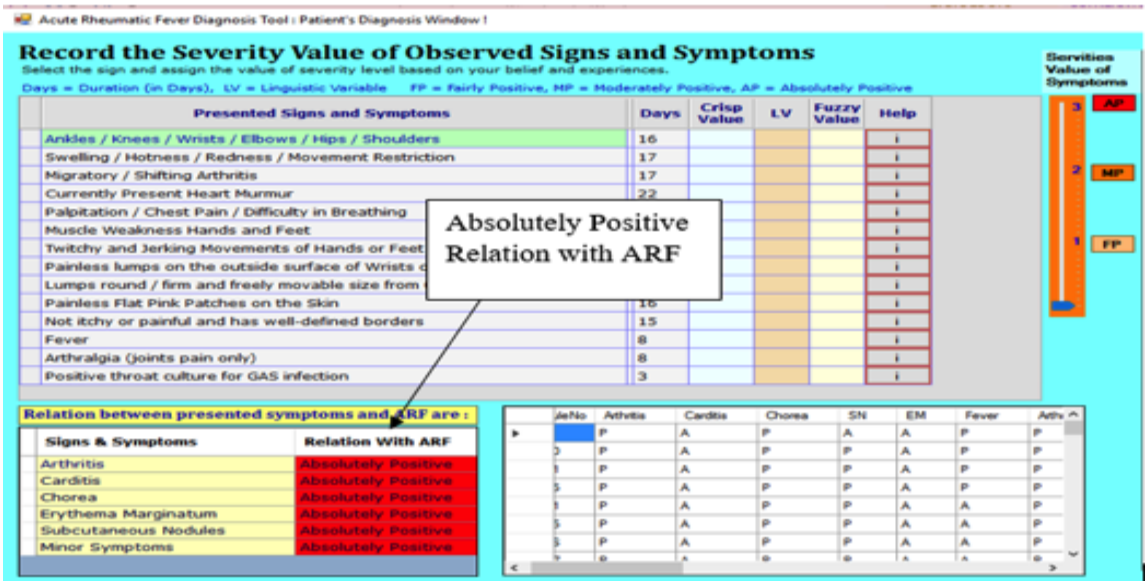


Figure 6.5 : Output of Tempoal Constraint of Absolutely Positive

6.5.2.2. Temporal Constraints for Very Positive

The temporal constraints equations number 35-40, are available in Research Methodology Chapter 4. These were designed and used to illustrate the very positive relation between symptoms and ARF which were tested with Application and Output presented in Figure 6.6.

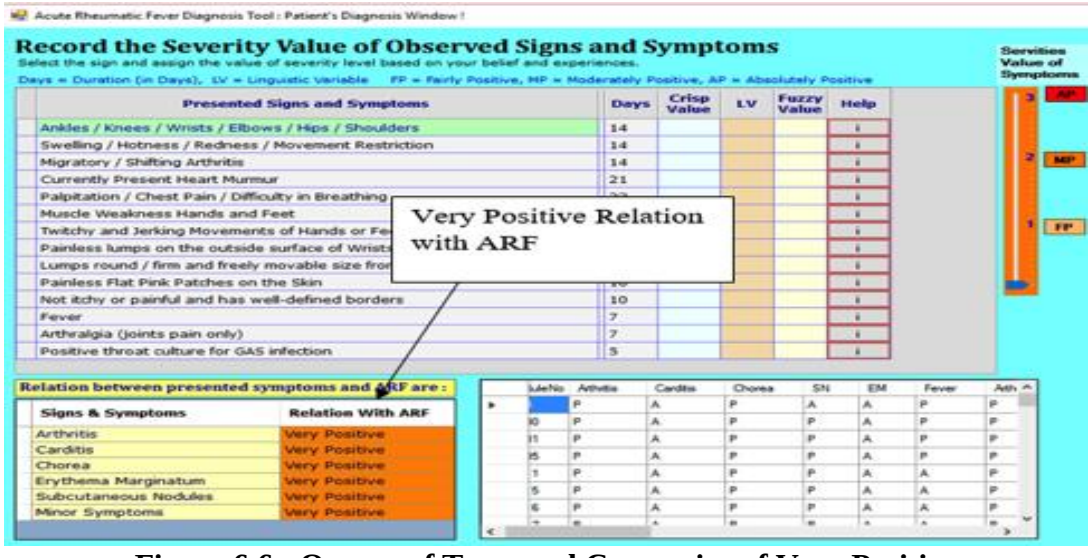


Figure 6.6 : Output of Temporal Constraint of Very Positive

6.5.2.3. Temporal Constraints for Relatively Positive

The temporal constraints equations numbers 41-46, are in the Research Methodology Chapter, 4. They were designed and used to illustrate relatively positive relationship between symptoms and ARF. They were tested with application and output and presented in Figure 6.7.

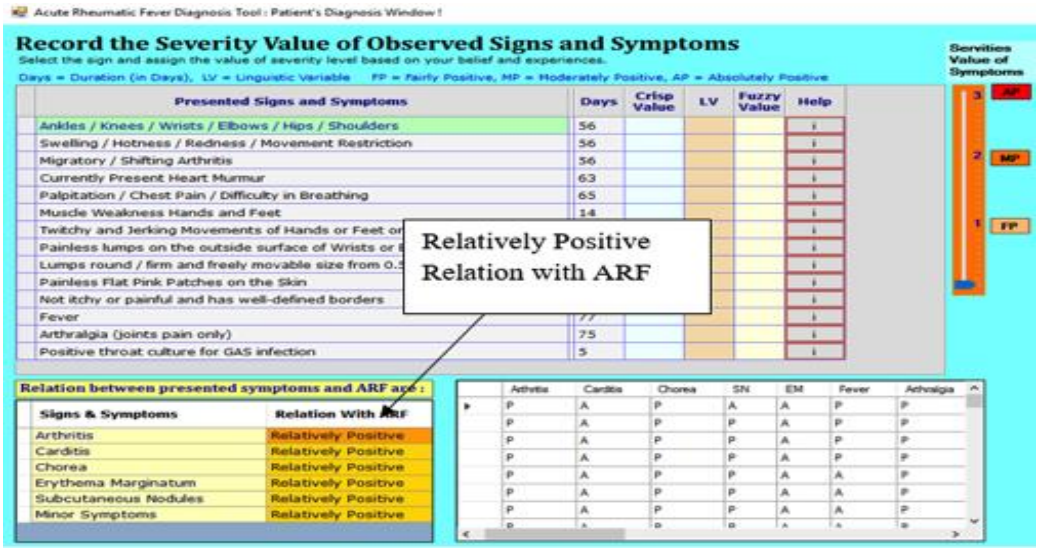


Figure 6.7 : Output of Tempoal Constraint of Relatively Positive

6.5.2.4. Temporal Constraints for Suspected

The temporal constraint equations numbers 47-52, are included in Research Methodology, Chapter 4. These were designed and used to illustrate suspected relations between symptoms and ARF, which were tested, with Application and Output, presented in Figure 6.8.

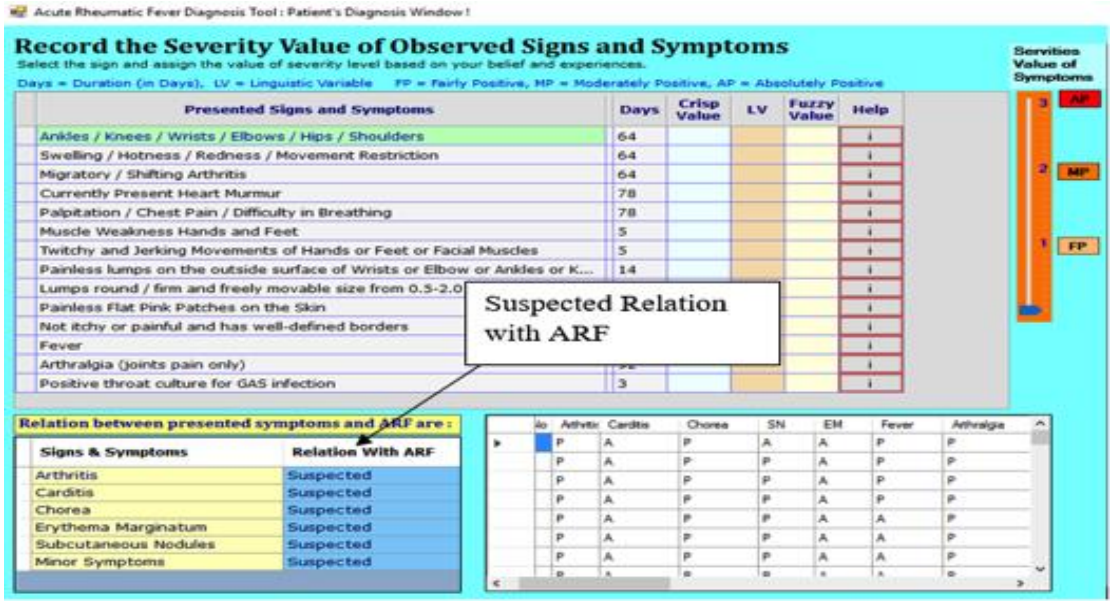


Figure 6.8 : Output of Temporal Constraints of Relatively Positive

The overall Temporal Model's view screenshot is provided in Figure 6.9.

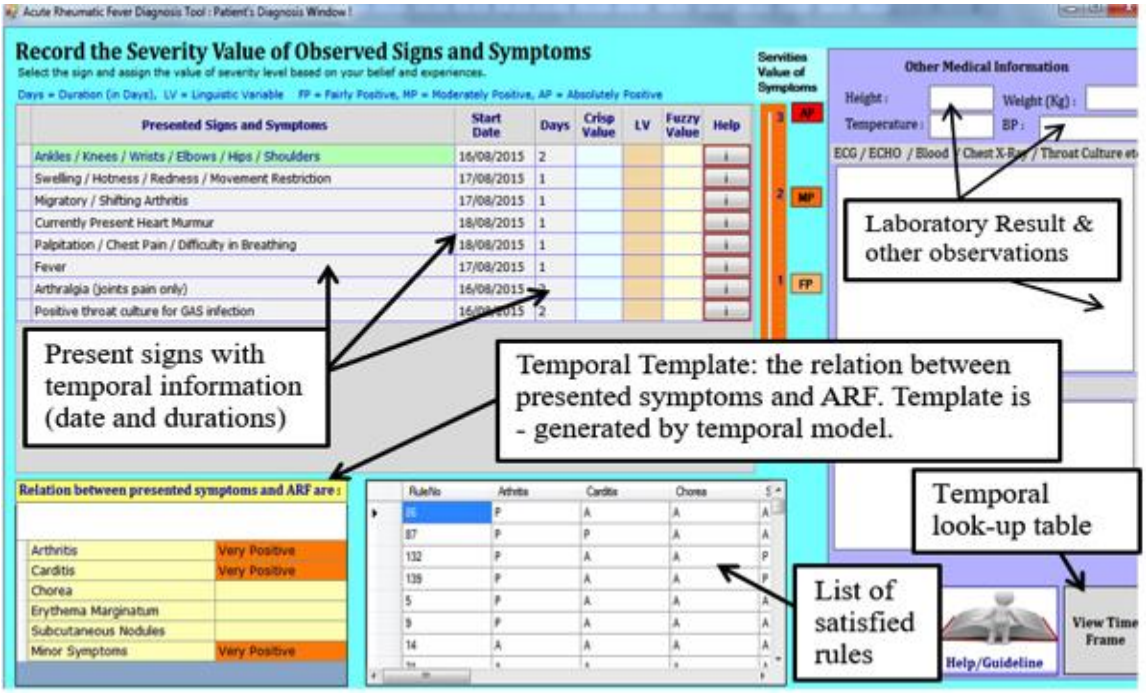


Figure 6.9 : Overall View of a Temporal Model

6.5.3. Experiment and Evaluation of the Fuzzy Model

In the Fuzzy Model, the user provides a Crisp Value (numerical) in numbers 0-3 for recording a patient's presented symptoms indicating impact or severity level based on his/her perception and belief. The user's judgement are recorded in linguistic terms as 'absolutely positive', 'moderately positive' and 'fairly positive' for any particular symptom. The fuzzy Process converts the user's belief into a numerical fuzzy value 0-1 which is defines degrees of belief values that can transferred into satisfied rules. Value of degrees of belief for each presented symptom will then be transferred into all "satisfied rules" for further process. Figure 6.9 shows a list of satisfied rules and the screenshot below shows the degree of belief value (fuzzy value) produced by the fuzzification process. This fuzzy mechanism will enable the user to deal with uncertainties and imprecise data such as 'severe pain in ankle', 'hotness in the large joint', 'weakness in the hands' etc. actually representing verbally some major symptoms of ARF. A question such as how severe is the pain; how severe is the perceived hotness in the large joint signifying how difficult is to obtain accurate, precise value measurements. When the Fuzzy Model is applied, it is shown to be capable of dealing with uncertainties of this kind. The sample screenshots of this process including diagnosis and treatment plan are shown in Figures 6.10 and 6.11.

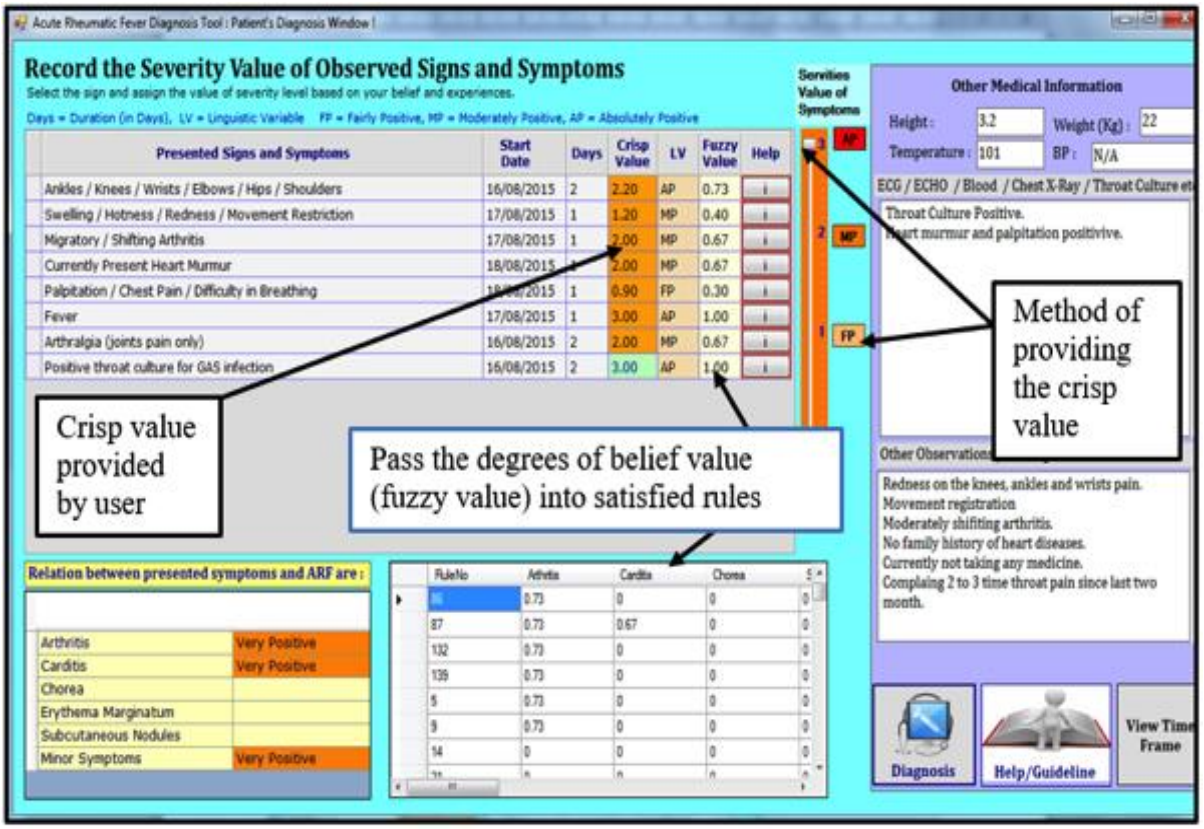


Figure 6.10 : Output of a Fuzzy Process

6.5.3.1 Diagnosis and Treatment Plan

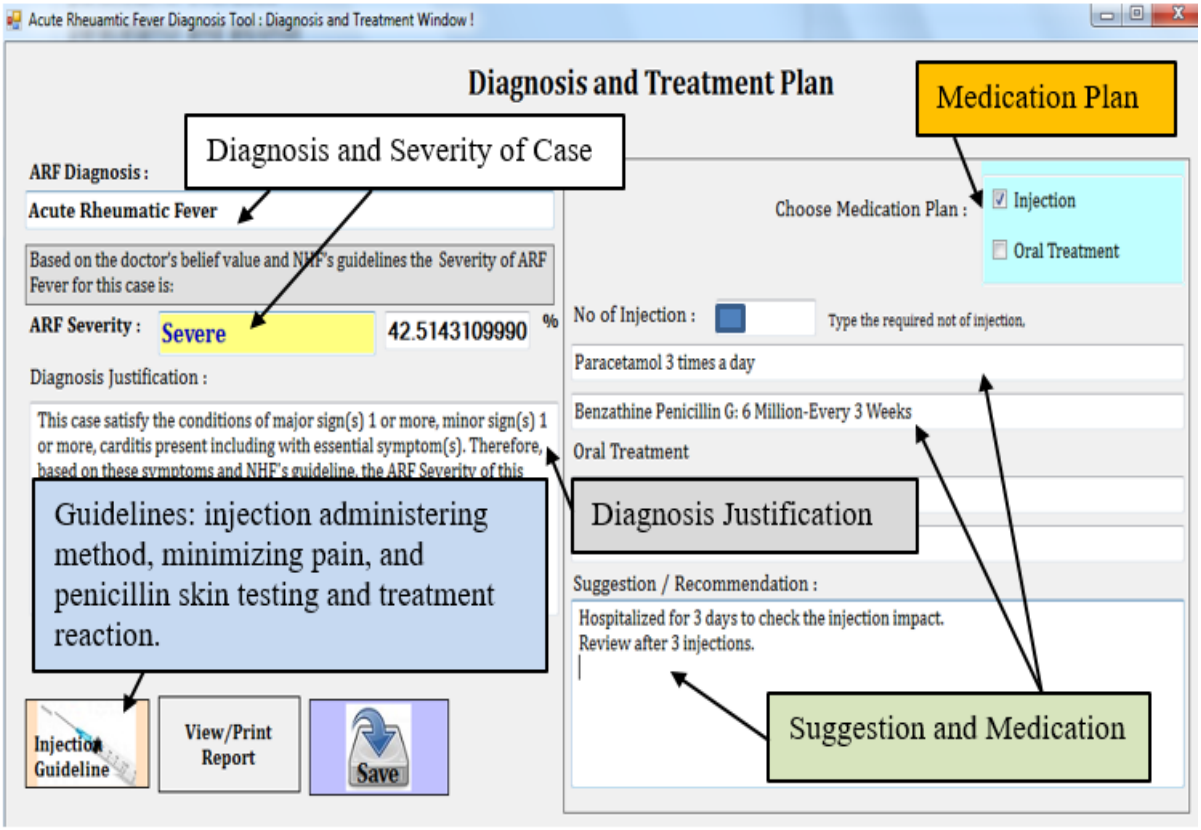


Figure 6.11 : Output of a Diagnosis and Treatment Plan

An example of a Patient Report Card is shown in screenshot Figure 6.12.

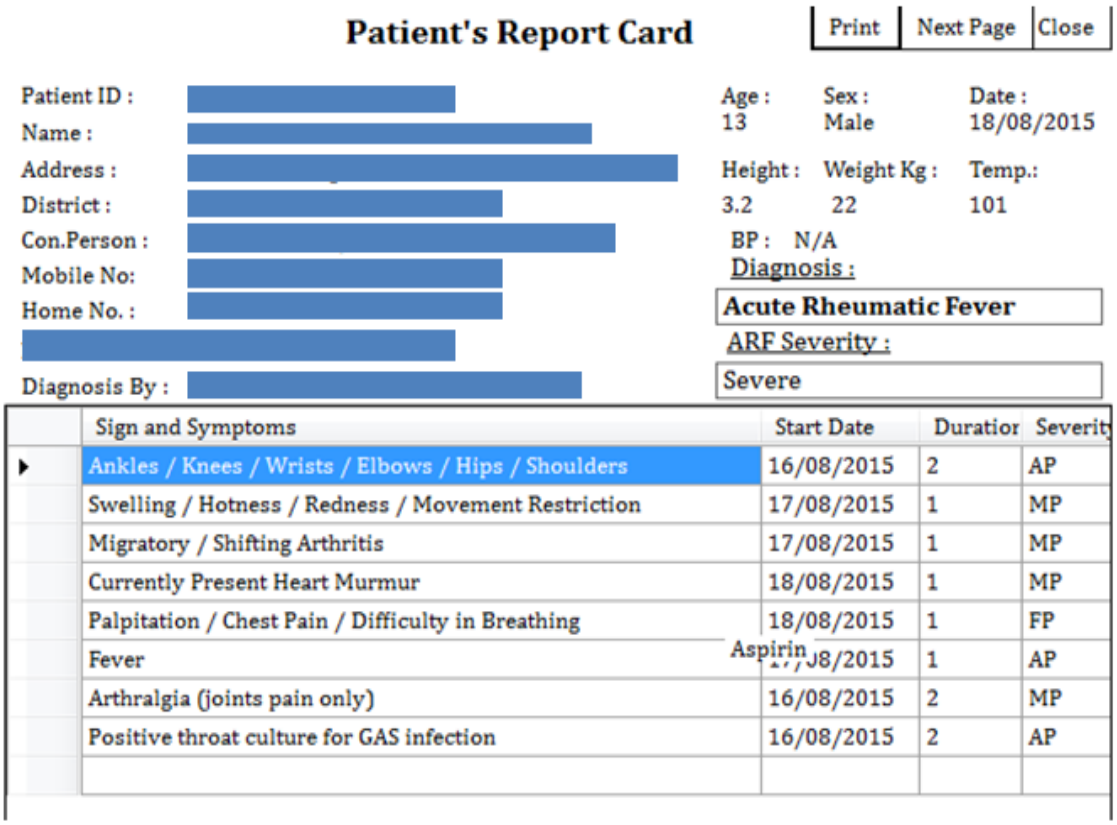


Figure 6.12: Sample of Patient Report Card

In the next page of the report, medication detail, laboratory report, other observations, doctor's suggestions and doctor's signature are included.

6.6. ARF Diagnosis Application: Comparison and Result

The comparison of ARF Diagnosis Application's result using NHF survey datasets are shown in Table 6.5 and overall match analyses are provided in Table 6.6.

Table 6.5: Comparison Result

Description	NHF registry data set's result	ARF Diagnosis Application's Result	Differences in number
Detected ARF Cases	87 (13.68%)	84 (13.21%)	3
Suspected ARF Cases	74 (11.64%)	73 (11.48%)	1
Not Detected Cases	475 (74.69%)	479 (75.31%)	4
Total Cases :	**636**	**636**	**8**

Based on the total 636 NHF survey datasets, 87 (13.68%) patients were recorded as Detected ARF cases; 74 (11.64%) patients were recorded as Suspected cases and 475

(74.69%) patients were recorded as Not detected. Similarly, 636 NHF' survey datasets were tested with our ARF Diagnosis Application. The result revealed that, 84 (13.21%) patients were identified as Detected cases; 73 (11.48%) patients were identified as Suspected and 479 (75.31%) patients identified as Not detected cases. There were only very few difference and Table 6.6 shows the comparison results in percentages.

Table 6.6: Comparison Result in Percentage

Description	Matching with NHF's data set	Not matching with NHF data set	Total
Detected ARF Cases	97%	3%	100%
Suspected ARF Cases	99%	1%	100%
Not Detected Cases	99%	1%	100%

Figure 6.13 shows the same comparison result graphic form.

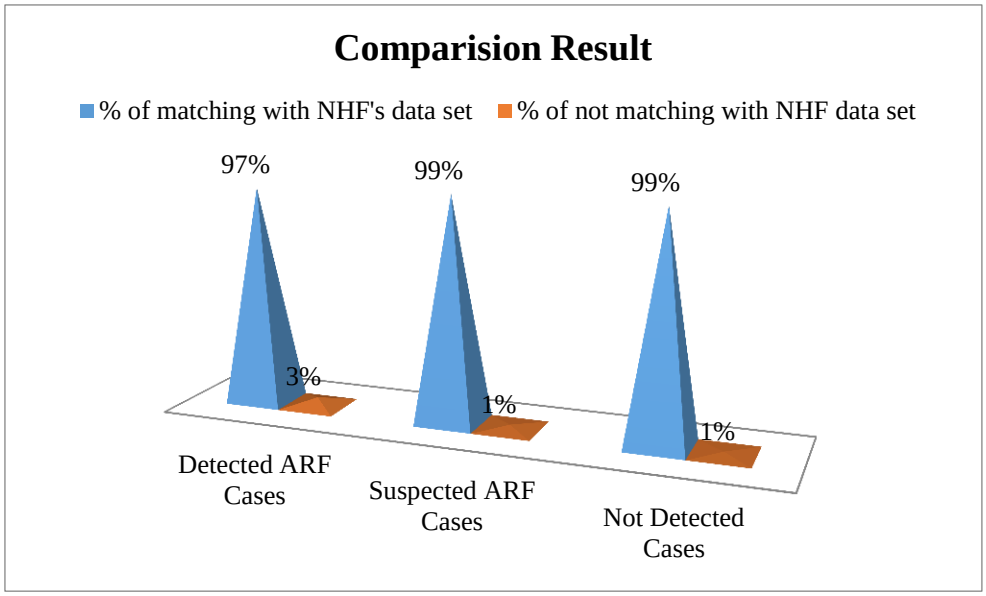


Figure 6.13: Graph showing Results of Comparison

Table 6.7 shows the overall comparison (match and not match cases of NHF ARF datasets) and results of our ARF Application using NHF datasets.

Table 6.7: Overall Comparison Result with NHF's Dataset

No. of matches cases with NHF's dataset :	**628**
No. of difference case (not matches cases) :	8
% of matches Case :	98.74
% of not matches Case :	1.26
Total :	100%

Figure 6.14 shows the overall comparison (matches, not matches cases of ARF) results of our ARF Application using NHF datasets are illustrated in a pie chart.

