

**THE PREVALENCE OF VECTOR BORNE
DISEASES IN TAMPIN HOSPITAL ,
NEGERI SEMBILAN**

GANGA DEVI A/P B. SINNIAH

UNIVERSITI SAINS MALAYSIA

2018

**THE PREVALENCE OF VECTOR BORNE
DISEASES IN TAMPIN HOSPITAL ,
NEGERI SEMBILAN**

by

GANGA DEVI A/P B. SINNIAH

**Thesis submitted in fulfilment of the requirements
for the degree of
Master of Sciences**

July 2018

ACKNOWLEDGEMENT

This author is very grateful to GOD ALMIGHTY for without His grace and blessings, this study would not have been possible.

My deepest appreciation to my supervisor, Associated Professor Dr. Zary Shariman Yahya, for his excellent guidance, his critical insights, motivation and his patience, willingness of time in sharing knowledge. He was extremely encouraging and instrumental in developing various ideas and arguments of this thesis. Thanks a lot Dr Zary Shariman, for giving me chances as a part time Master Student under your supervision.

I sincerely thank the Director of Tampin Hospital, Dr Hajjah Hatijah Bt Hj Mohd Tan for her guidance and encouragement in carrying out this project work. I also wish to express my gratitude to the staffs at Tampin Hospital who have rendered their help during the period of my study.

I would like to convey my gratefulness to all my friends, Rajiv and Azirah for their support and help during my experiment in laboratory. The skills and knowledge which I have gained throughout my experiment I perceive as very valuable component in my future development. Special thanks to the practical students in Lab 418 for inspiring and encouraging me as I was an older student among them.

Finally, I would like to acknowledge with gratitude, the support and love of my husband and children, my mother, brothers and also sisters. They all kept me going, and this thesis would not have been possible without them.

TABLE OF CONTENTS

ACKNOWLEDGEMENT.....	ii
TABLE OF CONTENTS.....	iii
LIST OF TABLES.....	iv
LIST FIGURES.....	v
LIST OF DIAGRAM.....	xv
LIST OF ABBREVIATIONS.....	xvi
ABSTRAK.....	xviii
ABSTRACT.....	xx
CHAPTER 1-INTRODUCTION	
1.1 Problems Statement.....	3
1.2 Research Objectives.....	5
1.2.1 General Objective.....	5
1.2.2 Specific Objective.....	5
CHAPTERS 2-LITERATURE REVIEW	
2.1 Vector Borne Disease.....	6
2.1.1 Introduction.....	6
2.1.2 Transmission of Vector-borne diseases in Malaysia.....	9
2.2 Major prevalent vector-borne diseases in Malaysia.....	25
2.2.1 Malaria.....	28
2.2.1(a) The Transmission of Malaria Cycle.....	30

2.2.1(b) Type of Malaria Parasites.....	32
2.1.1(b)(i) <i>Plasmodium falciparum</i>	33
2.1.1(b)(ii) <i>Plasmodium vivax</i>	35
2.1.1(b)(iii) <i>Plasmodium malariae</i>	37
2.1.1(b)(iv) <i>Plasmodium ovale</i>	38
2.1.1(b)(v) <i>Plasmodium knowlesi</i>	39
2.2.1(c) The Morphology of Malaria's Plasmodium spp.....	40
2.1.1(d) Clinical Features.....	41
2.1.1(e) Laboratory Finding.....	41
2.2.2 Dengue.....	43
2.2.2(a) Dengue Viral Transmission Cycle.....	45
2.2.2(b) Dengue Viral.....	47
2.2.2(c) Clinical Features.....	52
2.2.2(c)(i) Dengue Fever (DF).....	54
2.2.2(c)(ii) Dengue Hemorrhagic Fever (DHF).....	55
2.2.2(c)(iii)Dengue Shock Syndrome (DSS).....	56
2.2.3 Filariasis.....	57
2.2.3(a) Type of Filaria worms	61
2.2.3(a)(i) <i>Wuchereria bancrofti</i>	62
2.2.3(a)(ii) <i>Brugia malayi</i>	64
2.2.3(a)(iii) <i>Brugia timori</i>	65
2.2.3(a)(iv) <i>Brugia pahangi</i>	68
2.2.3(b) The Transmission of Filariasis	70
2.2.3(c) Clinical features.....	72
2.2.3(d) Laboratory Finding.....	72

CHAPTERS 3-METHODOLOGY

3.1 Blood Sampling.....	73
3.2 Subject and Inclusion Criteria.....	75
3.3 Laboratory Procedures.....	75
3.3.1 Blood Samples.....	75
3.3.2 Full Blood Count (FBC) method.