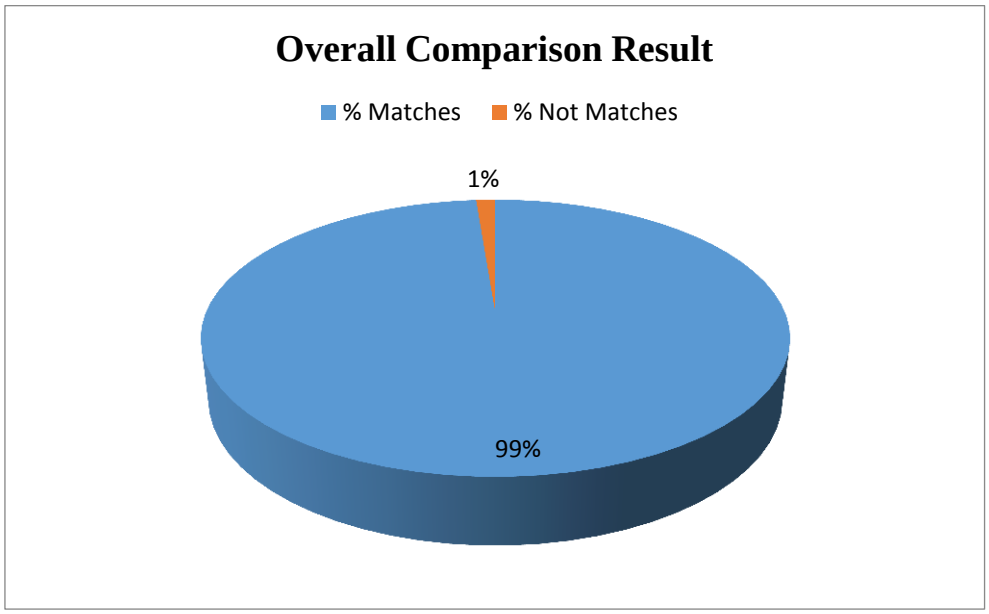


Figure 6.14: Overall Comparison Result with NHF's Dataset

The accuracy of our ARF Diagnosis Application is 98.74%. In the difference cases, the number of patients had already been diagnosed with heart disease and was taking medicine. These differences were revealed in the comparison result. This research did not consider the previous history of ARF and RHD diseases. Figure 6.15 shows comparison results of Detected, Suspected and Not detected cases.

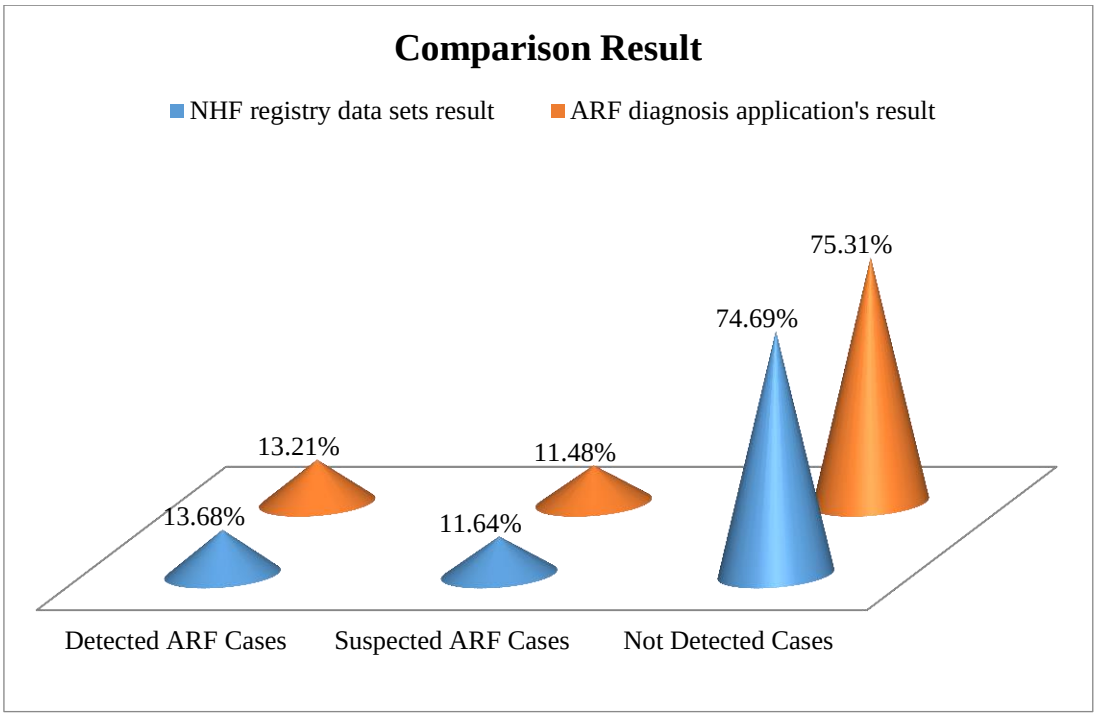


Figure 6.15: Comparison Result Chart

6.7. Evaluation of new ARF Diagnosis Application's Quality and Accuracy

Rensis Likert's article titled "*A simple and Reliable Method of Scoring the Thurstone Attitude Scales*" indicated the format of typical 5 level items ("strongly disagree", "disagree", "neither agree nor disagree", "agree", "strongly agree") referred to as Likert's scale questionnaires. There are some other versions as well e.g. extremely satisfied, very satisfied, somewhat satisfied, very dissatisfied etc. which can be used. These were included in the design of the evaluation of our ARF Diagnosis Application's performance test. These questionnaires were distributed to 9 users. The evaluation of the quality and accuracy of the Application was carried out by 4 NHF experts, (2 cardiologists and 2 physicians). All the questionnaires were returned on time with a 100% response rate.

The quality and accuracy of the identification of ARF stages from our Application revealed 75% of experts were very satisfied and 25% were satisfied. The identification of ARF stages was a key component of our ARF Diagnosis Application. For this, 100% of NHF experts were satisfied over the fact that production and definition of identification stages by our ARF Application were correct. Table 6.8 shows the questions and responses.

Table 6.8: Quality and Accuracy Result

Questions	**Very dissatisfied**	**Dissatisfied**	**Neutral**	**Satisfied**	**Very satisfied**
Identification of ARF Stage	0(0%)	0(0%)	0 (0%)	1 (25%)	3 (75%)
Knowledge representation	0(0%)	0(0%)	1 (25%)	1 (25%)	2 (50%)
Severity level of ARF	0(0%)	0(0%)	0 (0%)	1 (25%)	3 (75%)
New Rule Formation	0(0%)	0(0%)	0 (0%)	0 (0%)	4 (100%)
Rule Selection Mechanism	0(0%)	0(0%)	1 (25%)	1 (25%)	2 (50%)
Temporal Lookup Table/Rule & Temporal Template	0(0%)	0(0%)	0 (0%)	1 (25%)	3 (75%)
Patient Information Retrieval	0(0%)	0(0%)	0 (0%)	3 (75%)	1 (25%)
Diagnosis and medication/ treatment plan	0(0%)	0(0%)	0 (0%)	2 (50%)	2 (50%)
Sufficiency of supporting and technical information	0(0%)	0(0%)	1 (25%)	2 (50%)	1 (25%)
Meet the Nepalese setting (environment, lifestyle, NHF's procedure)	0(0%)	0(0%)	0(0%)	1 (25%)	3 (75%)

Figure 6.16 shows the application's quality and accuracy in the result column on the chart.

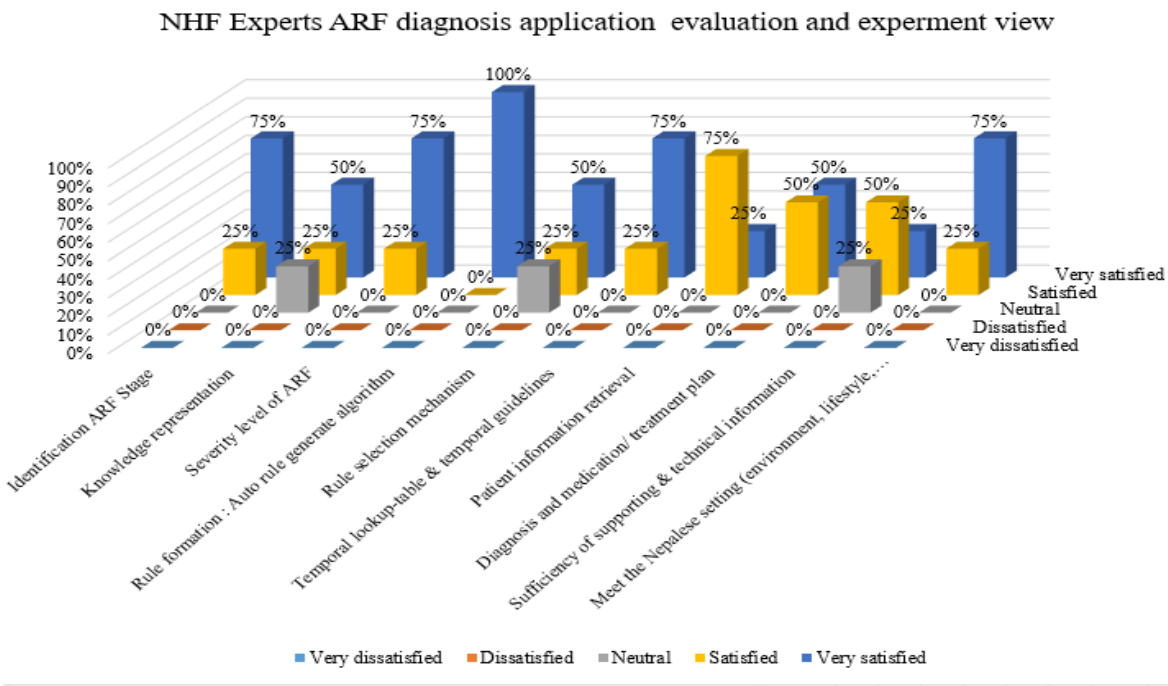


Figure 6.16: ARF Application's Quality and Accuracy Result on a Column Chart

6.8. Experiment and Evaluation of User Interfaces

In the ARF Diagnosis Application, the User Interface is a frontline where users can enter and access information. A user-centred design approach was applied to develop the Application that helped us to design a robust user interface. Moreover, it also helped us to fit the application conveniently into the Nepalese setting and lifestyles.

The Heuristic method is used for software usability evaluation. Evaluators will inspect the interface and identify any inherent problems (Zang J. *et al.*, 2003). Our ARF's Diagnosis Application's interface was examined by NHF's expertise from the outset. They provided verbal comments on the user interface and suggested further improvements. Their helpful comments covered windows size, font, form layout, sequence of windows, screen's text, instruction information, button's name, pictures, help information (Nepalese and English language, audio, video, images), Nepali calendar, error message, menu design, menu selection option, wording of menu, heading of each window form, report format etc. These were accepted and modified and introduced wherever appropriate. Some samples of the User Interface are provided for reference in Appendix 6.15.

A set of questions was answered by 9 users including NHF's experts (4), community rural health workers (3), NHF's IT expert internal (1), and IT expert external (1). The questions and output are listed in Table 6.9.

Table 6.9: User Interface Evaluation Result

Questions	Very hard	Hard	Neutral	Easy	Very easy
Reading texts on the screen	0 (0%)	1 (11%)	0 (0%)	3 (33%)	5 (56%)
Understand commands and instruction on the screen	0 (0%)	1 (11%)	0 (0%)	3 (33%)	5 (56%)
Memorability (remembering the process and sequences)	0 (0%)	2(22%)	0 (0%)	5 (56%)	2 (22%)
Learning and using application	0 (0%)	1 (11%)	0 (0%)	5 (56%)	3 (33%)
Providing input information e.g. date, duration etc.	0 (0%)	1 (11%)	0 (0%)	5 (56%)	3 (33%)
Select/remove : symptoms from the screen form	0 (0%)	0 (0%)	0 (0%)	1 (11%)	8 (89%)
Provide the Crisp value	0 (0%)	1 (11%)	0 (0%)	5 (56%)	3 (33%)
Correcting the error	0 (0%)	3 (33%)	0 (0%)	6 (67%)	0 (0%)

The following Figure 6.17 shows the user ARF Diagnosis Application's User Interface evaluation results in a column chart.

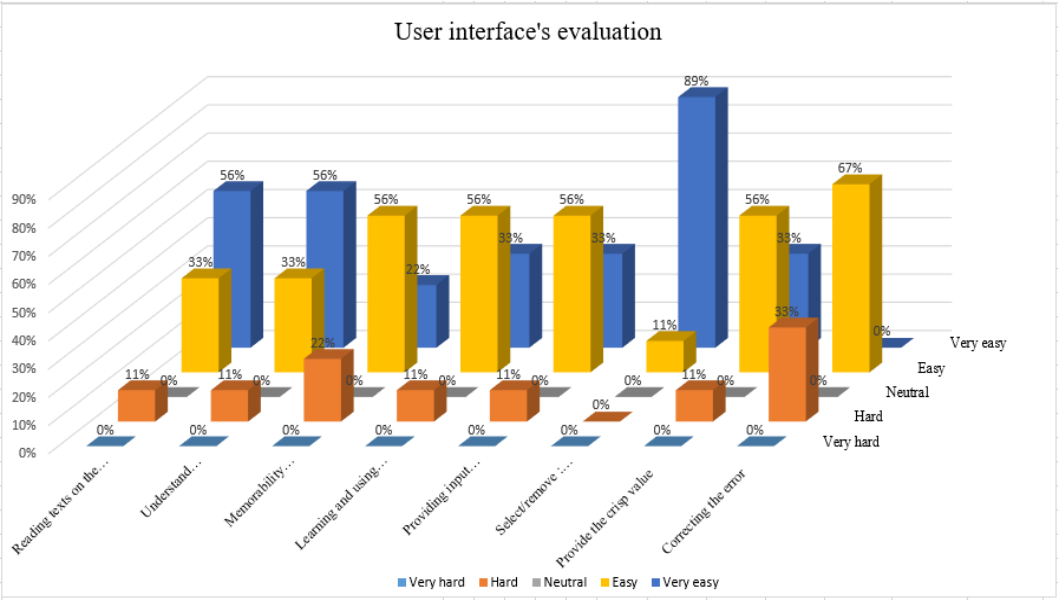


Figure 6.17: User Interface Evaluation Result on Column Chart

The ARF Diagnosis Application's information (help and supporting file information) pattern (text, audio, picture, Nepali and English language) and message (error message, warning message) evaluation results are shown in Table 6.10.

Table 6.10: Application's Information and Message Evaluation Result

Questions	**Very unhelpful**	**Unhelpful**	**Neutral**	**Helpful**	**Very helpful**
Supporting information on the screen.	0 (0%)	0 (0%)	1 (11%)	3 (33%)	5 (56%)
Layout/format and contents of the forms/supporting documents.	0 (0%)	0 (0%)	3 (33%)	5 (56%)	1 (11%)
Access of help files/documents.	0 (0%)	0 (0%)	0 (0%)	3 (33%)	6 (67%)
Error messages/format.	0 (0%)	0 (0%)	0 (0%)	5 (56%)	4 (44%)
Menu, login - format, style and sub-menu.	0 (0%)	0 (0%)	2 (22%)	5 (56%)	2 (22%)
Nepali calendar & information in Nepalese language.	0 (0%)	0 (0%)	0 (0%)	0 (0%)	9 (100%)

Figure 6.18 shows the information and message evaluation results.

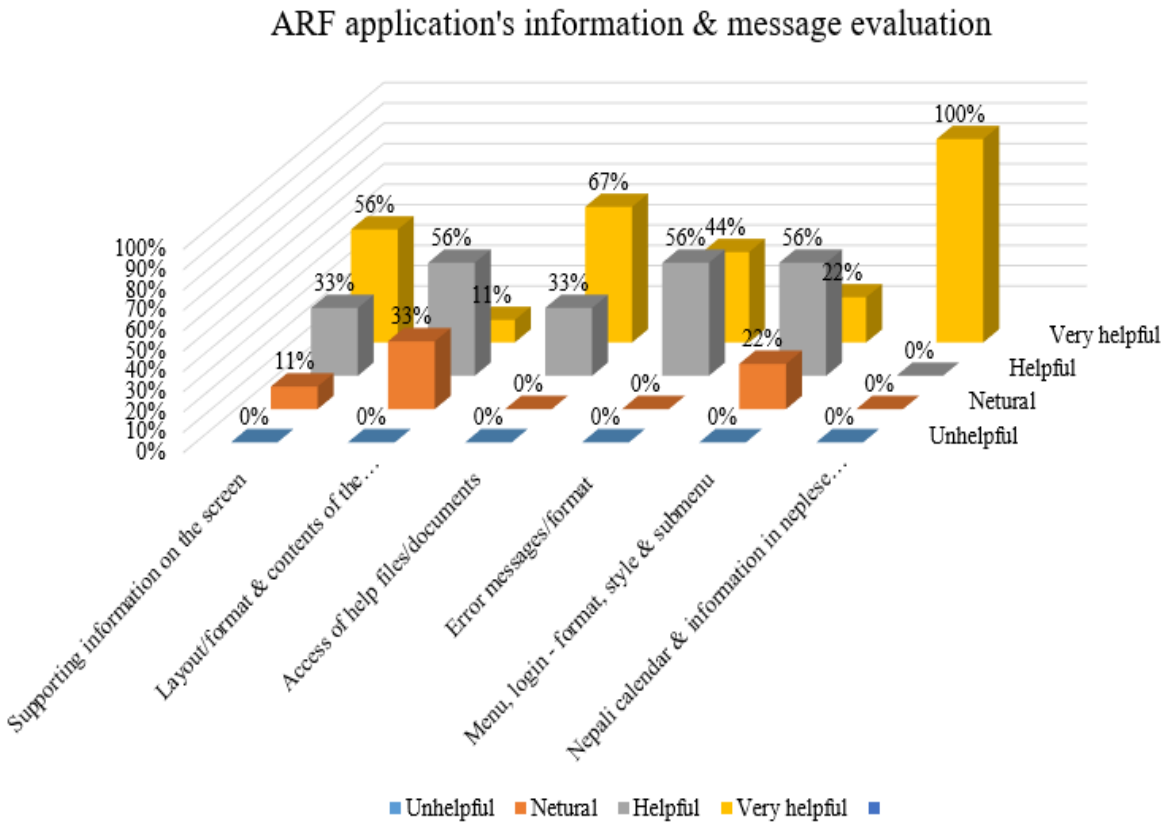


Figure 6.18: ARF Application's Information and Message Evaluation

Table 6.11 shows the ARF Application's overall performance result.

Table 6.11: Application's Overall Performance Evaluation and Result

Descriptions	**Strongly disagree**	**Disagree**	**Neutral**	**Agree**	**Strongly agree**
The ARF Diagnosis Application is easy to learn and use.	0 (0%)	1 (11%)	0 (0%)	3 (33%)	5 (56%)
I am satisfied with the User Interface (user friendly, simple).	0 (0%)	1 (11%)	0 (0%)	5 (56%)	3 (33%)
I understood and am satisfied with the sequence of the process.	0 (0%)	1 (11%)	1 (11%)	2 (22%)	5 (56%)
I am satisfied with the supporting documents that are in Nepali and English languages with image, video, sound; they are really helpful.	0 (0%)	0 (0%)	0 (0%)	2 (22%)	7 (78%)
I can effectively use this application for diagnosis of ARF.	0 (0%)	1 (11%)	0 (0%)	3 (33%)	5 (56%)
Temporal Guideline information is clear and highly supports me in diagnosis of ARF cases.	0 (0%)	0 (0%)	1 (11%)	3 (33%)	5 (56%)
I trust the output of the ARF Diagnosis Application.	0 (0%)	0 (0%)	1 (11%)	3 (33%)	5 (56%)
The Application gives error messages that help me to understand further processes.	0 (0%)	1 (11%)	0 (0%)	3 (33%)	5 (56%)
ARF Diagnosis Application meet the NHF diagnosis procedure, practice and guideline.	0 (0%)	0 (0%)	1 (11%)	3 (33%)	5 (56%)
I am happy with the Application's loading time, information processing and retrieving times.	0 (0%)	2 (22%)	0 (0%)	5 (56%)	2 (22%)
Application is suitable for Nepalese lifestyle and environment.	0 (0%)	0 (0%)	1 (11%)	3 (33%)	5 (56%)
Overall, I am fully satisfied to use this ARF Diagnosis Application in Nepal.	0 (0%)	0 (0%)	1 (11%)	2 (22%)	6 (67%)

Figure 6.19 shows our ARF Diagnosis Application's overall performance result.

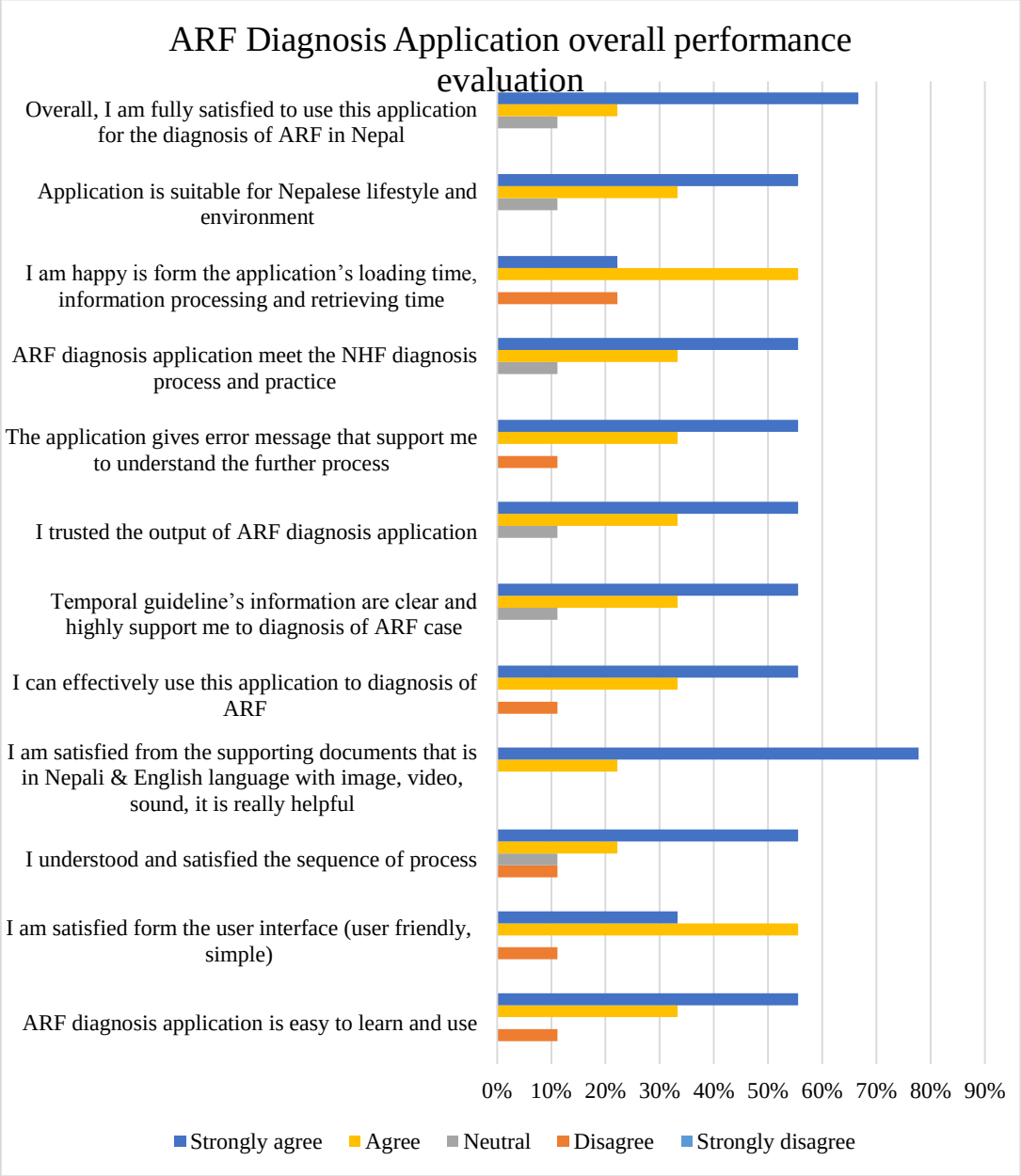


Figure 6.19: The Application's Overall Performance Evaluation Result

6.9. Sensitivity Analysis and Performance Evaluation

Our ARF Diagnosis Application had to be appropriate and useful for community rural health workers and inexperienced doctors, especially those who are working in the remote areas of Nepal. Our ARF Diagnosis Application was therefore designed and developed based on the Hybrid Approach, which is discussed in more detail in Research Methodology, Chapter 4. Each model has a specific process that performs a precise task, which makes the Application more robust. In the Sensitivity Analysis, we focussed on the following questions:

1. How confident are you with the KBS/Boolean Rule Model, Temporal and Fuzzy Models' results?
2. Check the importance of each model for ARF diagnosis; for example, what is the performance of our ARF Diagnosis Application likely to be if the Temporal Model is omitted.

6.9.1. Role of Each Model of ARF Diagnosis

The Knowledge-based model was used for the construction of Rules. The Boolean Rule Method was applied to represent the Knowledge. The Knowledge for diagnosis of ARF is straightforward, so that every portion of Knowledge can be formed into a Rule. We established a set of Rules, which is easy to read, understand and maintain for non-IT users especially for rural community health workers. Temporal Logic was used to model the event and time derived from a patient's verbal description during his/her explanation of perceived signs and symptoms. The Temporal Model was used to analyse the relationship between signs and the ARF and this enabled preparation of Temporal Template. Fuzzy Logic was used to model the uncertainties of symptoms and for making a final diagnosis, justification of the diagnosis and subsequent medication plan with guidelines and help subsets for ARF treatment, (Pandey S. *et al*., 2015).

In the diagnostic process of ARF, temporal information is essential because ARF symptoms are common, but some symptoms might indicate multiple diseases, and symptom appearance times can vary. For example, a patient can have a throat infection 3-7 days prior to other symptoms presenting or sometimes all symptoms will be present at the same time, or some symptoms will be present only after 2 weeks, a month, or even two months. Therefore, introduction of a Temporal Model is useful for the application that it can analyse properly the relationship between symptoms and ARF, length of the period between symptoms and relations between symptoms etc. Temporal rules are created by using temporal knowledge (Temporal Lookup Table) and will be interpreted for each patient's symptoms and how precisely they relate with the ARF case. Based on temporal interpretation and the patient's physical examination the doctor or community rural health worker will be able to provide a Crisp value for each sign and symptom and perform the further processes, which are discussed in the Research Methodology, Chapter 4.

Without a Temporal Model, the ARF Diagnosis Application is only able to identify the current stage of ARF. Therefore, to achieve our goal of making diagnosis more accurate and the Application more robust we recognised and agreed that inclusion of a Temporal Model is the key. The three models described are interrelated so that one model without another model cannot work. Further detail on this topic is provided in the Research Methodology, Chapter 4. Without a Temporal Model, a Fuzzy Model cannot be applied and without a KBS/Boolean Rule Model, the Temporal Model cannot apply. Introduction of a Temporal Model can unquestionably improve the accuracy and quality of ARF diagnostics. Each of the three key model's main tasks and outputs are shown in Table 6.12.

Table 6.12: Models and their Tasks and Outputs

Model Name	Task / Output
KBS/Boolean Rule Model	• Capture Patient's Symptoms. • Handle effectively Rule Pattern Matching, Rule Selection Mechanisms, New Rule Formation. • Identify the stage of ARF (Detected, Suspected, Not-detected). • If detected - identify the level of severity (Severe, Moderate, Mild). • Provide symptoms for Temporal Model process.
Temporal Model	• Capture temporal information of presented symptoms (date, duration). • Ordering symptoms (which signs appear first, second or together with other signs). • Analyses the relation between the presented symptoms and ARF. • Produce the Temporal Template by explaining how precisely related particular symptoms are to ARF. • Display the presented symptoms with duration, Temporal Template, and satisfied rule for Fuzzy Model process.
Fuzzy Model	• Fuzzy reasoning (fuzzification, reasoning and defuzzification). • Make a final diagnosis of ARF with explanation, % of severity level and justification of diagnosis. • Recommendation of the treatment e.g. oral or injection. • Prepare the medication plan e.g. dosages, duration, treatment period. • Guidelines for safe delivery of injections, allergies information. • Produce Patient Report Card.

6.9.1.1. Analysis of Temporal / Fuzzy Models' Outputs

In the NHF's datasets, only 129 record sets had temporal information and among them only 27 cases were detected or related to ARF. The NHF experts applied other random hypothesis datasets (120) for confidence in the Temporal Model as well as to evaluate related temporal constraints and rules. The dataset is given in Table 6.13. The output of comparing results is given in Table 6.14. We collaborated with NHF to setup the rules to identify the cases. Figures 4.1 and 4.3 in the Research Methodology, Chapter 4 and equations 1-11 were used to design the Rule for identifying and verifying detected ARFs.

Table 6.13: Dataset for Temporal / Fuzzy Model

Detected ARF	NHF's datasets Detected ARF case	Hypothesis Dataset	Total Dataset
Severe Case	4	40	44
Moderate Case	9	40	49
Mild Case	14	40	54
Total	**27**	**120**	**147**

Total datasets (120 + 127: Detected ARF 27, Not detected ARF 102) = 247.

Table 6.14: Comparision of Models and NHF's Temporal Constraints

Detected ARF	**NHF's datasets temporal constraints**	**Temporal + Fuzzy Model output**	**Differences**
Severe Case	44	44	0
Moderate Case	49	51	2
Mild Case	54	52	2
Total	**147**	**147**	**4**

Figure 6.20 shows comparison outputs between NHF dataset temporal constraints, Rule and Temporal and Fuzzy Models.

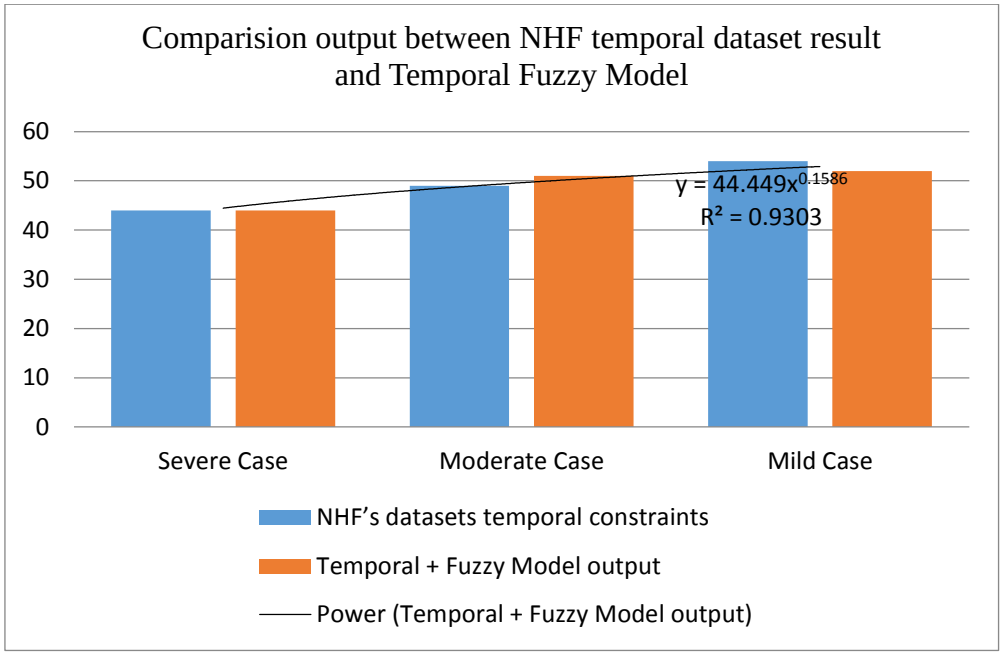


Figure 6.20: Comparison Output of NHF's and Temporal and Fuzzy Model

6.9.2. Performance Evaluation of ARF Application

A Confusion Matrix is applied for measuring and evaluating the ARF Application Diagnosis for testing its performance. In the matrix, Positive means detected ARF case while Negative means Not Detected ARF case. The Confusion Matrix is described in Tables 6.15 and 6.16.

Table 6.15: Confusion Matrix

Test Result	**Positive**	**Negative**	**Total (Row)**
Positive	True Positive (TP)	False Positive (FP)	TP + FP
Negative	False Negative (FN)	True Negative (TN)	EN + TN
Total (column)	**TP + FN**	**FP + TN**	**sum**

Table 6.16: Confusion Matrix for ARF Diagnostic Test

	Detected	**Suspected**	**Not Detected**	**Total (Row)**
Detected	84 (a)	0 (b)	3 (c)	87
Suspected	0 (d)	73 (e)	1 (f)	74
Not-Detected	0 (g)	0 (h)	475 (i)	475
Total (column)	84	73	479	636

Total (Column): ARF Diagnosis Application Result.

Total (Row): NHF Registry's Result.

Overall ARF Diagnostic Accuracy = (a + e + i) / n = (84+73+475)/636 = **99.36 %.**

Detected Case:

Positive Predictive Rate (Precision): a / (a + b + c) = 84/87 = 96.55 %.

False Positive Rate: c / (a + b + c) = 3/87 or = 3.45%.

True Positive Rate (Recall): a/ (a + d + g) = 84/84 = 100%.

Suspected Case:

Positive Predictive Rate (Precision): e / (d + e + f) = 73/74 = 98.65 %.

False Positive Rate: f / (d + e + f) = 1/74 = 1.35%.

True Positive Rate (Recall): e/ (b + e + h) = 73/73 = 100%.

Not-Detected Case:

Positive Predictive Rate (Precision): i / (g + h + i) = 475/475 = 100 %.

True Positive Rate (Recall) = i / (c + f + i) = 475/ (475 + 1 + 3) = 99.16%.

The overall accuracy of ARF Diagnosis Application was 99.36%. The true positive rate, also called **Sensitivity,** measures the number of cases that are correctly identified. The ARF stages test according to NHF guidelines matched very well with NHF datasets. Assessed overall, our ARF Diagnosis Application performance was rated as **very good**.

6.10. The ARF Treatment Implementation Plan

The Government of Nepal provided financial support to launch the "National Rheumatic Fever and Rheumatic Heart Disease Prevention and Control Program" from June 2007. Under this program, screening of school children is undertaken and penicillin injections for Rheumatic patients are made available through National, Regional and Zone Hospitals. Advocacy, training and awareness generation are other components of the programme. NHF has undertaken to exercise responsibility for the management and implementation of our ARF Diagnosis Application (NHF Report). The proposed action plans of the NHF are: (a) Prevention of GAS throat infection; meaning early diagnosis and proper treatment of GAS throat infections; (b) Secondary prevention – antibiotic prophylaxis; (c) requiring involvement of the Ministry of Health, Nepal Heart Foundation, Rural Health Care Centres, District Hospitals, other relevant organizations;

(d) provision of training for community rural health workers for ARF diagnosis; (e) develop a training curriculum or guidelines to teach ARF in each school of the country; (f) implement community awareness programs and home visit programs; (g) institute proper use of our newly developed model to identify ARF; (h) provide proper training for community rural health workers regarding the use of the model, and (i) Set up mobile ARF screening clinics at schools for our model to be used.

It was agreed that NHF will take overall responsibility for implementing our ARF Diagnosis Application. It is planed that the NHF will commence implementation the ARF Diagnosis Application July 2016. By this time, they will have setup their pre-implementation core plan which includes: 1) prepare a procedures and guidelines regarding use of the system; (2) prepare a hands outs and technical documentation for the Application; (3) identify the hospitals where required technology is available; (4) set-up and provide training for NHF staff regarding installation of the Application, data back-up, data management, handling of technical issues etc. and (5) set up a training plan for users describing how exactly to use the Application. Once these tasks have been completed, then ARF Diagnosis Application implementation plan will commence.

It has been agreed also that the Ministry of Health and the NHF will jointly implement the Application. It is already planned that in the first phase, the Application will be implemented at 38 district hospitals. The Application will be supervised so that all the diagnoses, medications and treatment plans will be verified by a medical health officer. When rural health workers become fully trained then the Application will be installed in the district public health offices where public health officers will be responsible for observation and verification of the diagnoses on a case-by-case basis. The initial implementation plan of the ARF Diagnosis Application is shown in Figure 6.21.

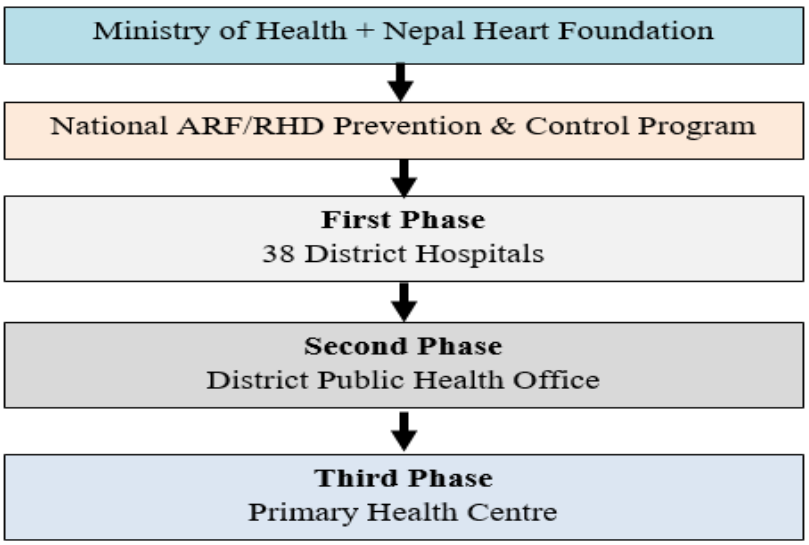


Figure 6.21: Initial Implementation Plan for the new ARF Diagnosis Application

The NHF experts will review, monitor and analyse the output of our ARF Diagnosis Application. Based on the results, the Application will be modified or updated the new information, or add new functionalities, if required. It is accepted that Sanjib Raj Pandey and Dr. Prakash Raj Regmi will be responsible for any re-engineering that may be required for the ARF's Application.

6.11. Chapter Summary

The aim of this chapter is to present experiment and evaluation results and overall performance and validation of our ARF Diagnosis Application including the basic concept of NHF's implementation plan regarding its future Application commencing in July 2016. The Application has been evaluated with NHF's survey datasets (636 records). Comparison of result shows that in total 98.74% matched with NHF's datasets and 1.26% did not match. The quality and accuracy of the methods, processes and functionalities of the Application were tested and evaluated by NHF experts. The accuracy of the identification of ARF stages was as follows: 75% were very satisfied and 25% were satisfied (100% satisfied overall). All participants who were surveyed stated that they were very satisfied with the accuracy and quality of our New Rule Formation process. So, in general 100% were satisfied that our Application was developed properly in accordance with their requirements. The overall accuracy of our ARF Diagnosis Application was found to be 99.36%.

Our ARF Diagnosis Application was thus successfully developed, experimented and evaluated meeting NHF's diagnosis criteria for treatment of ARF. The output of the evaluation was proof that the ARF Diagnosis Application we had developed in our

collaboration programme met the NHF's requirements. During experimentation and evaluation the following facts were identified as a key indicators and points for success of our ARF Diagnosis Application:

- Presented an interest and commitment of NHF's experts and users regarding the use of our innovative ARF Diagnosis Application.
- The Application's interface is user friendly.
- ARF Diagnosis Application suits the Nepalese environment and lifestyles.
- ARF knowledge and rules can be updated easily.
- The Temporal Template and other supporting materials can be updated easily.
- NHF application's supporting information was in both languages (Nepalese and English).
- Our ARF Diagnosis Application will be fully incorporated within the NHF diagnosis criteria since ARF diagnosis decisions are clear and transparent.

The following conclusions can be drawn from the system experiment and evaluation study:

- The application very well met the set of criteria established by the NHF.
- The Knowledge-based model can handle effectively the identification of ARF stages, Rule Pattern Matching and Rule Selection Mechanism, New Rule Formation.
- The quality and accuracy of New Rule Formation matched the set guidelines of NHF, and the Rule Selection Mechanism was shown able to select relevant rules from rule-based systems.
- The Temporal Lookup Table and temporal reasoning process can improve the accuracy and quality of ARF diagnostics.
- The fuzzy process can handle effectively al uncertainties pertaining to ARF symptoms.

Taken overall, it was shown that the proposed Hybrid Approach can provide a reliable tool for diagnosis of ARF cases. Moreover, the justification of diagnosis, recommendation of the treatment and medication planning added palpable strength to the Application. The next chapter concludes the description of our research and summarizes methodology, research contributions and indications for future work.

Chapter 7: Conclusion and Future Work

"A person who never made a mistake never tried anything new." - Albert Einstein

7.1. Introduction

This chapter summarises my whole research study. It highlights the important points of what was done during all the research activities as described in Section 7.2. Section 7.3 recapitulates my main findings. Section 7.4 explains the research contributions; Section 7.5 discusses the scope for future improvement; possible future research is discussed in Section 7.6.

7.2. Summary of research

It was found that CDSSs are not useful unless they are available at the time and point of patient care. Furthermore, it is clear that, any type of clinical diagnosis application must meet the users' requirements and must be user-friendly. My work shows the ARF Diagnosis Application which is the subject of my study, is the first computer-based decision support system in Nepal, designed and developed in the Nepalese setting. It is shown to be able to meet fully the NHF's requirements and is easy to use.

It is well accepted that late diagnosis of ARF is the common cause of heart damage and is a very serious problem in Nepal. In Nepal, 1000 children die each year due to ARF/RHD diseases, but are curable if the ARF symptoms are recognised and treated at an early stage. **No children are born to die from the late diagnosis of ARF**. Motivated by this, we strongly agreed with the NHF to proceed together in a collaboration research with UoG to develop a new, more effective application for ARF diagnosis. For our approach, we acknowledged that what was needed was a diagnosis model, which can: (a) assist rural health workers with diagnosis of ARF at an early stage; (b) provide a diagnosis model which will correctly recognize ARF symptoms and offer treatments that protect the heart from damage, (RHD); and save Nepali children's lives. I was also motivated strongly to investigate three problems that had not been addressed in the Artificial Intelligence community. These problems are: (i) ARF in Nepal historically has created a lot of confusion in the diagnosis and treatment domain, mainly due to lack of standard procedures; (ii) the adoption of foreign guideline is often not effective as they do not meet the needs of the Nepali environment and lifestyle; (iii) use of a Hybrid Approach (combination of Knowledge base, Temporal Theory and Fuzzy Logic) to design and

develop a system to diagnose ARF cases at an early stage in English and Nepali versions would be invaluable.

The main research question that I have tried to answer: "Is it feasible to apply Hybrid Approach (Knowledge-based system, Temporal Theory and Fuzzy Logic) to design and develop a cost effective CDSS model for the diagnosis of ARF that is suitable for the Nepalese environment and lifestyle?"

Realising that this key research question was of a general nature, I decided to define, more specific questions for my research programme and which I set out to answer. These included: 1) Is it appropriate for the diagnosis of ARF disease introduce a form which for an option to choose between "Detected ARF" (severity level: Severe Case, Moderate Case and Mild Case) or "Suspected ARF" (laboratory test) or "Not-detected ARF" (other diseases) in the Nepali environment? (2) Is it valid to develop a New Rule Formation process for the rule-based system for diagnosis of ARF? (3) Is it appropriate to indicate temporal constraints to show the relationship between the symptoms and ARF? (4) Is it feasible to feed a fuzzy value into pre-satisfied rules; justifying making a final decision on an ARF case? (5) Is it possible to develop the CDSS for diagnosis of ARF in Nepal based on the country's available ICT resources? (6) What type of user interface should be provided, suitable for doctors and community rural health workers and for those who are not familiar with using a clinical decision support system at all? (7) Is it practical to apply and implement an automated ARF Diagnosis Application in the rural areas of Nepal?

Based on these research questions, the assessable objectives of this research included: (a) examine the existing clinical practice and procedures of doctors and community rural health workers used to diagnose and manage ARF in Nepal; (b) investigate existing ARF/RHD diagnosis processes from the WHO, Jones' criteria, WHF, Australian and New Zealand systems, NHS Choice and NHF's expert guidelines; (c) acquire the required ARF knowledge (clinical dataset, diagnosis process and practice from the Nepalese environment and lifestyle) and use this research to develop English and Nepalese versions; (d) investigate the feasibility of employing the planned ARF Diagnosis Application with a Hybrid Approach using C#.NET, MS Access, Windows O/S; (e) develop techniques in Knowledge-based Systems, Temporal Theory and Fuzzy Logic for use in the ARF/RHD diagnosis model; (f) develop a suitable, easy to use and affordable

CDSS application for diagnosis of ARF in Nepal and (g) evaluate and verify the Application using NHF's real datasets.

The research carried out presents, validates and evaluates a proposed diagnosis method to diagnose ARF in three different stages: 1) Detected ARF; 2) Suspected and 3) Not-detected. It also underlined methods for identifying the severity level of detected ARF in the form of either "Severe Case", "Moderate Case" or "Mild Case". The research applied a Hybrid Approach to design, develop and implement an innovative ARF Diagnosis Application model. The Hybrid Approach was a combination of KBS/Boolean Rule Model, Temporal Model and Fuzzy Model. The research divided the overall ARF diagnosis problem and its requirements into several sub-problems and each model of the Hybrid Approach was organized to deal with a particular sub-problem. For example in identifying the stage of ARF we demonstrated a process of the KBS/Boolean Rule Model which was used to solve the problem of identifying the stage of ARF based on presented symptoms. Using this strategy every problem was handled by using a particular model's component/process and in this way I was significantly helped in finding ways to improve maintainability, reliability and the overall quality of our final ARF Diagnosis Application.

The ARF Diagnosis Application we prepared was experimented and evaluated by NHF's experts and in trials by users by using the NHF's datasets consisting of 676 records. The application matches 99% of cases of the NHF's datasets. We thus demonstrated and proved by experiment and evaluation of our ARF Diagnosis Application that: (1) our ARF Diagnosis Application can successfully identify the various stages of ARF; (2) our Rule Pattern Matching process, shows how an accurate rule can effectively detecting the number of positive signs and severity level of ARF; (3) our New Rule Formation process successfully and accurately generates a new rule in the rule-based system; (4) the Rule Selection Mechanism selects and displays the relevant rules automatically; (5) a Temporal Lookup Table/Rules show accurately the relationship between symptoms and ARF; (6) the Fuzzy Model handles all ARF uncertainties and makes a diagnosis of ARF with explanation and justification of diagnosis, recommended treatment method (oral, injection, dosages, duration, etc.), and provides treatment guidelines; (7) our Application integrates with help/supporting guidelines in Nepalese language including images, sounds, video and text; (9) our Application provides a cost-effective, user-friendly interface environment for medical practitioners. As a result, applied Hybrid Approach was conceived to support and facilitate the design of a new ARF diagnosis model.

7.3. Research Evaluation and Findings

Our collaboration research proved that it is logically and technically feasible to employ a Hybrid Approach for developing an ARF Diagnosis Application. An application was developed by us based on the NHF's requirement and guidelines. This proved to match the Nepalese setting and is suitable for use in the Nepalese environment and life style. The main findings addressing the research questions are given below:

1. The application we developed shows and proves that it is feasible and viable to use Hybrid Approach for developing an ARF Diagnosis Application.

2. It is appropriate and suitable for the diagnosis of ARF as either "Detected ARF" (severity level: Severe, Moderate, or Mild case) or "Suspected ARF" (laboratory test required) or "Not-detected ARF" (other diseases) in Nepal. This approach provides a quick treatment service to patients and community rural health workers. It prescribes the medication and follow up patient progress and if required it can recommend visiting the nearest hospital. Based on the premise that only severe cases need to visit hospital quickly. Normally rural health workers will prescribe medication themselves as a precaution to protect the heart from further damage. Suspected cases may also need to visit the nearest hospital for laboratory tests with ARF decisions only being made at the hospital based on laboratory results.

3. It is appropriate, very supportive and applicable to produce a Temporal Template which summarily explains the relationship in a specific case between the symptoms and ARF.

4. In Nepal, almost all hospitals are equipped with basic ICT infrastructure (computer with windows operating system, multimedia, office product 2007 or higher, printer, and scanner) which are sufficient to design and implement our ARF Diagnosis Application. Some hospitals certainly need to upgrade their machines and install Windows XP (or higher) operating systems with .NET framework 4.5, Access 2010, Office products and Acrobat reader. Meanwhile our ARF Diagnosis Application's installation kit is designed to have pre-installed: .NET framework 4.5, Acrobat reader, database file and other related files and program.

5. It was shown to be valid and applicable to feed the fuzzy value into pre-satisfied Rules and make a final decision on ARF. The Rule Selection Mechanism selects and

displays only the appropriate Rules from the Rule-based system. The fuzzy value will then feed into display rules so that the fuzzy inference mechanism makes a decision over the status of the ARF case. It is there not necessary to create a fuzzy rule since it does not make any significant difference to the accuracy of a diagnosis.

6. The designed and developed User Interface was shown to be appropriate and suitable for our ARF Diagnosis Application and its use. The Application's interface was accepted and well appreciated by NHF users.

7. We have demonstrated through our work that it is feasible to apply and implement an automated ARF Diagnosis Application in the rural areas of Nepal, where technologies are limited. The NHF has already made and agreed a plan to implement it initially at 38 district hospitals.

7.4. Research Contributions

The specific contribution of the thesis is divided into two parts and featured as follows:

7.4.1. Academic/Technical Contributions

- Our collaboration research developed a new CDSS framework for the diagnosis of ARF that integrates knowledge-based, temporal theory and fuzzy logic.

- This research developed techniques in temporal logic, fuzzy logic, rule selection and reasoning mechanisms for use in an ARF diagnosis model.

- This research developed a New Rule Formation process based on knowledge to generate a new rule for the ARF diagnosis model.

- This research developed Rule Selection; Rule Pattern Matching and reasoning mechanisms and New Rule Formation algorithm that are effective and appropriate for diagnosis of ARF.

- A main result is the design of a computer-based ARF diagnosis system that incorporates the concepts, ideas and procedures defined by our research study.

- We developed our Application based on three-tier architecture using an MS Access database which has the capability of managing and storing the Rules and patient's data. The C#.NET programming language was used to develop an Application which is portable, flexible, easy to use and implement and be cost effective.

- This research implemented and developed a help and support interface in both English and the Nepali language (some part) which can be accessed by users whenever required.

- This research developed an ARF Diagnosis Application that will inform/alert end users to any the changes of rules, or any guidelines related to ARF in Nepal.

- This research produced unique guidelines and procedures to diagnose ARF in Nepal, which suits the Nepalese environment and lifestyle.

7.4.2. Social Contributions in Nepal

- The Application we have developed will cut patients' costs and reduce the government's financial burden.

- Proper implementation and use of this Application will support the government in tracking down cases of ARF and RHD.

- Every individual obtains the same standard of service after using this Application.

- Community rural health workers and doctors can easily use the Application to diagnose ARF cases.

- It helps doctors and community health workers and others to perform their duties effectively and efficiently by minimising the chances of human error.

- It used NHF patients' real data in the research as evidence.

- Various statistical reports were produced which will help doctors or government to make further plans and policies to manage of ARF/RHD.

- ARF data will be available for further research.

- It will improve the practice of using technology in CDSSs.

7.5. Future Improvement

To prove the concept, a Hybrid Approach was used successfully to design, develop and implement a new ARF Diagnosis Application. It is shown that our Application accurately diagnoses ARF cases. NHF's procedure and guidelines were fully incorporated into our ARF Diagnosis Application. The final Application's results proved that the methods,

methodology, designed architecture and development process, met with the NHF's requirements. More importantly, the ARF Application's diagnostic performance was accepted for use by the NHF. Nevertheless we realize that many improvements are likely to done in the future, the most relevant of which is described below:

Develop and implement the newly adopted ARF Diagnosis Application (ours) in the Worldwide Web by applying suitable methodology. This extension within the functionality domain will certainly provide better ability for up-dating ARF data management, information management; better control and monitor applications; increase public awareness about ARF; facilitation of group training; monitoring work; group discussion and making objective clinical decisions regarding ARF case. Most importantly, rural health workers will be able to communicate swiftly with experts when they require support so that experts can also monitor and evaluate the diagnosis of a particular case with minimum time lags. Therefore, introduction of web-based system is likely to provide a much better service for users, patients and other related individuals and above all our ARF Diagnosis Application will have the potential to become available 24/7.

7.6. Future Research

Findings of our collaboration research reflects a positive and encouraging result about employing Hybrid Approach for developing ARF diagnosis applications using techniques for integrating the NHF's guidelines, process and practice for diagnosis of ARF in Nepal. This Hybrid Approach can be applied in other developing countries to design ARF Diagnosis Applications. We emphasise now that the significant potential for future research should consider two central issues:

1. In this Application, 6 different types of heart sounds were provided, which can help rural health workers to identify normal and abnormal heart sound. Rural health workers can use heart sounds for comparison with a patient's heart sound. This facility provides initial support to help care-workers to identify normal or abnormal heart situations in rural areas where expert support is often not available. This is a manual process and it depends entirely upon the judgment of an individual and his/her hearing capabilities. Therefore a potential research topic would be to record the heart sounds of a patient using computerized heart sound devices for those diagnosed with ARF or RHD and which can be stored on an appropriate database. Later, case-based reasoning methodology can be applied to search and compare the stored heart sound

for new cases. With this methodology the computer automatically records the heart sound of a patient and search and matches the sound in the database and is then able to retrieves those that match well within pre-determined guidelines. This is outstandingly useful for health-workers during diagnosis of ARF in the rural areas of Nepal.

2. Technology transfer for developed countries to developing countries can be useful but it has many obstacles which are discussed in the literature review. Investigation into means for capturing expert knowledge and experiences from developed countries and for transferring them to developing countries would be helpful for improving diagnosis, prognosis and patient treatment. Research could therefore focus upon design and development of a web-based tool to capture the expertise, knowledge and experiences of a particular domain and translate them into local vernacular versions thereby providing tangible benefit for health-care in all developing countries where such tools are not available.

Whilst our work indicates that many other productive researches could be conducted using the Hybrid Approach which we developed, there is a clear need to study and anticipate the many challenges that may lie ahead.

REFERENCES:

7CMU/SEI-2000-TR-028 (2000) *CMMISM for Systems Engineering/Software Engineering.* Version 1.02, Software Engineering Institute, November 2000. [Online], Available at: http://repository.cmu.edu/cgi/viewcontent.cgi?article=1101&context=sei, [Accessed: 22 Feb. 2015].

Abbod, M. F., von Keyserlingk, D. G., Linkens, D. A., and Mahfouf, M. (2001), 'Survey of utilisation of fuzzy technology in medicine and healthcare', *Fuzzy Sets and Systems*, vol.120, pp. 331-349, doi: 10.1016/S0165-0114(99)00148-7.

Abdulaziz Y., Mumtazeh S., (2010), 'Infant Cry Recognition System: A Comparison of System Performance based on Mel Frequency and Linear Prediction Campestral Coefficients', *International Retrieval & Knowledge Management*, IEEE, pp. 260 -263.

Achour, S. L., Dojat, M., Rieux, C., Bierling, P. & Lepage, E. (2001) *A UMLS-based knowledge acquisition tool for rule-based clinical decision support system development*. J Am Med Inform Assoc, vol. 8**,** pp. 351-360.

Adams AI, Chan M, Clifford PC, *et al.*, (1986), 'Computer -aided diagnosis of acute abdominal pain: a multi-center study', *British Medical Journal*, 293, pp. 800-805.

Adel Lahsasna, Raja Noor Ainon, Roziati Zainuddin, Awang Bulgiba (2012), 'Design of a Fuzzy-based Decision Support System for Coronary Heart Disease Diagnosis', *Journal of Medical Science*, vol.36, issue 5, pp. 3293-3306, 10.1007/s10916-012-9821-7.

Adlassnig, K-P. (1986), 'Fuzzy set theory in medical diagnosis', *IEEE Transaction on Systems, Man, and Cybernetics*, vol. 16, issue 2, pp. 260-265.

Agorastos, T., Koutkias, V., Falelakis, M., Lekka, I., Mikos, T., Delopoulos, A., Mitkas, P.A., Tantsis, A., Weyers, S., Coorevits, P., Kaufmann, A.M., Kurzeja, R. and Maglaveras, N. (2009), 'Semantic integration of cervical cancer data repositories to facilitate multicentre association studies: the ASSIST approach', *Cancer Informatics*, vol. 8, pp.31-44.

Akerkar, R.A. and Sajja, P.S. (2009). *Knowledge-based systems for development.* Jones & Bartlett Publishers, Sudbury, MA, USA.

Ali, S., Chia P, Ong, Ong, (1999), 'Graphical Knowledge-Based Protocols for Chest Pain Management', *Computer in Cardiology*, IEEE, pp. 309 -312.

Allen J. (1984), 'Towards a General Theory of Action and Time', *Artificial Intelligence*, vol. 23, pp.123-154.

Allen J.F. and Hayes P.J. (1989), 'Moments and Points in an Interval-based Temporal-based Logic', *Computational Intelligence*, vol.5 (4), pp. 225-238.

Allen, J.F., (1983), 'Maintaining knowledge about temporal intervals', *Communication of the ACM*, vol. 26, issue 11, pp. 832-843.

Ammenwerth E, Brender J, Nykanen P, Prokosch HU, Rigby M, Talmon J; HIS-EVAL (2004) workshop Participants, 'Visions and strategies to improve evaluation of health information systems', *Reflections and lessons based on the HIS-EVAL workshop in Innsbruck. Int J Med Inform*, vol. 73, issue 6, pp. 479-91.

Angele, J., Fensel, D., Landes, D., and Studer, R. (1998), 'Developing knowledge-based systems with MIKE', *Journal of Automated Software Engineering*, vol.5, issue 4, pp.389-418, 10.1023/A:1008653328901.

Awad, E. M. (2010) *Knowledge Management (2nd ed.).* North Garden, Virginia, USA: International Technology Group, LTD.

Bai, Y., Zhuang, H., Wang, D. (Eds.) (2006) *Fundamentals of Fuzzy Logic Control – Fuzzy Sets, Fuzzy Rules and Defuzzifications, Advanced Fuzzy Logic Technologies in Industrial Application.* 2006, XXV, pp. 334, with online files / update., ISBN 978-1-84628-468-7.

Bart Kosko, Satoru Isaka, (1993) *Fuzzy Logic.* Scientific American, July, 76-81, [Online]. Available at: http://sipi.usc.edu/~kosko/Scientific%20American.pdf, [Accessed: 04 April 2015]

Bates D.W., Kuperman G.J., *et al (2003)*, 'Ten Commandments for effective clinical decision support: Making the practice of evidence-based medicine a reality', *Journal of the American Medical Informatics Association*, vol. 10, issue 6, pp. 523-530.

Belacel N., Boulassel M.R., (2001), 'Multicriteria fuzzy assignment method: a useful tool to assist medical diagnoses, *Artificial Intelligence in Medicine* 21, 201±207.

Bellazzi R., Larizza C., Magni P., Montani S., Stefanelli M., (2000), 'Intelligent analysis of clinical time series: an application in the diabetes mellitus domain', *Artifical Intelligent in Medicine*, vol. 20, issue 1, pp. 37-57, doi>10.1016/S0933-3657(00)00052-X.

Benthem J.V. (1983) *The logic of Time*. Kluwer Academic Publisher, Dordrecht, Boston.

Bernadette Bouchon-Meunier, Mariagrazia Dotoli, Bruno Maione, (2007), 'On the Choice of Membership Functions in a Mamdani-Type Fuzzy Controller', *CiteSeer X.psu*: 10.1.1.52.8144

Bilge U., Bozkurt, S., & Durmaz, S. (2013), 'Application of data mining techniques for detecting asymptomatic carotid artery stenosis', *Computers and Electrical Engineering*, vol. 39, issue 5, pp.1499–1505, doi:10.1016/j.compeleceng.2012.12.010.

Boaz D., Shahar Y. (2003), 'IDAN a distributed temporal-abstraction mediator for medical databases', In: Dojat M, Keravnou ET, Barahona P, editors. *Proceedings of 9th Conference on Artificial Intelligence in Medicine in Europe (AIME 2003)*, Protaras, Cyprus, LNCS 2780, Springer Verlag, pp. 21-30.

Boehm, B. (1979) *Software engineering; R & D trends and defence needs*. In Research Direction in Software Technology (P.Wenger, ed.), Cambridge, MA: MIT Press, 1-9.

Boose J H. (1985) *A Knowledge Acquisition Program for Expert Systems Based on Personal Construct Psychology*. Int. J. Man-Mach. Stud., vol. 23, pp. 495-525.

Boose J H., Bradshaw J M. (1987) *Expertise Transfer and Complex Problems: Using AQUINAS as a Knowledge Acquisition Workbench for Knowledge-Based System.* Int. J. Man-Mach. Stud., vol. 26, pp. 3-28.

Burce B.C. (1972), 'A Model for Remporal References and Application in a Question Answering Program', Artificial *Intelligence*, vol. 3, pp.1-25.

Carapetis JR, Steer AC, Mulholland EK, Weber M, (2005) *The global burden of group A*

streptococcal diseases. Lancet Infectious Disease, vol. 5, pp. 685–694.

Carlo Combi and Yuval Shahar, (1997), 'Temporal Reasoning and Temporal Data Maintenance in Medicine: Issues and Challenges', *Computers in Bilogoy and Medicine*, vol. 27, issue 5, pp. 353-68.

Carter J. H., (1999) *Clinical Decision Support Systems.* E.S. Berner, Ed. (Springer-Verlag, New York, 1999), pp.169-198.

Carter, J. H. (2007) *Design and Implementation Issues* IN BERNER, E. S. (Ed.), *Clinical Decision Support Systems: Theory and Practice.* 2nd ed. New York, Springer-Verlag.

Çelik, Yıldıray ; Yamak, Sultan , (2013), 'Fuzzy soft set theory applied to medical diagnosis using fuzzy arithmetic operations', *Journal of Inequalities and Applications*, vol.1, pp.1-9.

Cesar Uribe1, Claudia Isaza1, and Jose F. Florez-Arango, (2011), 'Qualitative-Fuzzy Decision Support System for Monitoring Patients with Cardiovascular Risk', *2011 Eighth International Conference on Fuzzy Systems and Knowledge Discovery (FSKD)*, 978-1-61284-181-6/11©2011 IEEE

Chandrasekaran B. (1986), *Generic tasks in knowledge-based reasoning : High-level building blocks for expert system design*. IEE Expert, (1) pp. 23-30

Chang-Shing Lee, Senior Member, *IEEE*, and Mei-Hui Wang (2011), 'A Fuzzy Expert System for Diabetes Decision Support Application', *IEEE transactions on systems, man, and cybernetics-part b: cybernetics*, vol. 41, no. 1, pp. 139.

Chen, H.-L., Huang, C.C., Yu, X.G., Xu, X., Sun, X., Wang, G., (2013), 'An efficient diagnosis system for detection of Parkinson's disease using fuzzy k-nearest neighbor approach', *Expert Systems with Applications*, vol. 40, pp. 263–271, doi:10.1016/j.eswa.2012.07.014.

Chen, M. S. and Wang, S. W. (1999) *Fuzzy clustering analysis for optimizing membership functions.* Fuzzy Sets and Systems, 103, pp.239–254.

Chittaro L, Del Rosso M, Dojat M. (1995), 'Modeling medical reasoning with the event calculus: an application to the management of mechanical ventilation', *In: Barahona P, Stefanelli M, Wyatt J, (eds) Artificial Intelligence in Medicine, LNAI 934*, Berlin Heidelberg, Springer, pp. 79 - 90.

Chou, S.M., Lee, T.-S., Shao, Y. E., & Chen, I. F. (2004), 'Mining the breast cancer pattern using artificial neural networks and multivariate adaptive regression splines', *Expert Systems with Applications*, vol. 27, pp.133–142, doi:10.1016/j.eswa.2003.12.013

Cilliers A. M (2006), 'Rheumatic fever and its management', *British Medical Journal BMJ*, 333(7579), pp.1153-6.

Cindy, Marling, Jay, Shubrook& Franck. Schwartz (2008), 'Case-Based Decision Support for Patients with Type 1 Diabetes on Insulin Pump Therapy', *9th European Conference, ECCBR*, Springer-Verlag, Berlin, pp.325-339.

Clayton P.D., Pryor T.A., O.B. Wigertz, and G. Hripcsak (1989), 'Issues and structures for sharing medical knowledge among decision-making systems: The 1989 Arden homestead retreat', *In Proceedings of the Annual Symposium on Computer Application in Medical Care.*

Clinfowiki, 'Timme of the Development of Clinical Decision', [Online], Available at: http://clinfowiki.org/wiki/index.php/Timeline_of_the_Development_of_Clinical_Decision, [Assessed: 11 Feb. 2015].

Connolly, T.M. and Begg, C.E. (2010) *Database systems: a practical approach to design, implementation, and management*. 5th edition Boston; London: Addison-Wesley.

Cooke, N.J. (1994), 'Varieties of knowledge elicitation techniques', *International Journal of Human-Computer Studies*, vol. 41 no. 6, pp. 801-49.

D Tadaki (2009), 'Advanced Surgical Imaging', *Biomedical Science & Engineering Conference*, IEEE, pp.1-1.

Darlene Berge (1988-2000), 'A brief history of medical diagnosis and the birth of the clinical laboratory: Part 1-Anicient times through the 19th Century', [Online]. Available at: http://www.academia.dk/Blog/wp-content/uploads/KlinLab-Hist/LabHistory1.pdf, [Accessed: 13 April 2015].

Das G., Gunopulos D. and Mannila H., (1997), 'Finding similar time series', *In proceedings of 1st the European Symposium on Principles of Data Mining and Knolwedge Discovery form Database*, Trondheim, Norway, pp.88-100.

David Sutton & Vivek Patkar, (2009), 'CommonKADS analysis and description of a knowledge based system for the assessment of breast cancer', *Expert Systems with Applications*, vol. 36, pp. 2411–2423.

David Boaz and Yuval Shahar (2003) *Idan: A Distributed Temporal-Abstraction Mediator for Medical Databases.* Artificial Intelligence in Medicine, pp. 21-30, 10.1007/978-3-540-39907-0_3.

David, B. Leake (1996) *Case-Based Reasoning: Experiences, Lessons, and Future Directions*. MIT press.

Davis R, Lenat D. (1982) *Knowledge-Based System in Artificial Intelligence*. New York, MacGraw-Hill.

Demmer-Fushman D., Lin J. (2007), 'Answering Clinical Question with Knowledge-Based and Statistical Techniques', *Association for Computational Linguistics*, pp.63-103.

Diederich J (Ed.) (2008) *Rule Extraction from Support Vector Machines*. Springer Studies in Computational Intelligence, vol. 80.

Diederich J., Ruhmann I and Mark May (1987), 'KRITON: a knowledge-acquisition tool for expert system', *Internal Journal of Man-Machine Studies*, CiteSeerx vol. 26, pp. 29-40.

Dorr, D., Bonner, L., Cohen, A., Shoai, R., Perrin, R., Chaney, E. & Young, A. (2007), *Informatics systems to promote improved care for chronic illness a literature review*. American Medical Informatics Association, vol.14, issue 2, pp. 156–163.

Druzdzel, M. J. and R. R. Flynn (1999) *Decision Support Systems.* Encyclopedia of Library and Information Science. A. Kent, Marcel Dekker, Inc.

Duch W (2000) *Similarity based methods: a general framework for classification, approximation and association.* Control and Cybernetics, vol. 29, issue 4, pp. 937-968.

Duch, W., Grudzinski, K. (2001), 'Prototype based rules-a new way to understand the data', *International Joint Conference on Neural Networks*, proceedings '01 2001, vol.3, pp.1858-1863.

Duftschmid G. et.al, (2002). 'Verification of temporal scheduling constraints in clinical practice guidelines', *Artificial Intelligence in Medicine*, vol. 25, issue 2, pp.93-121, DOI : 10.1016/S0933-3657(02)00011-8.

Durkin, J. (1994) *Expert Systems Design and Development.* Prentice Hall, Englewood Cliffs, NJ.

Dxplain: [Online]. Availabe at: http://www.mghlcs.org/projects/dxplain , [Accessed: 28 Feb 2015].

Dzeroski, S., and Nada Lavrac (1996), 'Rule induction and instance-based learning applied in medical diagnosis', *Technology and Health Care,* 4.2, pp. 203-221.

Edward Samuel A. and Balamurugan M. (2012) *Fuzzy Max-Min Composition Technique in Medical Diagnosis Applied Mathematical Sciences*, vol. 6, no. 35, pp. 1741-1746.

Efraim Turban & Jay E. Aronson (2001) *Decision Support Systems and Intelligent Systems.* 6th edition Copyright 2001, Prentice Hall, Upper Saddle River, NJ.

Encyclopedia (2009), 'Medical Decision Making', Contribution by J. Hilden, j.hilden@biostat.ku.dk.

Engel ME, Stander R, Vogel J, *et al* (2011), 'Genetic susceptibility to acute rheumatic fever: a systematic review and meta-analysis of twin studies', *PLoS One, 2011; 6 (9): e25326, doi: 10.1371/journal.pone.0025326, Epub 2011 Sep 30.*

English PC. (1999) *Rheumatic fever in America and Britain. A biological, epidemiological and medical history*. New Jersey: Rutgers University Press; pp. 17-52.

Enrico Coiera (2003) *Chapter 25 Clinical Decision Support System.* In: Enrico Coiera, editor. Guide to Health Informatics 2nd Edition. Hodder Arnold.

Esposito, Massimo; De Pietro, Giuseppe, (2011) *An ontology-based fuzzy decision support system for multiple sclerosis, Engineering Applications of Artificial Intelligence.* 2011, vol. 24, issue 8, pp.1340-1354.

Feinstein, A.R., Wood, H.F., Epstein, J.A., Taranta, A., Simpson, R., and Tursky, E. (1959), ' A controlled study of three methods of prophylaxis against streptococcal infection a population of rheumatic children II: results of the first three years of the study including methods for evaluating the maintenance of oral prophylaxis', *N Engl J Med*. 260, pp. 689–702.

Finlay, P. N. (1994), *Introducing decision support systems.* Oxford, UK Cambridge, Mass., NCC Blackwell; Blackwell Publishers.

Ford, D.N. and Sterman, J.D. (1998) *Expert knowledge elicitation to improve mental and formal models.* System Dynamics Review, vol. 14 no.4, pp. 309-30.

Fox J, Johns N, Rahmanzadeh A, Thomson R, (1996), 'PROforma: A method and language for specifying clinical guidelines and protocols', *Proceedings of Medical Informatics Europe* Amsterdam.

Fox J., Johns N., and Rahmanzadeh A. (1998), 'Disseminating medical knowledge: the

proforma approach', *Artificial Intelligence in Medicine*, vol. 14, pp.157-181.

Fuzzy toolbox: [Online]. Avaialbe at: http://www.mathworks.co.uk/help/toolbox/fuzzy/fp72.h [Accessed: 2013, 2014, 2015].

Galton A, (1990) *A critical Examination of Allen's Theory of Action and time*. Artificial Intelligence, vol. 42, pp. 159-188.

Ganapathy S., Sethukkarasi R., Yougesh P., Vijayakumar P. and Kannan A. (2014), 'An intelligent temporal pattern classification system using fuzzy temporal rules and particle swarm optimization', *Indian Academy of Science*, Sadhanna, vol. 29, Part 2, pp. 283-302.

Garbay, C. (2000) *Knowledge Acquisition and Representation*. The Biomedical Engineering Handbook: Second Edition. Ed. Joseph D. Bronzino, Boca Raton: CRC Press LLC.

Gennari, John H ; Musen, Mark A ; Fergerson, Ray W ; Grosso, William E ; Crubézy, Monica ; Eriksson, Henrik ; Noy, Natalya F ; Tu, Samson W, (2003), 'The evolution of Protégé: an environment for knowledge-based systems development', *International Journal of Human - Computer Studies*, vol.58, issue 1, pp.89-123.

González A, Pérez R, Valenzuela A (1995), 'Diagnosis of myocardial infarction through fuzzy learning techniques', *Proc Sixth International Fuzzy Systems Association World Congress* (IFSA'95) pp. 273–276.

Goralwalla, Iqbal A., Özsu, M.Tamer, Szafron, Duane, (1997) *Modeling medical trials in pharmacoeconomics using a temporal object model*. Computers in Biology and Medicine, vol.27, issue 5, pp. 369-387, doi: 10.1016/S0010-4825(97)00011-5.

Guralnik V & Srivastava J. (1999), 'Event detection from time series data', *In Proceedings of the 5th ACM SIGKDD International Conference on Knowledge Discovery and Data Mining* (KDD'99), San Diego, CA, pp:33-42.

Hajioff S. (1998), 'Computerized decision support systems: an overview', *Health Informatics Journal*, doi: 10.1177/146045829800400104, vol. 4 no. 1, pp. 23-28

Hansen, W. (1971), 'User Engineering Principles for Interactive Systems', *AFIPS Conference Proceedings 39*, AFIPS Press, pp. 523-532.

Hartwich, F., & Janssen, W. (2000) *Setting research priorities: An example from agriculture using the analytic hierarchy process*. Research Evaluation, vol. 9, issue 3, pp. 201-210.

Health Evaluation Through Logical Processing (HELP), 'Knowledge-based hospital information system', [Online], Available at: http://www.openclinical.org/aisp_help.html [Accessed: 14 April 2015].

Hongwei Zhu, Stuart E. Madnick, Michael D. Siegel, (2004), 'Effective Data Integration in the Presence of Temporal Semantic Conflicts', *MIT Sloan School of Management*, 30 Wadsworth Street, Cambridge, MA 02142, USA, [Online], Available at: http://ebusiness.mit.edu [Accessed: 14 May 2015].

Houeland, T. G., & Aamodt, A. (2009), 'Towards an introspective architecture for meta-level reasoning in clinical decision support systems', *In 7th Workshop on CBR in the Health Sciences*, ICCBR pp. 136-147.

Hu-Chen Liu, Long Liu, Qing-Lian Lin, Nan Liu, (2013), 'Knowledge Acquisition and

Representation Using Fuzzy Evidential Reasoning and Dynamic Adaptive Fuzzy Petri Nets', *IEEE Transactions on Cybernetics*, vol .43, issue 3, pp.1059-1072.

Ian Sommerville (2001) *Software Engineering 6th Edition.* ISBN 0-201-39815-X, Addison Wesley.

Ida Sam *et al*, (2001), 'Clinical Decision Support Systems for the Practice of Evidence-based Medicine', *The Journal of the American Medical Informatics Association*, vol. 8, issue 6, pp. 527–534.

ISABEL, *"the diagnosis checklist"*, [Online], Available at: http://www.isabelhealthcare.com/home/default, [Accessed: 28 Feb. 2015].

James F. Allen and Patrick J. Hayes (1987), 'Moments and Points in an Interval-Based Temporal Logic', *Departments of Computer Science and Philosophy The University of Rochester*, Rochester, NY 14627, urresearch.rochester.edu.

Jang, J. S. R., Sun, C. T., & Mitzutani, E. (1997) *Neuro-Fuzzy and Soft Computing: A Computational Approach to Learning and Machine Intelligence*. Upper Saddle River, USA: Prentice Hall Inc., pp. 8-33.

Jeong S., Youn C.-H., Y.-W. Kim, Shim S.-O. (2014), 'Temporal progress model of metabolic syndrome for clinical decision support system', IRBM, vol.35, issue 6, pp.310-320, doi:10.1016/j.irbm.2014.08.003.

Jim Warren, Gleb Beliakov and Berend van der Zwaag (2000), 'Fuzzy logic in clinical practice decision support systems', *Proceedings of the 33rd Hawaii International Conference on System Sciences* 2000.

Jin, B., Tang, Y. C., and Zhang, Y.Q. (2007), 'Support vector machines with genetic fuzzy feature transformation for biomedical data classification', *Information Sciences*, 177, pp. 476-489. doi:10.1016/j.ins.2006.03.015

Jones T.D. (1994), 'Diagnosis of rheumatic fever', *Journal of the American Medical association*, vol.126, pp.481-484.

Jose Palma, Jose M. Juarez, Manuel Campos, Roque Marin (2006), 'Fuzzy theory approach for temporal model-based diagnosis: An application to medical domains', *Artificial Intelligence in Medicine*, vol. 38, pp.197-218.

Kahn G, Nowlan S, McDermott J. (1985), 'MORE: an Intelligent Knowledge Acquisition Tool', *Proceedings AAAI* '85. pp. 581-584.

Kahn M. G. & K. A. Marrs (1995), 'Creating Temporal Abstractions in Three Clinical Information Systems', *ProcAnnuSympComputAppl Med Care*, 392–396. PMCID: PMC257912.

Kavan Sedighiani, Seyed Sasan Hashemi Khabir (2009), 'Constructing interpretable genetic fuzzy rule-based system for Breast Cancer Diagnostic', *Global Congress on Intelligent Systems*, 978-0-7695-3571-5/09 © 2009 IEEE Computer Society, DOI 10.1109/GCIS.2009.349

Kaya, M. and Alhajj, R. (2003), 'A clustering algorithm with genetically optimized membership functions for fuzzy association rules mining', *12th IEEE International Conference on*

Fuzzy Systems., vol. 2, pp.881–886.

Kazem Sadegh-Zadeh (2000), 'Fuzzy Health, Illness, and Disease', *In: The Journal of Medicine and Philosophy*, vol. 25, pp. 605-638.

Keen, P. G. W. and M. S. Scott Morton (1978) *Decision support systems : an organizational Perspective.* Reading, Mass., Addison-Wesley Pub. Co.

Kellogg W.K. (2004), W.K. Kellogg Foundation Evaluation Handbook, [Online], Available at: www.wkkf.org/~/media/62EF77BD5792454B807085B1AD044FE7.ashx [Assessed: 8 July 2015].

Kemal Polata, Salih Güne¸sa, Sülayman Tosunb (2006) *Diagnosis of heart disease using artificial immune recognition system and fuzzy weighted pre-processing.* Elsevier, Pattern Recognition, vol. 39 pp. 2186 - 2193.

Kensaku Kawamoto, Caitlin A Houlihan, E Andrew Balas, David F Lobach (2005), '"Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to successes, *BMJ 330* (7494): 765, doi: 10.1136 /bmj.38398.500764.8F. PMC 555881, PMID 15767266.

Klaus-Peter Adlassnig, Carlo Combi, Amar K. Das, Elpida T. Keravnou, Giuseppe Pozzi (2006), 'Temporal representation and reasoning in medicine: Research directions and challenges', *Artificial Intelligence in Medicine, Temporal Representation and Reasoning in Medicine,* vol.38, issue 2, pp.101-113.

Klopper H., Andersson H., *et al* (2006), 'Strategies in assessing post-operative pain-A South African study', *Intensive and Critical Care Nursing*, pp. 12-21.

Kosko, B. (1986), 'Fuzzy Cognitive Maps', *International Journal of Man-Machine Studies*, vol. 24, pp. 65-75.

KOSKO, B. (1992) *Neural networks and fuzzy systems.* Prentice Hall, 1992.lected.

Kris Verlaene, Wouter Joosen, Pierre Verbaeten (2007), 'Arriclides: An Architecture Integrating Clinical Decision Support Models', hicss, pp.135c, *40th Annual Hawaii International Conference on System Sciences (HICSS'07).*

L.Brownston, R. Farrell, E. Kant & N.Martin (1986) *Programming Expert Systems in OPS5, An Introduction to Rule Based Programming.* Addison Wesley Publishers, USA.

Lai, J.K., Lau, F. and Shaw, N. (2009), 'A study of information technology use and implementation of electronic medical record systems in BC medical practices', *BC Medical Journal*, vol. 51, no. 3, pp.114-21.

Lalande, A. *et al*. (1997), 'Automatic detection of cardiac contours on MR images using fuzzy logic and dynamic programming', *Procedding AMIA Ann. Fall Symp*., pp. 474-478.

Legind Larsen (2005) Aalborg University Esbjerg, 'Fundamentals of fuzzy sets and fuzzy logic ', *Computer Science / Course in Fuzzy Logic*.

Levashenko, V. and Zaitseva, E. (2012), 'Fuzzy Decision Trees in medical decision Making Support System', *2012 Federated Conference on Computer Science and Information Systems*, pp.213-219.

Lim, C. K., K. M. Yew, K. H. Ng, and B. J. J. Abdullah (2002), 'A proposed hierarchical fuzzy inference system for the diagnosis of arthritic diseases', *Australasian Physics & Engineering Sciences in Medicine*, vol. 25, no. 3 pp. 144-150.

Limberg, Julia; Seising, Rudolf (2007) 'Fuzzy Health, Illness, and Disease Sadegh-Zadeh's framework and a program to identify diseases', *Fuzzy Systems Conference, FUZZ-IEEE 200*, IEEE International, DOI 10.1109/FUZZY.2007.4295467.

Liu F., Ng G. S., Quek C., Loh T. F. (2006), 'Artificial Ventilation Modeling using Neuro-Fuzzy Hybrid System', *International Joint Conference on Neural Network*, Sheraton Vancouver Wall Centre Hotel, Vancouver, BC, Canada.

Lotfi A. Z (1956) *Fuzzy sets.* Information and Control, vol. 8, pp. 338-353.

Lotfi A. Z (1983) *The role of fuzzy logic in the management of uncertainty in expert systems*. Fuzzy Sets and Systems, vol. 11, issue 1, Pages 197-198.

Lotfi A. Zadeh (2004), 'Fuzzy logic systems: origin, concepts and trends', [Online], Available at: http://wi-consortium.org/wicweb/pdf/Zadeh.pdf [Accessed: 12 July 2015].

Lotfi A. Zadeh (2008), 'Is there a need for fuzzy logic?', *Information Sciences*, vol. 178, pp. 2751-2779.

Luca Anselma, Paolo Terenziani, Stefania Montani, Alessio Bottrighi (2006), 'Towards a comprehensive treatment of repetitions, periodicity and temporal constraints in clinical guidelines', *Artificial Intelligence in Medicine*, vol. 38, pp. 171-195, doi: 10.1016/j.artmed.2006.03.007.

Lundsgaarde H. (1987), 'Evaluating medical expert systems', *Soc Sci Med* 1987; 24: 805-819.

Ma J. (2007), 'Ontological Considerations of Time, Meta-Predicates and Temporal Propositions, Applied Ontology', vol.2, issue 1, pp. 37-66, IOS Press Amsterdam, ISSN: 1570-5838.

Ma J., Knight B. (2003), 'Representing The Dividing Instant', *the Computer Journal*, vol. 46, issue 2, pp. 213-222.

Ma J., Knight B. (1994), 'A General Temporal Theory', *the Computer Journal*, vol.37, issue 2, pp.114-123.

Magoulas, G. D., Plagianakos, V. P., & Vrahatis, M. N. (2004), 'Neural network-based colonoscopic diagnosis using on-line learning and differential evolution', *Applied Soft Computing*, 4, 369–379. doi:10.1016/j.asoc.2004.01.005.

Mahfouf, M., Abbod, M. F., & Linkens, D. A. (2001), 'A survey of fuzzy logic monitoring and control utilisation in medicine', *Artificial Intelligence in Medicine*, vol. 21, pp. 27–42, doi: 10.1016/S0933-3657(00)00072-5.

Marakas, G. M. (1999) *Decision support systems in the twenty-first century*. Upper Saddle River, N.J., Prentice Hall.

Marijon E, Ou P, Celermajer DS, *et. al* (2007), 'Prevalence of rheumatic heart disease detected by echocardiographic screening', *The New England Journal of Medicine*, 357:470–476.

Mason, D., Linkens, D. & Edwards, N. (1997), 'Self-learning fuzzy logic control in medicine', *Procedding AIME'97, (E. Keravnou et al., eds.), Lecture Notes in Artificial Intelligence*

1211, Springer -Verlag: Berlin, pp. 300-303.

Mayhew, Deborah (1992) *Principles and Guidelines in Software User Interface Design*. New Jersey: Prentice-Hall.

McDermott, Drew (1982) *A Temporal Logic for Reasoning about Processes and Plans.* Cognitive Science, vol.6, issue 2, pp.101-15

Mendel J. M. (1995), 'Fuzzy logic systems for engineering: A tutorial', *Proceedings of the IEEE*, vol. 83, issue 3, pp. 345-377.

Meyer, B. (2008), 'Seven principles of software testing', *IEEE Computer*, vol. 41, issue 10, pp. 99-101.

Michael D Seckeler, Tracey R Hoke, (2011) *The worldwide epidemiology of acute rheumatic fever and rheumatic heart disease*. Clin Epidemiol, vol. 3, pp.67–84, doi: 10.2147/CLEP.S12977 PMCID: PMC3046187.

Microsoft 2, "*Introduction to the C# Language and the .NET Framework*", [Online], Available at: https://msdn.microsoft.com/en-gb/library/z1zx9t92.aspx [Accessed: 14 Jan 2015]

Microsoft 3, "*The .NET Framework System Requirements*", [Online], Available at: https://msdn.microsoft.com/en-us/library/8z6watww.aspx [Accessed: 14 Jan 2015]

Microsoft,*"NET Framework Conceptual Overview"*, [Online], Available at: https://msdn.microsoft.com/en-us/library/zw4w595w%28v=VS.100%29.aspx [Accessed: 14 Jan 2015]

Mitchell T (1997) *Machine Learning.* New York: McGraw Hill.

MIZUMOTO, M. (1988) *Fuzzy controls under various fuzzy reasoning methods.* In Information Sciences 45.

Nabil Belacel (2000), 'Multicriteria assignment method PROAFTN: Methodology and medical application', *European Journal of Operational Research* 125, 175±183.

Nauck D, Klawonn F, Kruse R (1997) *Foundations of Neuro-Fuzzy Systems.* Chichester: Wiley.

Nepal Himalayan Times (2015), [Online], Available at : http://thehimalayantimes.com/kathmandu/computer-based-arf-diagnosis-system-developed/

NHF (2011), 'National Seminar on RF/RHD Prevention and Control in Nepal', *July 2011.*

Nielsen J. (Ed.) (1993) *What is usability? Usability Engineering.* Academic Press, Chapter 2.

Nielsen, J. (1994) *Heuristic evaluation.* In Nielsen, J., and Mack, R.L. (Eds.), Usability Inspection Methods, John Wiley & Sons, New York, NY.

Noor Akhmad Setiawan1, P.A. Venkatachalam2 and Ahmad Fadzil M.Hani (2009), 'Artificial Intelligence Based Decision Support System', *Proceedings of the International Conference on Man-Machine Systems (ICoMMS)*, Batu Ferringhi, Penang, MALAYSIA.

Ohno-Machado L., Gennari J.H., *et al* (1998), 'The guideline interchange format: a model for representing guidelines', *Journal of the American Medical Informatics Association*.

Ongenae, Femke ; Dhaene, Tom ; De Turck, Filip ; Benoit, Dominique ; Decruyenaere, Johan

(2010), 'Design of a probabilistic ontology-based clinical decision support system for classifying temporal patterns in the ICU: a sepsis case study Computer-Based Medical Systems', *23rd IEEE International symposium, Proceedings.*

Open Clinic: Absru, [Online], Available at: http://www.openclinical.org/gmm_asbru.html, [Accessed: 11 August 2015].

Open Clinic: Glif, 2000, [Online], Available at: http://www.openclinical.org/gmm_glif.html, [Accessed: 11 August 2015].

Open Clinic: Guide, 1998, [Online], Available at: http://www.openclinical.org/gmm_guide.html, [Accessed: 12 August 2015].

Open Clinic: Prodigy, [Online], Available at: http://www.openclinical.org/gmm_prodigy.html, [Accessed: 12 August 2015].

Open Clinic: Arden Syntax, [Online], Available at: http://www.openclinical.org/gmmsummaries.html#arden, [Accessed: 2 Sept. 2015].

Open Clinical, 'Knowledge Management for Medical Care, Decision Support System', [Online], Available at: http://www.openclinical.org/dss.html [Accessed: 28 Feb. 2015]

Ozsoyoglu G, Snodgrass RT (1995), 'Temporal and real-time database: a Survey', IEEE *Transactions on Knowledge and Data Engineering* vol. 7, issue 4, pp. 513-532.

Pandey Sanjib Raj, Ma Jixin and Lai, Choi-Hong (2014),'Fuzzy membership function and input/output parameter for diagnosis of rheumatic fever', *International Transactions on Information Science and Technology (ITIST)*, 2 (6). pp. 10-15. ISSN 2325-6567 (Print), 2325-6575.

Pandey Sanjib, Ma Jixin and Lai Choi-Hong (2015), 'Development of Decision Support System for the Diagnosis of Arthritis Pain for Rheumatic Fever Patients: Based on the Fuzzy Approach', *Journal of Algorithms and Computational Technology*, vol. 9, issue 3, pp. 265-290, DOI: http://dx.doi.org/10.1260/1748-3018.9.3.265.

Pandey, B., & Mishra, R. B. (2009), 'Knowledge and intelligent computing system in medicine', *Computers in Biology and Medicine*, vol. 39, pp. 215-230. doi:10.1016/j.compbiomed.2008.12.008

Peleg M., Tu S., and Bury J. (2002), 'Comparing models of data and knowledge for guideline-based decision support: A case study approach', *Report SMI*-2002-0923.

Pena-Reyes C.A. and Sipper M, (2002), 'Combining Evolutionary and Fuzzy Techniques in Medical Diagnosis', *Computational Intelligence Processing in Medical Diagnosis*, vol. 96, pp. 391-426, DOI: 10.1007/978-3-7908-1788-1_14.

Pena-Reyes C.A. and Sipper M. (1999), 'A Fuzzy –genetic approach to breast cancer diagnosis', *Artificial Intelligence in Medicine*", vol. 17, issue 2, pp.131-155.

Pena-Reyes, C. A., & Sipper, M. (2000), 'Evolutionary computation in medicine: an overview', *Artificial Intelligence in Medicine*, vol. 19, pp. 1-23, doi:10.1016/S0933-3657(99)00047-0.

Pinciroli F, Combi C, Pozzi G, Rossi R (1992), 'MS/2Cardio: Toward a Multi-Service Medical Software for Cardiology', *Methods of Information in Medicine*, vol. 31, issue 1, pp.18-27,

PMID 1569890.

Polanyi M. Gloucester, MA: Peter Smith; Polanyi M. (1966) *The tacit dimensio*n. Peter Smith, Gloucester, MA, pp. 4.

Power D. J., Frada Burstein and Ramesh Sharda (2011) *Chapter 2 Reflections on the Past and Future of Decision Support Systems: Perspective of Eleven Pioneers*. Decision Support, Annals of Information System 14, DOI: 10.1007/978-1-4419-6181-5_2.

Power, D. J. (1997), 'What is a DSS?', *The On-Line Executive Journal for Data-Intensive Decision Support,* vol. 1, No. 3, other DSS's materials, information and resources, [Online], Available at: http://dssresources.com/papers/dssarticles.html, http://dssresources.com/papers/whatisadss/index.html [Accessed: 2 April 2015].

Power, D. J. (2002) *Decision support systems: concepts and resources for managers*. Quoroum Books division Greenwood Publishing, book code Q497, ISBN: 156720497X.

Power, D.J (2007), 'A Brief History of Decision Support Systems. DSSResources*'*, COM, [Online], Available at: http://DSSResources.COM/history/dsshistory.html, version 4.0, March 10, 2007, and others Available at: http://www.dssresources.com/dsstypes/ [Accessed: 05 April 2015].

Prasath V., Lakshmi N., Nathiya M., Nithya Bharathan,Neetha N.P (2013), 'A Survey on the Applications of Fuzzy Logic in Medical Diagnosis', *International Journal of Scientific & Engineering Research*, vol. 4, issue 4, ISSN 2229-5518.

Preece, A. (1994), 'Validation of knowledge-based systems', *The state-of-the-art in north America, Journal of communication and cognition - Artificial intelligence* 11: 381– 413.

Preece, A. (1998), 'Building the right system right - Evaluating V&V methods in knowledge engineering', *Proceedings of the eleventh workshop on Knowledge Acquisition, Modeling and Management (KAW'98)*, Voyager Inn, Banff, Alberta, Canada.

Preece, A. D. & Shinghal, R. (1994), 'Foundation and application of knowledge base verification', Int J Intell Syst, vol. 22, issue 8, pp 23-41.

Professor Diana Lennon *et al*., (2006), 'Evidence-based, best practice New Zealand Guidelines for Rheumatic Fever', *The National Heart Foundation of New Zealand,* ISBN: 0-9582743-0-4,[Online], Available at: http://www.waikatodhb.health.nz/assets/for-health-professionals/Primary-care-management-guidelines/Guidelines-for-Rheumatic-Fever-1-Diagnosis-Management-and-Secondary-Prevention.pdf [Accessed: 12 May 2014].

Professor Jonathan Carapetis , Dr Alex Brown, Dr Warren Walsh (2006), 'Diagnosis and management of acute rheumatic fever and rheumatic heart disease in Australia, An evidence-based review', *National Heart Foundation of Australia*, ISBN 1 921226 02 1, [Online], Available at: http://www.heartfoundation.org.au/SiteCollectionDocuments/PP-590-Diagnosis-Management-ARF-Evidence-Based-%20Review.pdf, [Accessed: 12 May 2014].

Protégé (2015), 'A free, open-source ontology editor and framework for building intelligent system', *Stanford Centre for Biomedical Informatic Research,* Protégé official web site [Online], Available at: http://protege.stanford.edu/, [Accessed: 18 Jan. 2015].

Quinlan, J.R. (1993) *C4.5: Programs for Machine Learning*. Machine Learning, Morgan

Kaufmann, Publishers, vol. 16, issue 3, pp 235-240, 10.1007/BF00993309.

Rabelo, A., Rocha, A. R., Souza, A. D., Ximenes, A. A., Lobo, N., Filho, J. C. S., *et al*. (1996), ' An expert system for diagnosis of acute myocardial infraction', *In ACM*, 0-89791-658-1, pp. 96-100.

Raymond, R.C. (1996), 'Use of the Time-sharing Computer in Business Planning and Budgeting', *Management Science*, vol. 12, issue. 8, B363-381.

Regmi P R, *et al* (2012), *'Prevalence of Sydenham's Chorea in Patients with Acute Rheumatic Fever in Nepal'*, *Nepalese Heart Journal*, vol.9, No.1, pp 30-32, [Online], Available at: www.nepjol.info/index.php/nhj/article/download/8345/6794 [Accessed: 27 Feb. 2015].

Regmi, P. R., & Wyber, R. (2013), 'Prevention of rheumatic fever and heart disease: Nepalese experience', *Global Heart*, vol. 8, issue 3, pp. 247.

Remenyi, B., Carapetis, J., Wyber, R., Taubert, K., Mayosi, B.M. (2013), 'Position statement of the World Heart Federation on the prevention and control of rheumatic heart disease', *Nat Rev Cardiol*, vol.10, pp. 284-292.

Rokach L, Maimon O (2009) *Data Mining with Decision Trees: Theory and Applications*. World Scientific Publishing Company, ISBN: 9812771719.

Rudolf Seising (2006), 'From vagueness in medical thought to the foundations of fuzzy reasoning in medical diagnosis', *Artificial Intelligence in Medicine* vol. 38, pp. 237-256.

Sanjib Pandey, Ma Jixin and Lai Choi-Hong (2015), 'A Conceptual Framework to Diagnosis of Acute Rheumatic Fever Based on the Temporal and Fuzzy Logic Approach', *Canadian International Journal of Science and Technology*, vol. 2, pp 397-426 (print), The Anglo-Egyptian Bookshop, ISBN: 2356-9085.

Schreiber G, Akkermans H, Anjewierden A, de Hoog R, Shadbolt, Nigel, Van de Velde W, Wielinga B. (2000) *Knowledge Engineering and Management: The CommonKADS Methodology*. Cambridge, MA: The MIT Press.

Sean N. Ghazavi, Thunshun W. Liao, (2008), 'Medical data mining by fuzzy modelling with selected features', *Artificial Intelligence in Medicine*, vol. 43, issue 3, pp. 195-206.

SGNHC (2007), 'Annual Report', *Shahid Gangalal National Health Centre, Nepal*, [Online], Available at: http://www.sgnhc.org.np/report-2007/main%20Page%201%20to%2066.pdf, [Accessed: 27 Feb. 2015].

Shadbolt, N.R. and Burton, A.M. (1995), 'Knowledge elicitation: a systematic approach', *Wilson, J.R. and Corlett, E. (Eds), Evaluation of Human Work: A Practical Ergonomics Methodology*, Taylor & Francis, London.

Shahar Y. and Cheng C. (1999), 'Model-Based Visualization of Temporal Abstractions', [Online], Available at: www.ise.bgu.ac.il/courses/trp/SMI-1999-0807.pdf, [Accessed: 4 Jan. 2015].

Shengbing Jiang ; Kumar, R. (2006), 'Diagnosis of repeated failures for discrete event systems with linear-time temporal-logic specifications', *IEEE Transactions on Automation Science and Engineering*, vol.3, issue 1, pp. 47-59.

Shneiderman, Ben. (1992) *Designing the User Interface: Strategies for Effective Human - Computer Interaction.*, Massachusetts: Addison –Wesley.

Shoham, Y. (1987), 'Temporal Logics in AI: Semantical and Ontological Considerations', *Artificial Intelligence*, vol. 33, pp. 89-104.

Shortliffe EH (1987), 'Computer programs to support clinical decision making', *JAMA: the journal of the American Medical Association*, vol. 258, issue 1, pp. 61-6.

Shyi-Ming Chen, (1994), 'A weighted fuzzy reasoning algorithm for medical diagnosis', *Decision Support Systems*, vol. 11, issue 1, pp. 37-43.

Silvana Badaloni and Marco Falda (2010), 'Temporal-Based medical diagnoses using a fuzzy temporal reasoning system', *Journal of International Manufacture*, vol. 21, issue 1, pp. 145-153, 10.1007/s10845-008-0171-8.

Smith, R. (1996), 'What clinical information do doctors need?', *BMJ313* (7064), pp.1062-1068.

Snodgrass, R. and Ahn, I (1986), 'Temporal databases', *IEEE Computer*, vol. 19, issue 9, pp. 35-42.

Special Writing Group of the Committee on (1992), 'Rheumatic Fever, Endocarditis and Kawasaki Disease of the Council on Cardiovascular Disease in the Young of the American Heart Association Guidelines for the diagnosis of rheumatic fever', *Jones Criteria*, 1992 *Update*, JAMA, 268, pp. 2069-2073.

Sprague, R. H. and E. D. Carlson (1982) *Building effective decision support systems*. Englewood Cliffs, N.J., Prentice-Hall.

Steiguer, J. E., Duberstein, J., & Lopes, V. (2003), 'The analytic hierarchy process as a means for integrated watershed management', *In Proceedings of the 1st interagency conference on research in the Watersheds*, USA, pp. 736-740.

Stephen L.Chiu (1996) 'Selecting Input Variables for Fuzzy Models', *Journal of Intelligent & Fuzzy Systems*, vol.4, no.4, pp.243-256.

Stuart McTaggart (2008) *Chapter 4 Clinical decision support systems*. Using Medical Information, Christine Bond, series editor Radcliffe Publishing Ltd, UK, ISBN 13:978 1 857756906.

Subasi, Abdulhamit (2012), 'Medical decision support system for diagnosis of neuromuscular disorders using DWT and fuzzy support vector machines', *Computers in Biology and Medicine*, vol. 42, issue 8, pp. 806-815.

Szmidt, E.; Kacpizyk, J. (2003), 'Recent advances in intelligent paradigms and applications', *An intuitionistic fuzzy set based approach to intelligent data analysis: an application to medical diagnosis*, Physica-Verlag GmbH; Heildelberg, Germany.

Thomas K Chin, And Lawrence K Jung (2014), 'Pediatric Rheumatic Fever Clinical Presentation', [Online], Available at: http://reference.medscape.com/article/1007946-clinical#b4 [Accessed: 18 June 2015].

Thomas M Hsieh, Yi-Min Liu, Chun-Chih Liao, Furen Xiao, I-Jen Chiang, Jau-Min Wong (2011),'Automatic segmentation of meningioma from non-contrasted brain MRI integrating fuzzy clustering and region growing', *BMC Med Inform Decis Mak*, vol. 11,

doi: 10.1186/1472-6947-11-54, PMCID: PMC3189096.

Tim Thornton (2006), 'Tacit knowledge as the unifying factor in evidence based medicine and clinical judgement', Med. Vol. 1: 2, Doi: 10.1186/1747-5341-1-2.

Timeline of the Development of Clinical DSS – Clinfowiki, [Online] Available at: http://clinfowiki.org/wiki/index.php/Timeline_of_the_Development_of_Clinical_Decision_Support, [Accessed: 13 April 2015].

Ting S.L., Wang W.M., Tse Y.K., W.H. Ip (2011), 'Knowledge elicitation approach in enhancing tacit knowledge sharing', *Industrial Management & Data Systems*, vol. 111, issue 7, pp.1039-1064.

Tsipouras, M. G., Exarchos, T. P., Fotiadis, D. I., Kotsia, A. P., Vakalis, K. V., Naka, K. K. (2008). 'Automated diagnosis of coronary artery disease based on data mining and fuzzy modelling', *IEEE Transactions on Information Technology in Biomedicine*, vol. 12, pp. 447–458

Tu, S.W., Eriksson, H., Gennari, J.H., Shahar, Y., and Musen, M.A. (1995), 'Ontology-based configuration of problem-solving methods and generation of knowledge acquisition tools: The application of PROTÉGÉ-II to protocol-based decision support', *Artificial Intelligence in Medicine*, vol.7, issue 3, pp. 257-289.

Turban, Aronson, and Liang (2005) *Decision Support Systems and Intelligent Systems*. Seventh Edition, © 2005, Prentice Hall.

Turban, E. (1995) *Decision support and expert systems: management support systems*. Englewood Cliffs, N.J., Prentice Hall, ISBN:0024216631.

Turban, E. (1967), 'The Use of Mathematical Models in Plant Maintenance Decision Making', *Management Science*, vol. 13, issue 6, B342-359.

United Nations (2013), 'World Statistics Pocketbook 2013 Edition', *NY: United Nations, Department of Economic and Social Affairs, Statistics Division*, series v. no. 37. New York,

Urban, G.L. (1967), 'SPRINTER: A Tool for New Products Decision Makers', *Industrial Management Review*, vol. 8, issue 2, pp. 43-54

Uzoka, F. M. E., Obot, O., & Baker, K. (2009), 'A performance comparison of fuzzy logic and AHP as engines for the development of intelligent medical diagnosis system', *In Procedding of 9th International Conference. Nigeria Computer Society, (MacGlobe'09)*, Abuja, vol. 20, pp. 135.

Victor E. Ekong, Udoinyang G. Inyang, Emmanuel A. Onibere (2012*)," Intelligent Decision Support System for Depression Diagnosis Based on Neuro-fuzzy-CBR Hybrid"*, Modern Applied Science ISSN 1913-1844 (Print) ISSN 1913-1852 (Online)

Vijaya, K., Nehemiah, H. K., Kannan, A., & Bhuvaneswari, N. G. (2010), 'Fuzzy Neuro Genetic Approach for Predicting the Risk of Cardiovascular Diseases', *International Journal of Data Mining, Modelling & Management*, vol. 2, issue 4, pp. 388-402. http://dx.doi.org/10.1504/IJDMMM.2010.035565

Vilain M. & Kautz H.A. (1986), 'Constraint propagation algorithms for temporal reasoning', *in Proceedings of the Fifth National Conference of the American Association for Artificial*

Intelligence (AAAI-86), Philadelphia, PA, Morgan Kaufmann, San Mateo, CA, , pp. 377-382.

Medasani, S., Kim, J., and Krishnapuram, R. (1998), 'An overview of membership function generation techniques for pattern recognition', *International Journal of Approximate Reasoning,*, vol. 19, pp. 391-417.

Vili Podgoreleca, Peter Kokola, Milojka Molan Stiglicb, Marjan Heričkoa, Ivan Rozmana (2005), 'Knowledge discovery with classification rules in a cardiovascular dataset', *Computer Methods and Programs in Biomedicine*, vol.80 (Suppl.1),S39–S49, doi:10.1016/S0169-2607(05)80005-7.

Wan, H., Wan, I., & Fadzilah, S. (2006), 'Artificial Intelligence in Medicine', *Journal of Health Informatics*, [Online], Available at: http://hi-europe.info/files/2002/9980.htm, [Accessed: 12 March 2012].

Wetter T (2002), 'Lessons learnt from bringing knowledge-based decision support into routine use', *Artificial Intelligence in Medicine*, vol. 24, issue 3, pp. 195-203.

Word Heart Federation (2007), 'Diagnosis and Management of Acute Rheumatic Fever and Rheumatic Heart Disease', [Online], Available at: http://www.world-heart-federation.org/fileadmin/user_upload/documents/RHD-net/RHD%20Curriculum.Oct.2008.pdf [Accessed: 18 June 2012; 12 May 2014].

World Health Organization (2001), 'Rheumatic Fever and Rheumatic Heart Disease', *Report of a WHO Expert Consultations, Geneva*, WHO Technical Report Series.

World Health Organization (2005), 'The Current Evidence for the Burden of Group A Streptococcal Diseases', [Online], Available at: http://whqlibdoc.who.int/hq/2005/WHO_FCH_CAH_05.07.pdf, [Accessed: 25 Feb 2014].

World Health Organization (2014), 'Country Cooperative Strategy at a glance. Federal Democratic Republic of Nepal', [Online], Available at: http://www.searo.who.int/nepal/ccs_countryprofile.pdf?ua=1 [Accessed: 25 Jan. 2015].

World Health Organization, Technical Report Series, (2004), 'Rheumatic Fever and rheumatic heart disease: report of a WHO expert consultation. Geneva: World Health Organization', [Online], Available at: http://www.who.int/cardiovascular_diseases/resources/en/cvd_trs923.pdf, [Accessed: 11 Nov. 2011; 12 Feb. 2012].

World Heart Federation (2012), 'Rheumatic Heart Disease', [Online], Available at: http://www.world-heart-federation.org/press/fact-sheets/rheumatic-heart-disease/, [Accessed: 18 June 2015].

World Heart Federation (2012), 'Word Heart Federation' [Online], Available at: http://www.world-heart-federation.org/press/fact-sheets/rheumatic-heart-disease/, [Accessed: 18 June 2015].

Wyatt J and Spiegelhalter D (1991), 'Field trials of medical decision-aids: potential problems and solutions', *Proc Annu Symp Comput Appl Med Care*, pp.3-7, PMCID: PMC2247484.

Yager R. R. and Filev D. P. (1994) *Essentials of Fuzzy Modelling and Control*. John Wiley & Sons., New York, DOI**:** 10.1016/0967-0661(95)90104-3.

Yardimci, A. (2009), 'Soft computing in medicine', *Applied Soft Computing*, vol. 9, pp. 1029-1043, doi:10.1016/j.asoc.2009.02.003.

Yuval Shahar (1987), 'Temporal Logic Past and Future', *Lecturer Note*, [Online], Available at: www.ise.bgu.ac.il/courses/trp/TR-in-CS-and-AI.revised [Accessed: 11 Dec. 2014].

Yuval Shahar (1998), 'Time is Everything, Time-Oriented Clinical Information', West J Med, vol.168, pp.105-113.

Zahlmann, G., Scherf, M. & Wegner, A. (1997), 'A neurofuzzy classifier for a knowledge-based glaucoma monitor', *Procedding AIME'97, (E. Keravnou et al., eds.), Lecture Notes in Artificial Intelligence*, 1211, Springer-Verlag, Berlin, pp. 273-284.

Zhang J, Johnson TR, Patel VL, Paige DL, Kubose T.(2003), 'Using usability heuristics to evaluate patient safety of medical devices', *J Biomed Inform*, vol. 36 (1-2), pp. 23-30.

Appendixes

Appendix 1: Award & Publications

AWARD: selected as the winner of the award for the best refereed application paper: Sanjib Raj Pandey, Jixin Ma and Chong Hong Lai (2015), "*Development of Temporal Logic-Based Fuzzy Decision Support System for Diagnosis of Acute Rheumatic Fever/Rheumatic Heart Disease*", Research and Development in Intelligent Systems XXXII, Springer International Publishing, pp 213-228, 2015, 978-3-319-25030-4, DOI :10.1007/978-3-319-25032-8_17

Journal Papers:

Pandey Sanjib, Ma Jixin and Lai Choi-Hong (2015) "*A Conceptual Framework to Diagnosis of Acute Rheumatic Fever Based on the Temporal and Fuzzy Logic Approach*" Canadian International Journal of Science and Technology" Vol2 May 2015, pp 397-426 (print), The Anglo-Egyptian Bookshop, ISBN: 2356-9085

Pandey Sanjib, Ma Jixin and Lai Choi-Hong (2015) "*Development of Decision Support System for the Diagnosis of Arthritis Pain for Rheumatic Fever Patients: Based on the Fuzzy Approach*" Journal of Algorithms and Computational Technology, Sep 2015, Vol. 9, Issue 3, pp. 265-290, DOI: http://dx.doi.org/10.1260/1748-3018.9.3.265

Pandey Sanjib, Ma Jixin and Lai Choi-Hong (2014) "*Fuzzy Membership Function and Input / Output Parameter for Diagnosis of Rheumatic Fever",* International Transactions on Information Science and Technology (ITIST), 2 (6), pp.10-15. ISSN 2325-6567 (Print), 2325-6575

Conferences/Workshop Papers:

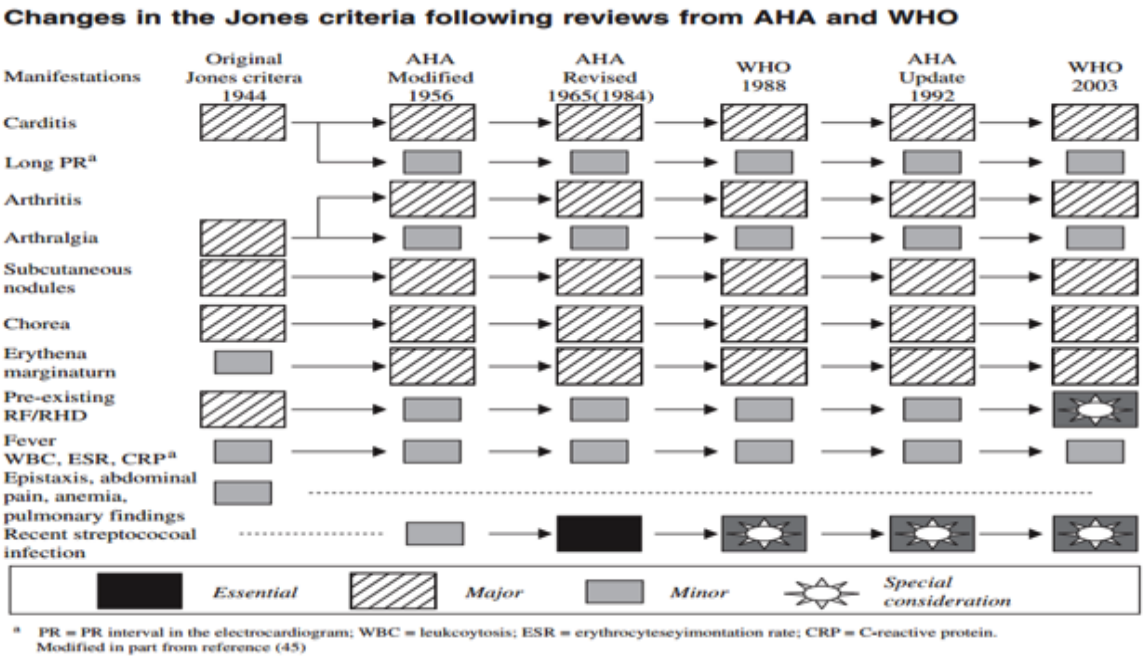
S. Pandey, J. Ma, C. Lai and C. Najovu (2013) "*A Fuzzy Logic-Based Decision Support System for the diagnosis of Arthritis Pain for Rheumatic Fever Patients*", SGAI Conference, Research and Development in Intelligent Systems XXX, 2013, pp 259-264. Springer, ISBN 978-3-319-026206, DOI 10.1007/978-3-319-02621-3

Sanjib Raj Pandey, Dr. Chiyaba Njovu, Professor Choi-Hong Lai (2012) "A Decision Support System for Diagnosis of Rheumatic Fever in Nepal", proceeding of 7th Asia Pacific Medical Informatics Conferences, Beijing, China, 22-25th October 2012.

S. Pandey, J. Ma and C. Lai (2013) "*Temporal Logic-Based Fuzzy Decision Support System for Rheumatic Fever and Rheumatic Heart Diseases in Nepal*", Oral Presentation and abstract submitted, Nepalese Doctor Association UK, 28th Annual Conference, 26th - 28th July 2013, Birmingham, UK

Sanjib Raj Pandey, Choi-Hong Lai, Chiyaba Njovu (2012) "*A Fuzzy Decision Support System for Rheumatic Fever in Nepal*", Oral Presentation and abstract submitted, EGH2012 workshop on Applied and Numerical Mathematics, 7-8 June 2012, University of Greenwich, London, UK.

Appendix 2.1: Changes to the Jones Criteria [WHO, pp.28, 2004**]**



Appendix 2.2: Developed Clinical Decision Support System

An early attempt to implement automated reasoning under uncertainty (1972), De Dombal's system, developed at Leeds University, was designed to support the diagnosis of acute abdominal pain and, based on analysis, the need for surgery. The system's decision making was based on the naive Bayesian approach [Open Clinical].

Pople and Myers begin work on INTERNIST, one of the first clinical decision support systems, designed to support diagnosis, in 1970. Later, INTERNIST-I was a rule-based expert system designed at the University of Pittsburgh in 1974 for the diagnosis of complex diagnosis of complex problems in general internal medicine [Open Clinical].

"Isabel" is a Web-based diagnosis reminder and knowledge mobilising system developed and delivered by Isabel Healthcare Inc in the USA and Isabel Healthcare Ltd in UK/Europe/India [Open Clinical, ISBEL].

*Diagnosist Decision Support System **(DXplain)** was developed by Lab. of Computer Science, Massachusetts General Hospital in 1987. The current DXplain knowledge base (KB) includes over 2400 diseases and over 5000 clinical findings (symptoms, signs, epidemiologic data and laboratory, endoscopic and radiologic findings) [Open Clinical,Dxplain]*

MYCIN was a rule-based expert system designed to diagnose and recommend treatment for certain blood infections (antimicrobial selection for patients with bacteraemia or meningitis) it was developed in the mid-1970s by Ted Shortliffe and colleagues at Stanford University [Open Clinical].

HELP:Knowledge-based hospital information system, developed by Department of Medical Informatics, University of Utah, Salt Lake City [Open Clinical].

Quick Medical Reference (QMR (1980) QMR was Developed by the University of Pittsburgh and First Databank, California. QMR is a diagnostic decision-support system with a knowledge base of diseases, diagnoses, findings, disease associations and lab information. With information from the primary medical literature on almost 700 diseases and more than 5,000 symptoms, signs, and labs. [Open Clinical]

ACRON (1987) : Hybrid rule-based & Bayesian system for advising on management of chest pain patients in the emergency room, applied Hybrid, rule-based, Bayesian, decision support system at Accident & Emergency Department, Westminster Hospital, London, The system was in routine use at Westminster during 1987-90 < http://www.openclinical.org/aisinpracticeAcute.html>

Automedon (2001) : Knowledge-based system for the management of mechanical ventilation in Intensive Care Units (ICUs), developed by French National Institute for Health and Medical Research (INSERM). It is a knowledge based workbench and methodology for computerizing, automating and executing clinical guidelines applied to critical care ventilator. < http://www.openclinical.org/aisinpracticeAcute.html>

SmartCare(2003): knowledge-based system for the management of mechanical ventilation in Intensive Care Units, developed by Dräger Medical GmbH & Co KGaA, Lübeck, Germany in association with Hôpital Henri Mondor and INSERM, Créteil, France. http://www.openclinical.org/aisinpracticeAcute.html

ATHENA (2002): Assessment and Treatment of Hypertension: Evidence-Based Automation is a Decision support system for the management of hypertension in primary care, developed by Stanford Medical Informatics, VA Palo Alto Health Care System, and Stanford Center for Primary Care and Outcomes Research. http://www.openclinical.org/aisinpracticeDSS.html>

APACHE III (1991) Acute Physiology and Chronic Health Evaluation, Prognostic scoring system for intensive care units, developed by William A. Knaus, an intensive-care physician at George Washington University, and colleagues. http://www.openclinical.org/aisinpracticeDSS.html>

PARIS (2001) Physician assistant Artificial Intelligence System is a diagnostic decision support system developed by Dr. AM Mohan Rao, Logic Medical Systems, Hyderabad, India, It is design to help doctors to help difficult cases. http://www.openclinical.org/aisinpracticeDSS.html

LISA (2003) : Clinical information and decision support system for collaborative care in childhood acute lymphoblastic leukaemia developed by A collaboration between three departments at Cancer Research UK: the Children's Cancer Group at St Bartholomew's Hospital, the Advanced Computation Laboratory and Information Systems. Cancer, childhood acute lymphoblastic leukaemia, shared care, collaborative care

Becton Dickinson Systems (1990) : rule based system for (1) QBC™ AUTOREAD™ Plus System for point-of-care haematology testing (2) The Sceptor™ MIC interpreter, developed by Becton Dickinson. http://www.openclinical.org/aisinpracticeLab.html

DoseChecker (1994): Expert system that screens prescriptions for correct medication dosages - monitors potentially toxic drugs orders which must be carefully dosed. Used expert system, knowledge –based system. Developed by Barnes-Jewish Hospital Pharmacy Department and Medical Informatics researchers, Washington University, St. Louis. http://www.openclinical.org/aisinpracticeLab.html

GermAlert (1993): Detection and reporting of emergency hospital infections. Used rule based system, alert infection control in hospitals. Developed by Washington University, St. Louis

PERFEX (apprx 1991): expert system for automated interpretation of Cardiac SPECT data. Used Expert systems, rules-based systems. Cardiology, coronary artery disease, 3D Myocardial Perfusion, cardiac SPECT data, diagnosis. Developed by Georgia Tech., Emory University Hospital http://www.openclinical.org/aisinpracticeLab.htm

Web-based clinical application

http://www.openclinical.org/applicationsWWW.html

Breast Cancer Risk Assessment Tools (2003): Interactive tool to assess breast cancer risk in patients. Evidence-based medicine, clinical guidelines, decision support, risk assessment, clinical calculators. Developed by halls.md - Steven B. Halls, MD, FRCPC. http://halls.md/breast/risk.htm

TheraDoc Antibiotic Assistant (2003): Antibiotic management decision support tool, developed by TheraDoc, Inc., Salt Lake City, USA http://www.theradoc.com/

eMedicine (1996) : Comprehensive clinical knowledge base. Clinical knowledge base, medical reference, evidence-based medicine, CME. Developed by WebMD.http://emedicine.medscape.com/

eRx Now ( ) : Electronic prescribing system. Evidence-based medicine, decision support etc used. Developed by Allscripts in association with members of the US National ePrescribing Patient Safety Initiative (NEPSI). http://www.allscripts.com/products-services/products/eprescribe-deluxe/free-eprescribe

Ganyfd (2005-2006) : Wiki-based textbook of medicine, developed by Collaborative wike community. Started in the UK and now involves medical practitioners from other English-speaking countries. Used medical knowledge base, medical wiki, medical textbook, etc http://www.ganfyd.org/index.php?title=Main_Page

Appendix 3.1: NHF guidelines on penicillin skin testing

1. **Perform penicillin allergy skin test in the following situations :**
   - Before first penicillin injection
   - With change in batch number.
   - With change in brand name.
2. **Steps for penicillin skin test:**
   - Use 23-G needle.
   - Clean the middle of forearm with spirit swab.
   - Inject 0.1 ml of diluted BPG intradermal on the forearm.
   - Wait for 15 to 20 min.
   - Look for local signs and symptoms of allergy (e.g., redness, inflammation, itching, erythema, swelling, blistering).
   - If any of the local signs are present and if the swelling is >10 mm, the test is considered positive.

Appendix 3.2: Safe benzathine penicillin injection delivery

1. Take consent from the patient or his/her relative before the first penicillin injection, with change in batch number and brand.
2. Record the brand name and batch number of the BPG.
3. Reconstitute the BPG powder with 3.5 ml of sterile distilled water.
4. Use 2 separate needles: 1 for pricking the vial and the other for injecting into the patient.
5. Use 10 ml syringe and 21-G needle for deep intramuscular injection.
6. Patient should lie down on trolley or bed on abdomen with head resting on pillow in a comfortable and relaxed position. In hospital settings, bed should be portable to rush the patient to the intensive care unit in case of emergency.
7. Inject BPG deep intramuscularly in the upper outer quadrant of the buttock.
8. Stay prepared for the treatment of possible anaphylaxis. The following medicines and instruments should be ready for emergency use:
   a. Adrenaline injection: l ampoule pre-loaded into the syringe.
   b. Atropine injection.
   c. Dexamethasone or antihistamine injection.
   d. Intubation set.
   e. Suction machine.

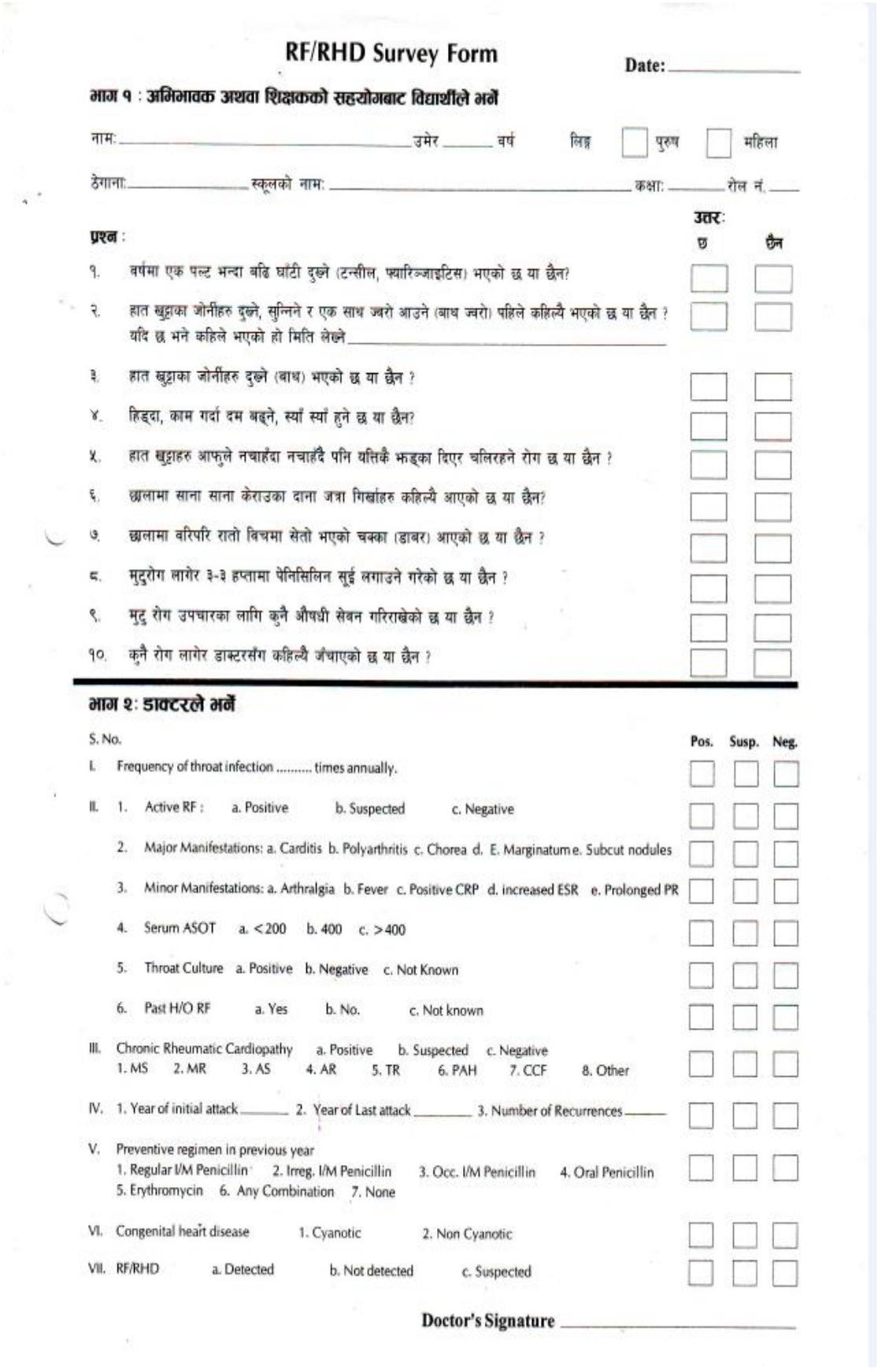
Appendix 3.3: Treatment guideline for anaphylactic reaction and vasovagal reaction

Anaphylactic reaction	• Low blood pressure • Tachycardia • Sweating • Dizziness • Dyspnea • Syncope	If not treated immediately, it may lead to death. Treat anaphylaxis with adrenaline injection. Repeat injection after 2 to 3 min if necessary.
Vasovagal reaction	• Low blood pressure • Bradycardia • Syncope	Treat vasovagal reaction with atropine injection.

Appendix 3.4: Guidelines for reduce the pain of BPG injection

- Shake the powdered BPG vial after adding 3.5 ml of distilled water until the powder dissolves and an opaque, viscous, suspension is formed with a final volume of ~5.0 ml. The penicillin crystal can easily pass through a 21- to 23-G needle. If the crystals are attached to each other, they form large particles that get clogged inside the needle. To avoid this situation, reconstitution of the powder with 3.5 ml of distilled water rather than 3 ml is advised.
- Use 21-G taper cut needle for intramuscular injection.
- Properly select the injection site and apply finger pressure for 10 s.
- Stretch the skin at the injection site with the thumb and index finger.
- Inject the liquid medicine at 90° angle with taper cut needle tip facing downward in vertical plane, which will cause minimum nerve end damage.
- Never double prick with the same needle.
- Push the syringe slowly, applying sufficient pressure in a gradually increasing manner to allow the crystals in the viscous medicine to flow smoothly. It may take up to 1 min to push 5.0 ml of solution.
- Distract the attention of the patient away from the injection.
- Maintain the injection delivery room temperature below 30°C. In hot air and moist skin, the injections are more painful.
- Apply ice pack in case of pain immediately after injection.
- Mix 0.5 to 1.0 ml of 1% lignocaine with the BPG solution for reducing pain if all other techniques fail.

Appendix 3.5: Questionnaire of RF/RHD survey form



RF/RHD Survey Form

Date: _____

भाग १ : अभिभावक अथवा शिक्षकको सहयोगबाट विद्यार्थीले भर्ने

नाम: _____ उमेर _____ वर्ष लिङ्ग ☐ पुरुष ☐ महिला

ठेगाना: _____ स्कूलको नाम: _____ कक्षा: _____ रोल नं. _____

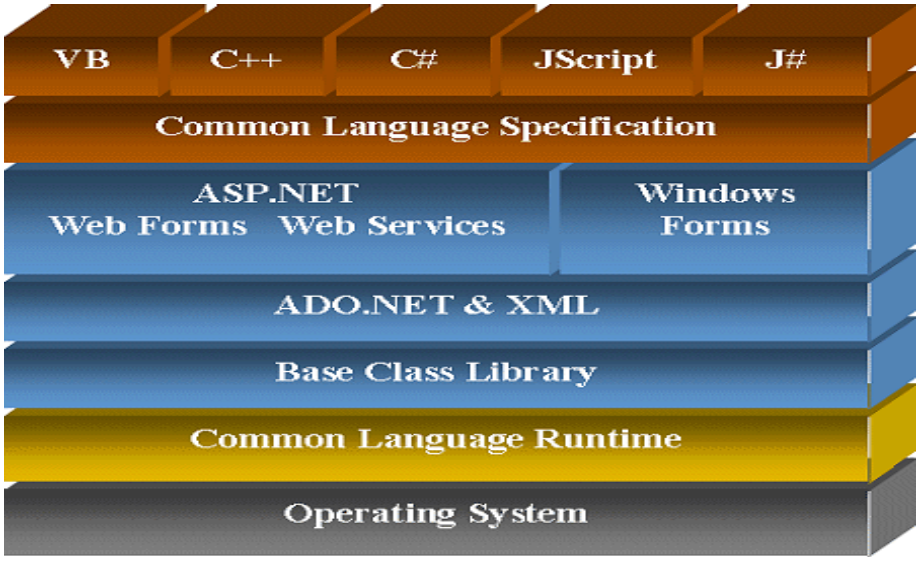
प्रश्न :	**उत्तर:** छ	छैन
१. वर्षमा एक पल्ट भन्दा बढि घाँटी दुख्ने (टन्सील, फ्यारिन्जाइटिस) भएको छ या छैन?	☐	☐
२. हात खुट्टाका जोर्नीहरु दुख्ने, सुन्निने र एक साथ ज्वरो आउने (बाथ ज्वरो) पहिले कहिल्यै भएको छ या छैन ? यदि छ भने कहिले भएको हो मिति लेख्ने _____	☐	☐
३. हात खुट्टाका जोर्नीहरु दुख्ने (बाथ) भएको छ या छैन ?	☐	☐
४. हिड्दा, काम गर्दा दम बढ्ने, स्याँ स्याँ हुने छ या छैन?	☐	☐
५. हात खुट्टाहरु आफुले नचाहँदा नचाहँदै पनि यत्तिकै झड्का दिएर चलिरहने रोग छ या छैन ?	☐	☐
६. छालामा साना साना केराउका दाना जत्रा गिर्खाहरु कहिल्यै आएको छ या छैन?	☐	☐
७. छालामा वरिपरि रातो बिचमा सेतो भएको चक्का (डाबर) आएको छ या छैन ?	☐	☐
८. मुटुरोग लागेर ३-३ हप्तामा पेनिसिलिन सुई लगाउने गरेको छ या छैन ?	☐	☐
९. मुटु रोग उपचारका लागि कुनै औषधी सेवन गरिराखेको छ या छैन ?	☐	☐
१०. कुनै रोग लागेर डाक्टरसँग कहिल्यै जँचाएको छ या छैन ?	☐	☐

भाग २: डाक्टरले भर्ने

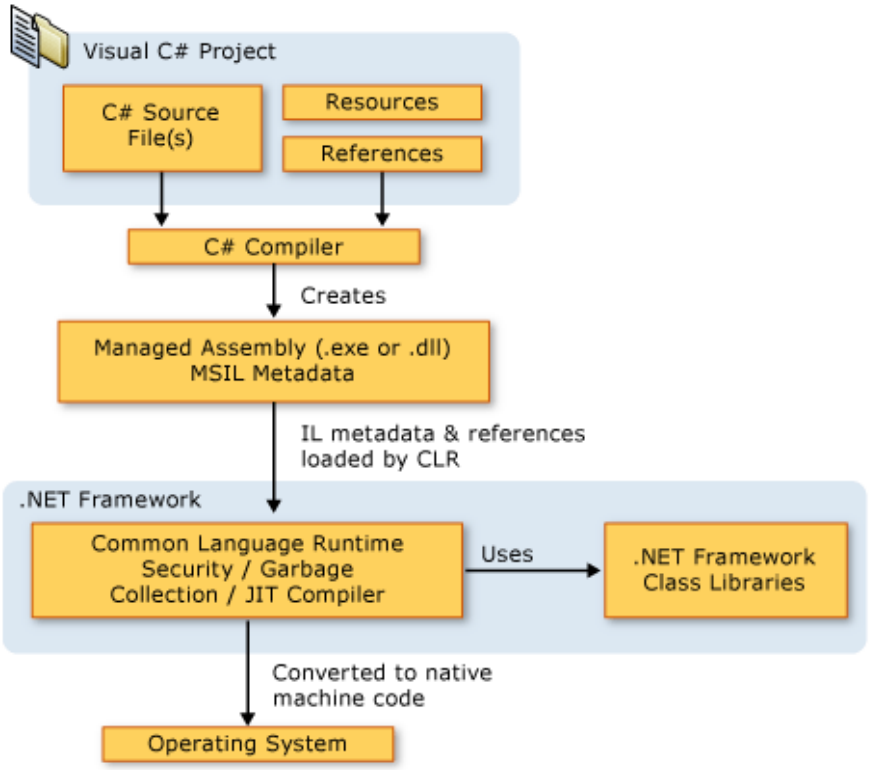
S. No.	Pos.	Susp.	Neg.
I. Frequency of throat infection ..... times annually.	☐	☐	☐
II. 1. Active RF : a. Positive b. Suspected c. Negative	☐	☐	☐
2. Major Manifestations: a. Carditis b. Polyarthritis c. Chorea d. E. Marginatum e. Subcut nodules	☐	☐	☐
3. Minor Manifestations: a. Arthralgia b. Fever c. Positive CRP d. increased ESR e. Prolonged PR	☐	☐	☐
4. Serum ASOT a. <200 b. 400 c. >400	☐	☐	☐
5. Throat Culture a. Positive b. Negative c. Not Known	☐	☐	☐
6. Past H/O RF a. Yes b. No. c. Not known	☐	☐	☐
III. Chronic Rheumatic Cardiopathy a. Positive b. Suspected c. Negative 1. MS 2. MR 3. AS 4. AR 5. TR 6. PAH 7. CCF 8. Other	☐	☐	☐
IV. 1. Year of initial attack _____ 2. Year of Last attack _____ 3. Number of Recurrences _____	☐	☐	☐
V. Preventive regimen in previous year 1. Regular I/M Penicillin 2. Irreg. I/M Penicillin 3. Occ. I/M Penicillin 4. Oral Penicillin 5. Erythromycin 6. Any Combination 7. None	☐	☐	☐
VI. Congenital heart disease 1. Cyanotic 2. Non Cyanotic	☐	☐	☐
VII. RF/RHD a. Detected b. Not detected c. Suspected	☐	☐	☐

Doctor's Signature _____

Appendix 5.1: Main components of .NET Framework



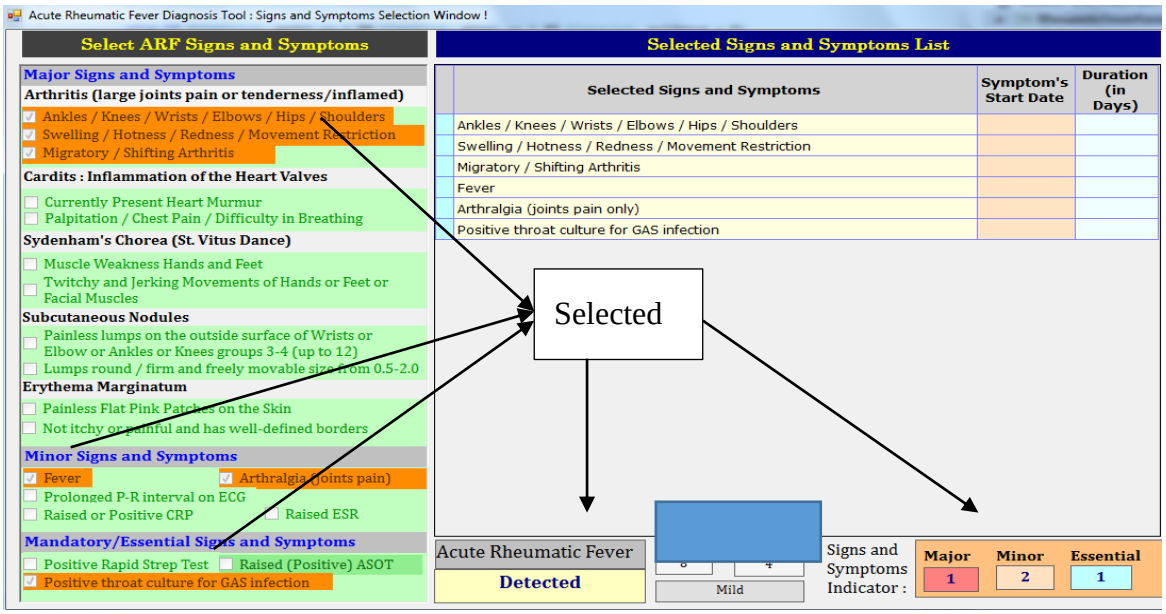
Appendix 5.2 the following diagram is adopted from Microsoft that shows the relationships of C# and .Net framework [Microsoft 2].



Appendix 6.1: Screenshot of test 1 output

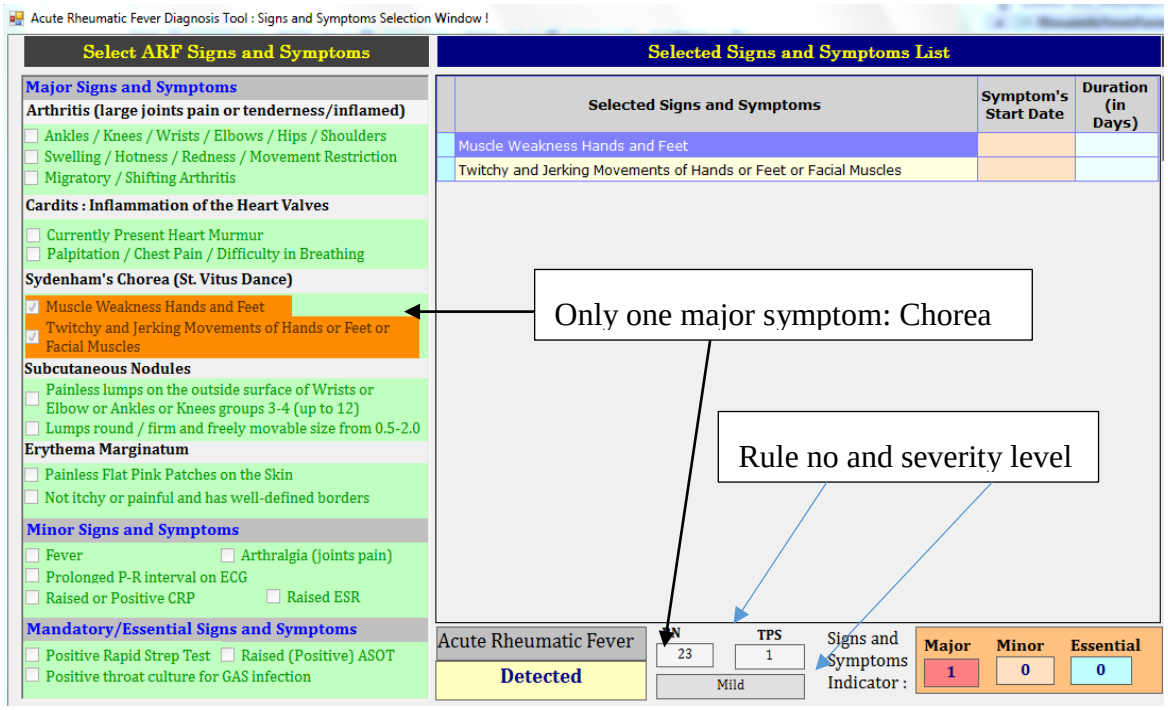
Detected ARF

SN. : $Detected\ ARF = (major\ sign \geq 1 \wedge minor\ signs \geq 2 \wedge essential\ sign(s) \geq 1)$



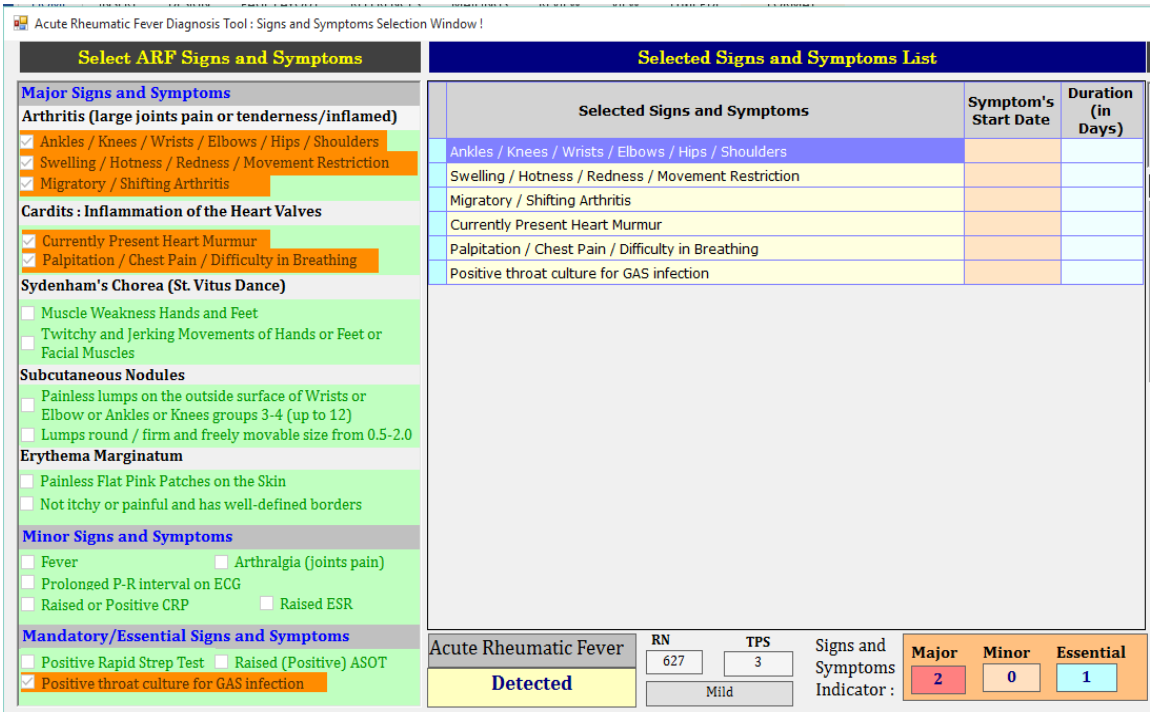
SN. 2: $Detected\ ARF = (Major\ (Chorea\ sign))$

Appendix 6.2: Screenshot of test 2 output



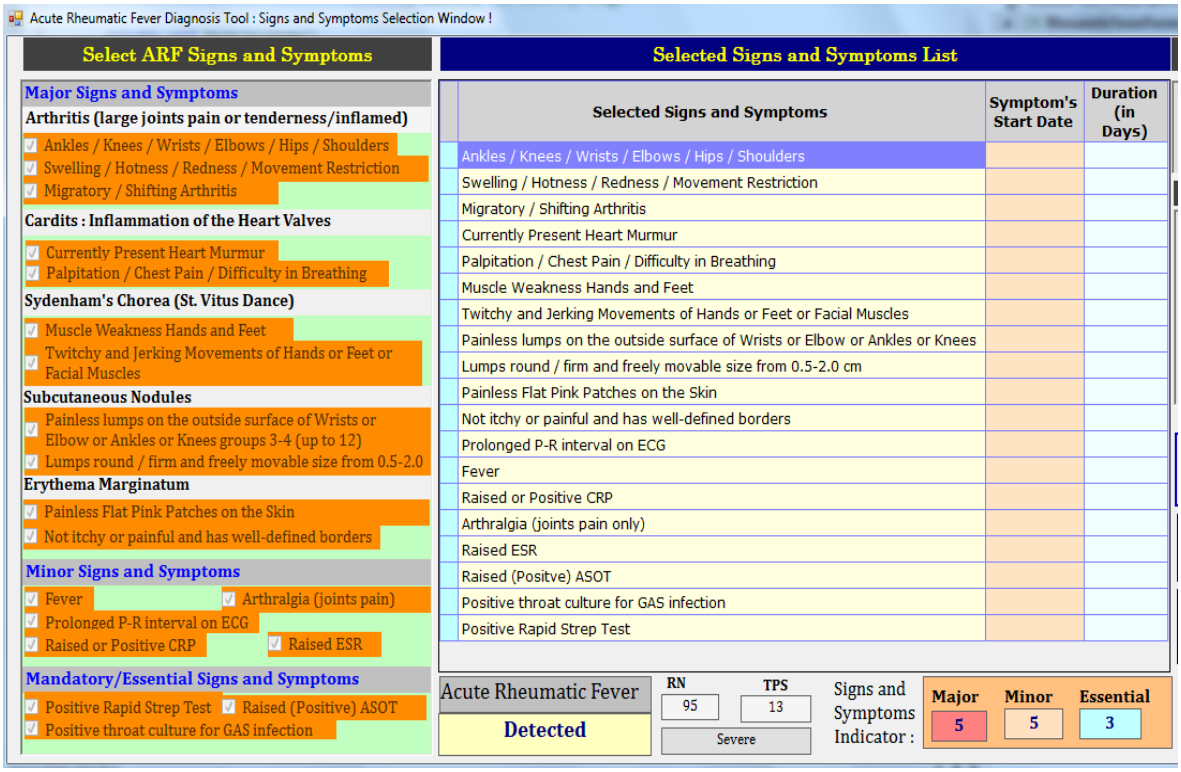
SN.3: $Detected\ ARF = (major\ signs \geq 2 \wedge minor\ sign = 0 \wedge essential\ sign(s) \geq 1)$

Appendix 6.3: Screenshot of test 3 output



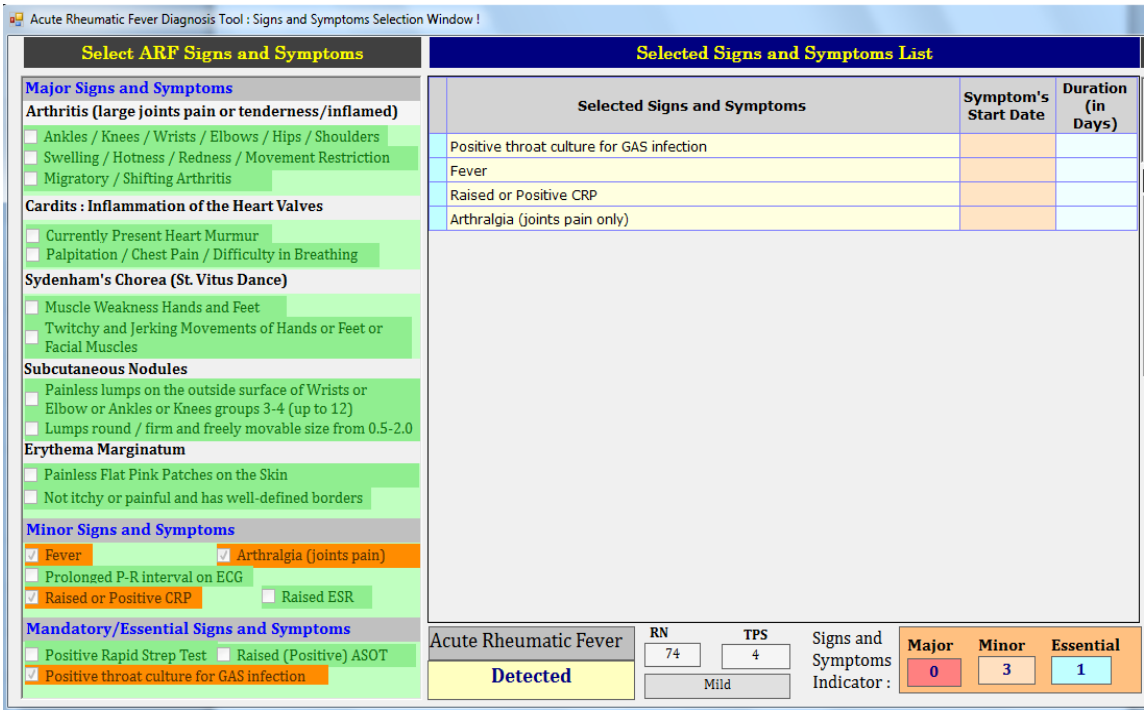
SN. 4: $Detected\ ARF = (major\ signs = 5 \wedge minor\ signs = 5\ \wedge essential\ signs = 3)$

Appendix 6.4: Screenshot of test 4 output



SN. 5: $Detected\ ARF = (Art_{13} \wedge\ Fe_{12}\ \wedge Crp_{15} \wedge essential\ sign(s)\ \geq 1)$

Appendix 6.5: Screenshot of test 5 output

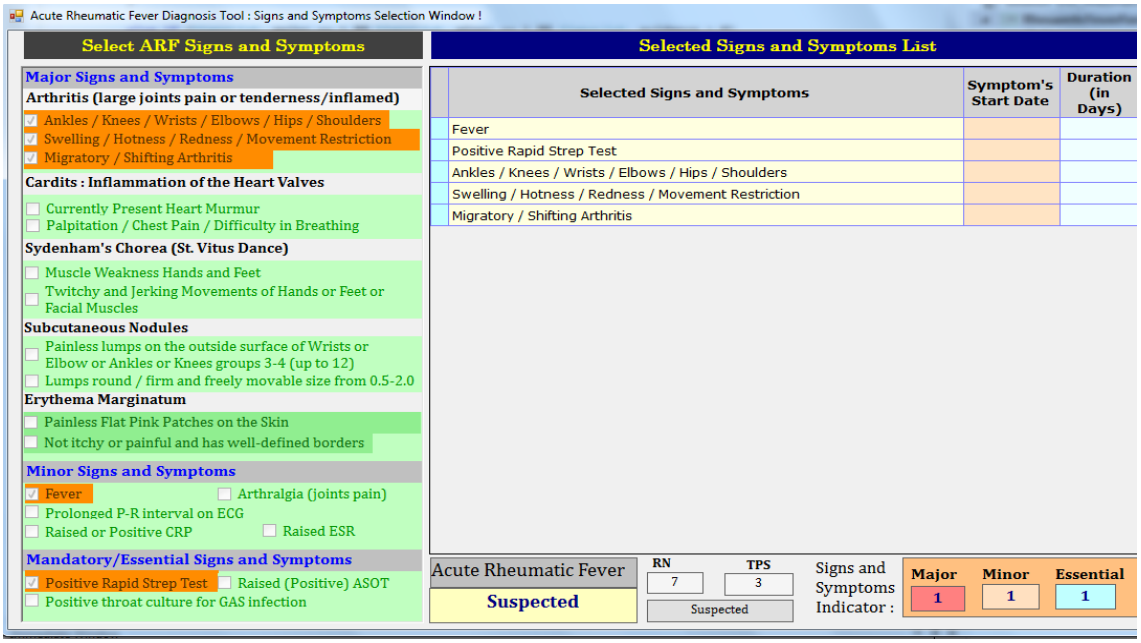


Suspected ARF

SN.6: $Suspected\ ARF =$

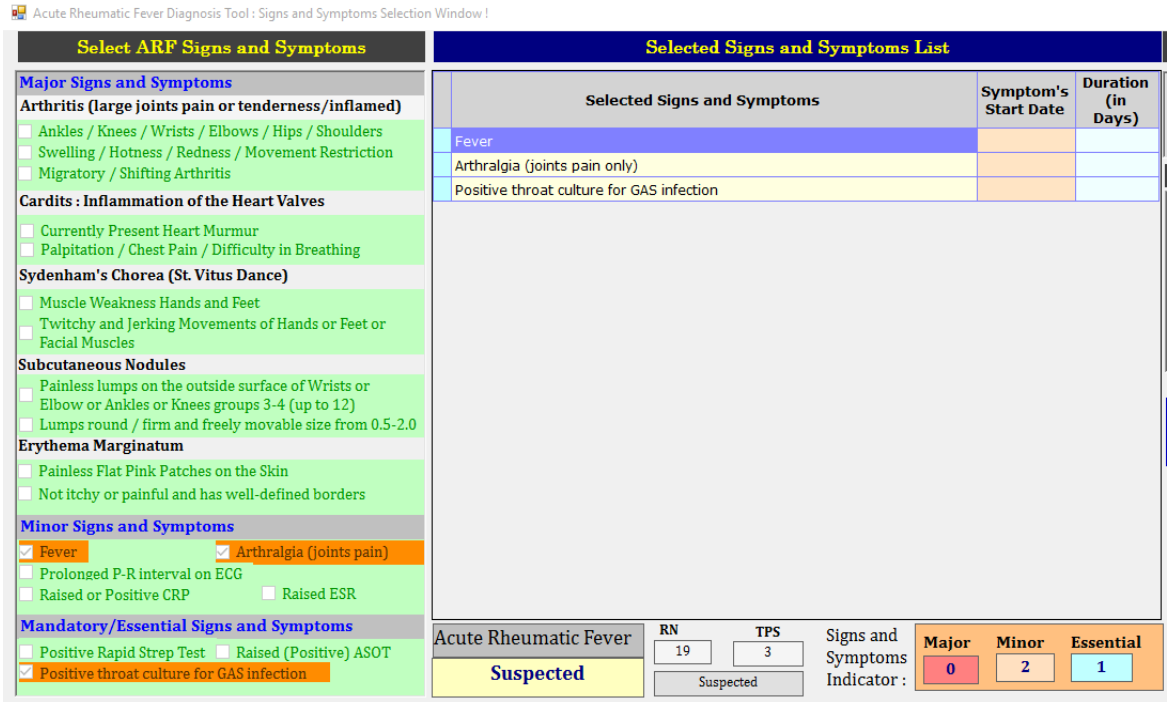
$(major\ sign = 1\ \wedge \neg Chorea\ \wedge\ minor\ sign = 1\ \wedge\ essential\ sign(s) \geq 1)$

Appendix 6.6: Screenshot of test 6 output



SN. 7: $Suspected\ ARF = (Art_{13} \wedge\ Fe_{12}\ \wedge essential\ sing(s)\ \geq 1)$

Appendix 6.7: Screenshot of test 7 output

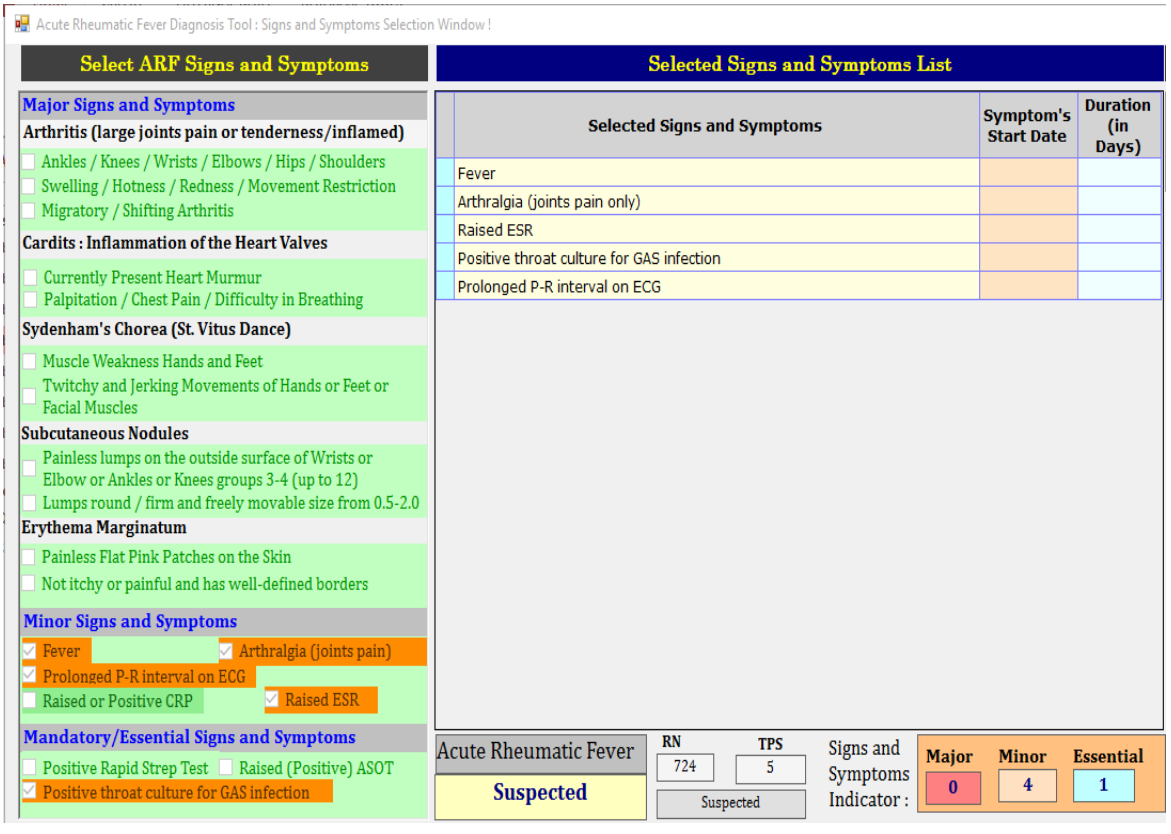


SN. 8: $Suspected\ ARF = (Art_{13} \wedge Fe_{12} \wedge Ecg_{14} \wedge essential\ sing(s) \geq 1)$

SN. 9: $Suspected\ ARF = (Art_{13} \wedge Fe_{12} \wedge Esr_{16} \wedge essential\ sing(s) \geq 1)$

SN. 10: $Suspected\ ARF = (Art_{13} \wedge Fe_{12} \wedge Ecg_{14} \wedge Esr_{16} \wedge essential\ sing(s) \geq 1)$

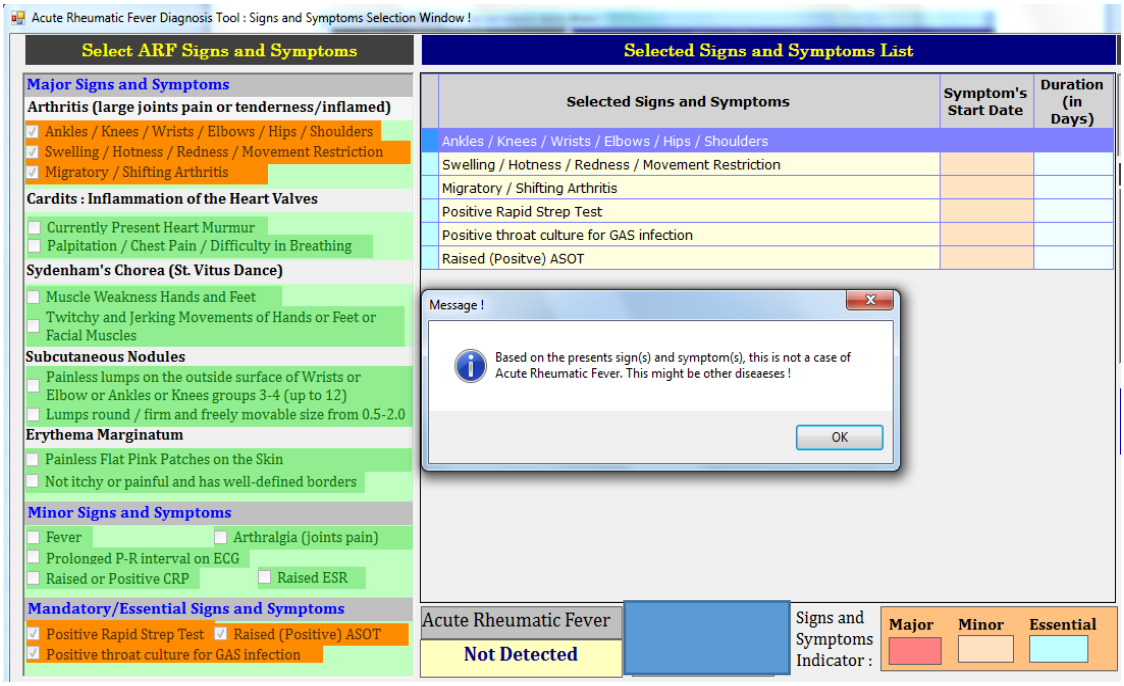
Appendix 6.8: Screenshot of test 8,9,10 output



Not Detected

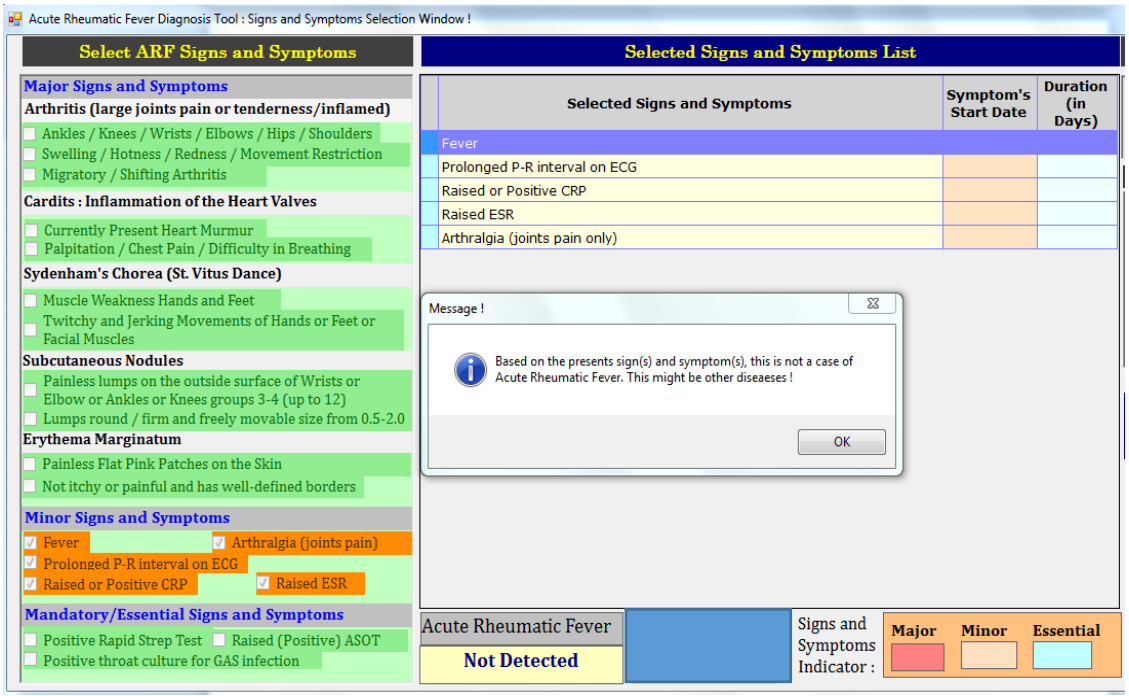
SN.11: $Not - detected\ ARF = (major\ sign = 1 \wedge \neg Chorea \wedge 0\ minor\ sign(s) \wedge essential \geq 1)$

Appendix 6.9: Screenshot of test 11 output



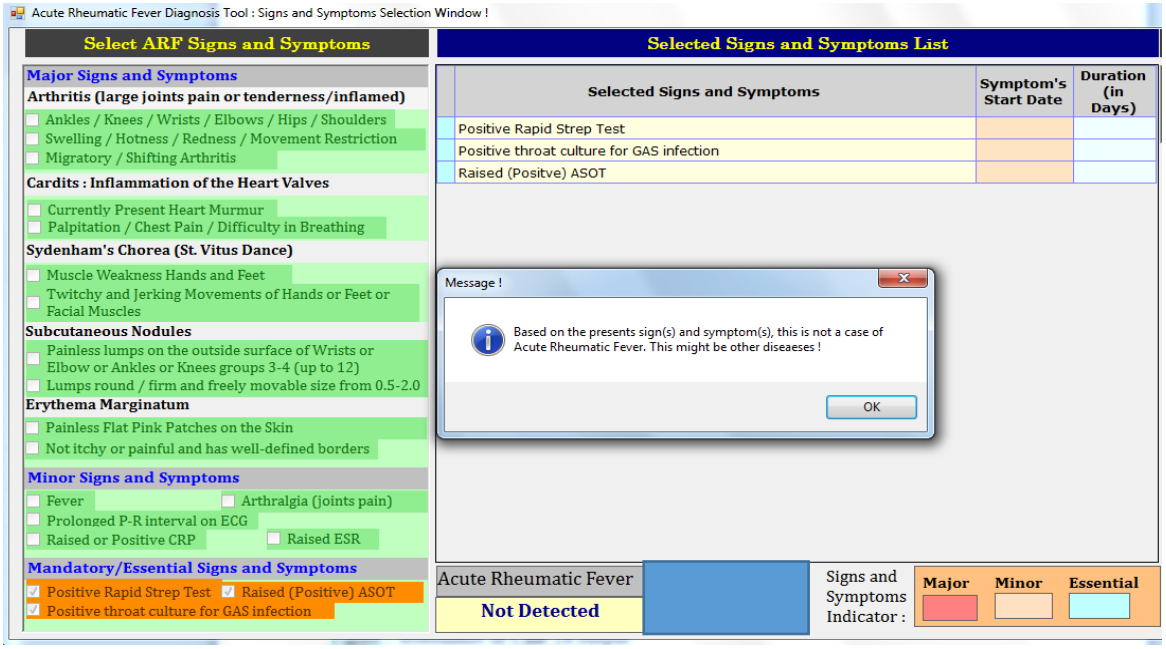
SN. 12: $Not - detected\ ARF = (major\ sign = 0 \wedge 1\ or\ all\ minor\ signs \wedge essential = 0)$

Appendix 6.10: Screenshot of test 12 output



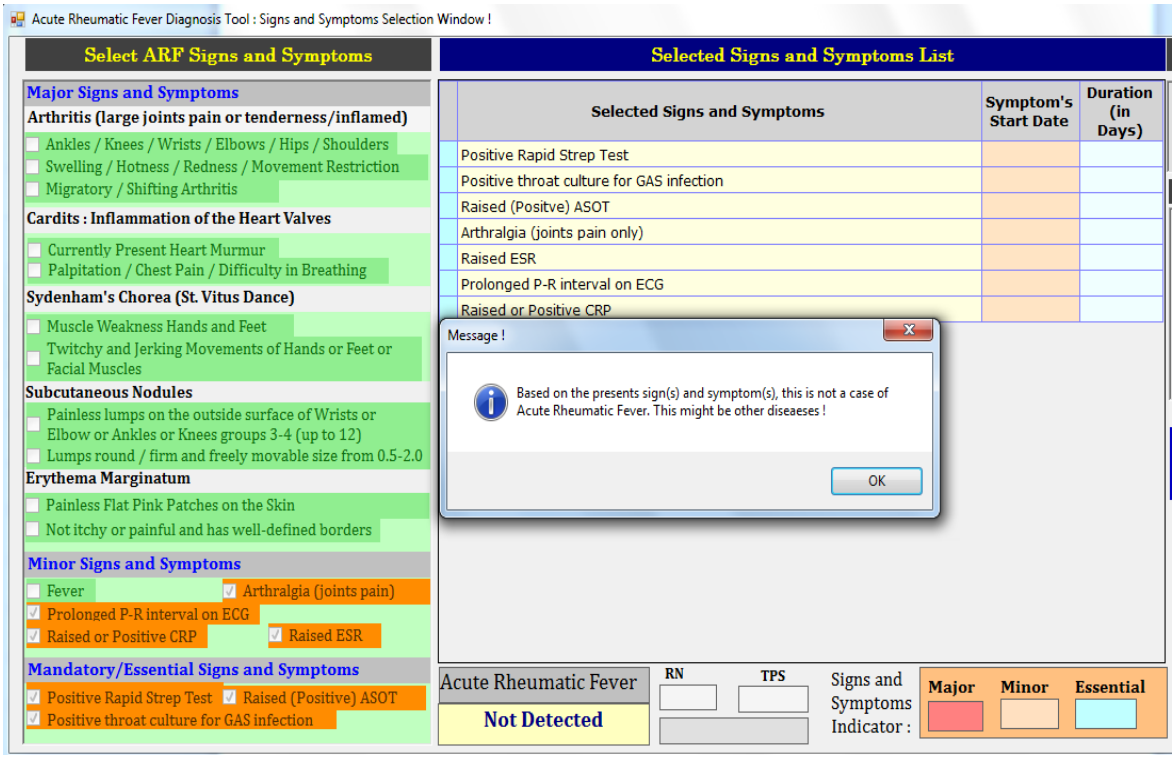
SN.13:$Not - detected\ ARF = (major\ sign = 0 \wedge minor\ sign = 0 \wedge essential\ signs \geq 1)$

Appendix 6.11: Screenshot of test 13 output



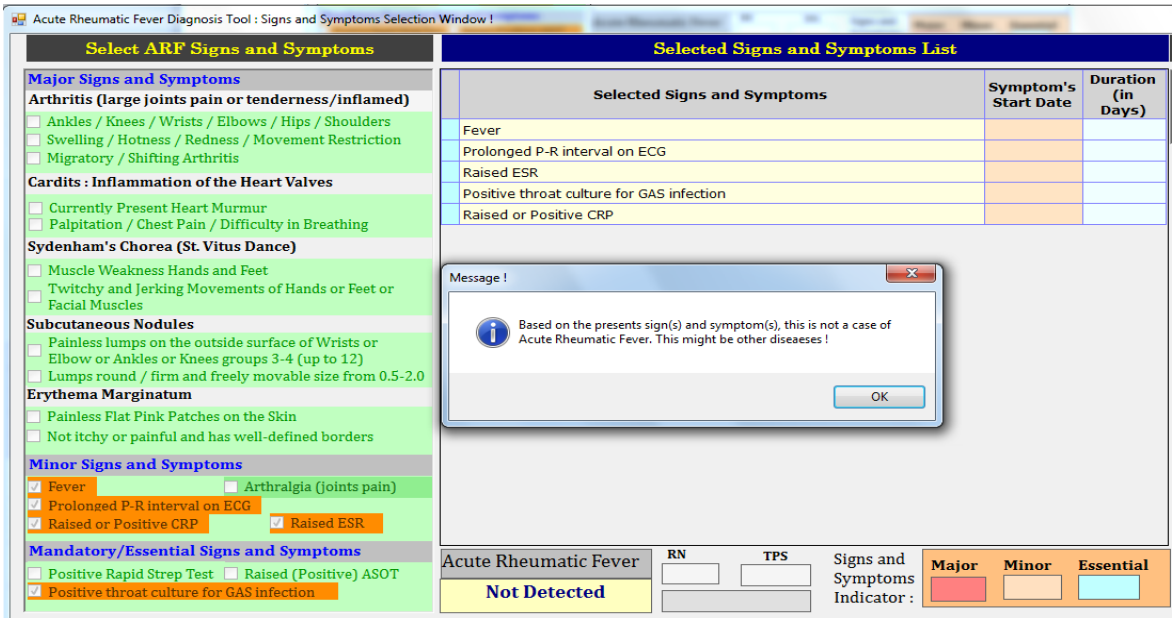
SN.14:$Not - detected\ ARF = (major\ sign = 0 \wedge (Art_{13} \vee Ecg_{14} \vee Crp_{15} \vee Esr_{16}) \wedge essential\ signs \geq 1)$

Appendix 6.12: Screenshot of test 14 output



SN.15: $Not - detected\ ARF = (major\ sign = 0 \wedge (Fe_{12} \vee Ecg_{14} \vee Crp_{15} \vee Esr_{16}) \wedge essential\ signs \geq 1)$

Appendix 6.13: Screenshot of test 15 output



Appendix 6.14: Format and Sample of Excel data

Rheumatic Fever / Rheumatic Heart Diseases Survey Form

Nepal Heart Foundation

Tri-Padma Vidyashram Higher Secondary School, Pulchowk, Lalitpur, Nepal

Record entered on 17/04/2014

By : Sanjib Raj Pandey

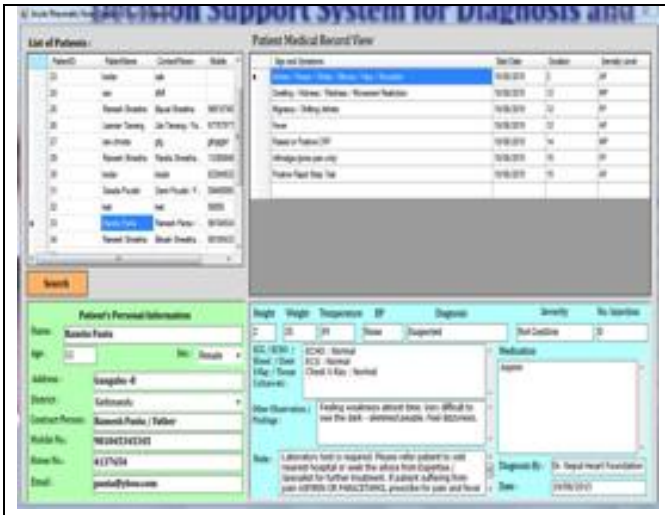
Part 1 : Fill - up by Parents or Class Teacher														Part 2 : Fill-up by doctors
S.N.	Name	Age	Sex	Class	Q101 (GAS)	Q102 (Arthritis)	Q103 (Arthriligia)	Q104 (Carditis)	Q105 (Chorea)	Q106 (SN)	Q107 (EM)	Q108 (RHD/Fever)	Q109 (Med/Heart)	Q110 (Visit Hospital)	Part 2 : Fill-up by doctors / RF/RHD
1		8	M	1	N	N	N	N	N	N	N	N	N	N	Not Detected
2		8	F	1	Y	Y	Y	N	N	N	N	N	N	N	Suspected
3		11	M	1	N	N	N	N	Y	N	N	N	N	Y	Detected
4		6	M	1	N	N	N	N	N	Y	Y	N	N	Y	Not Detected
5		6	F	1	Y	N	N	N	N	N	N	N	N	Y	Not Detected
6		8	F	1	N	N	N	N	N	N	N	N	N	N	Not Detected
7		7	F	1	N	N	N	N	N	N	N	N	N	Y	Not Detected
8		6	M	1	Y	N	N	N	N	N	N	N	N	N	Not Detected
9		9	M	1	N	N	N	N	N	N	N	N	N	Y	Not Detected
10		7	M	1	N	N	N	N	N	N	N	N	N	Y	Not Detected
11		7	M	1	N	N	N	N	N	N	N	N	N	Y	Not Detected
12		8	F	1	N	N	N	N	N	N	N	N	N	N	Not Detected
13		8	F	1	N	N	N	N	N	N	N	N	N	Y	Not Detected

14		7	F	1	N	N	N	N	N	N	N	N	N	Y	Not Detected
15		7	F	1	N	N	N	N	N	N	N	N	N	Y	Not Detected
16		9	M	1	N	N	N	N	N	N	N	N	N	Y	Not Detected
17		7	F	1	Y	N	N	N	N	N	N	N	N	Y	Not Detected
18		7	M	1	N	N	N	N	N	N	N	N	N	Y	Not Detected

Appendix: 6.15: ARF Diagnosis Application's sample of user interface

User interface (start-up window)

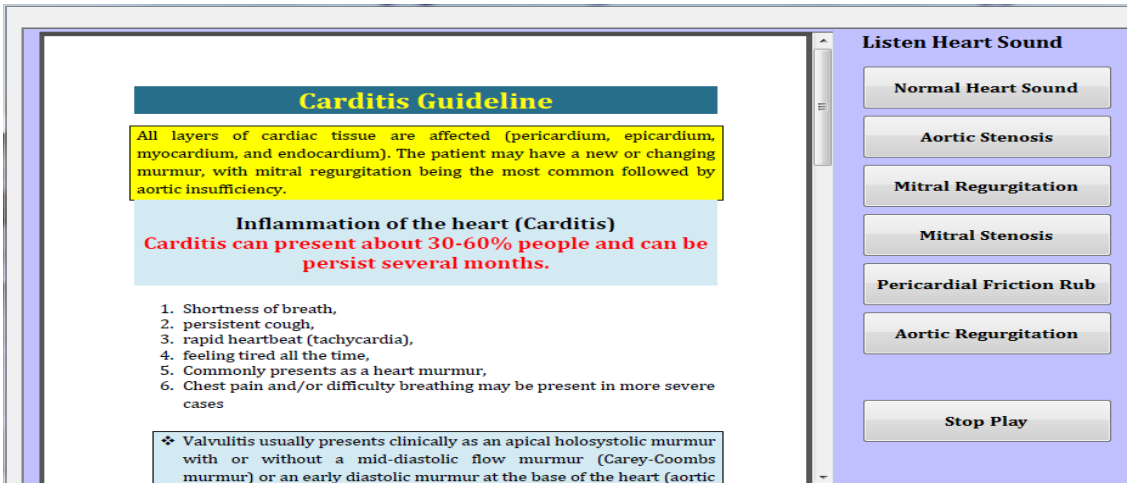
Patient information retrieval, supporting files in Nepalese language



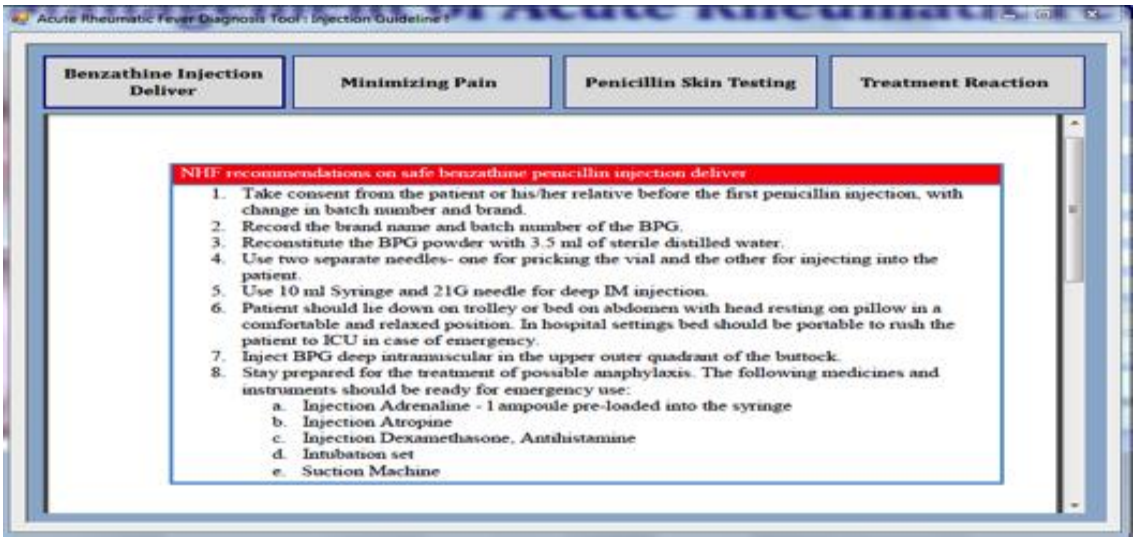
Patient's record retrieval

ARF help/guidelines in Nepalese language

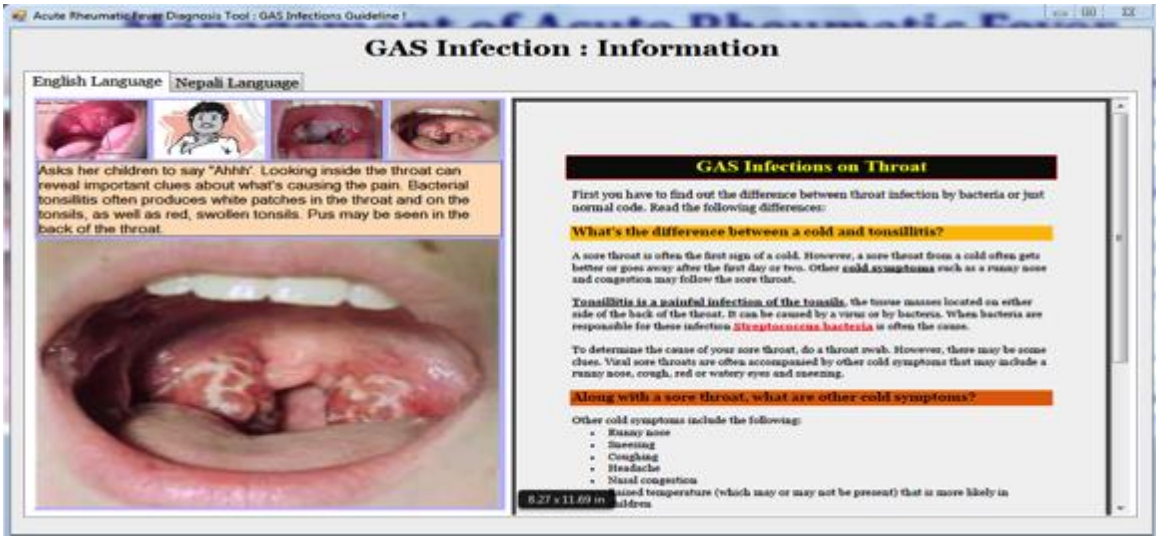
Carditis: Guidelines & heart sound



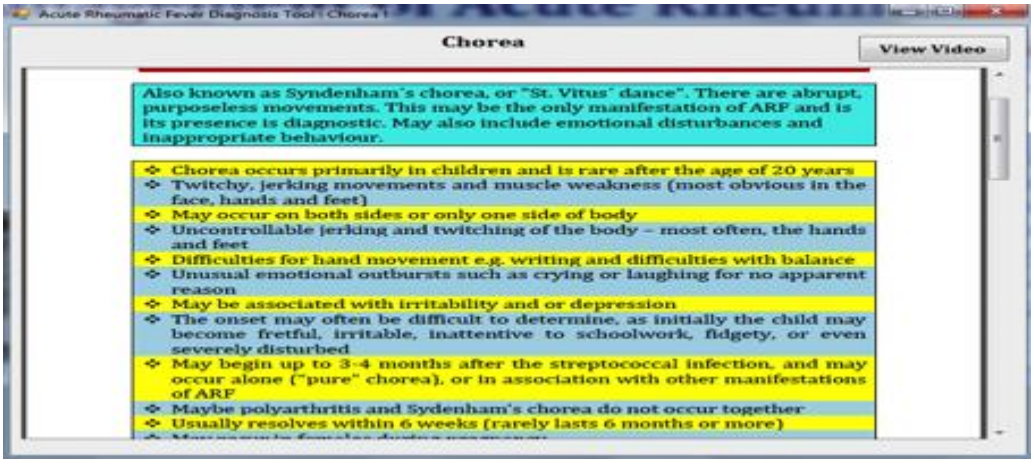
Injection Guideline



GAS Infection: Guidelines

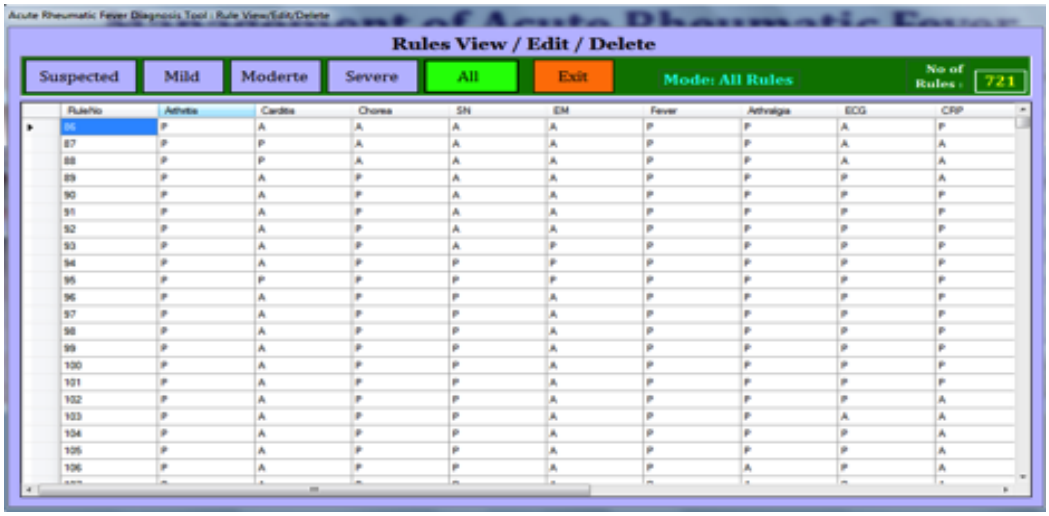


Chorea Guidelines

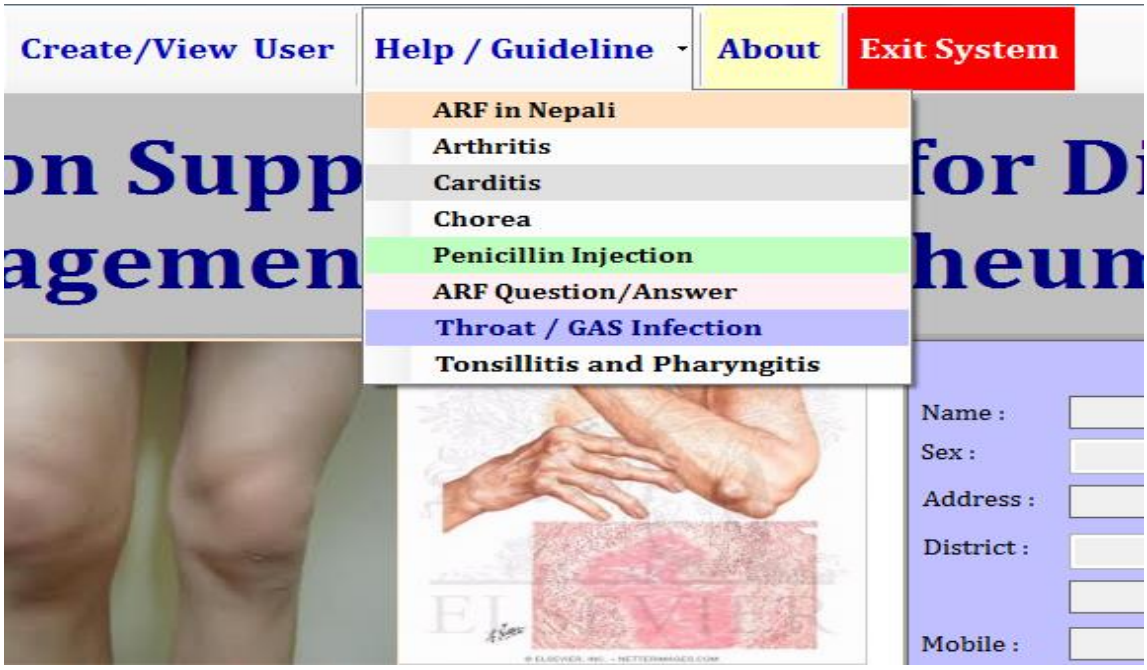


ARF/RHD: Question and Answer (symptoms, medication etc.)

Rules View



Help and Guidelines options



About system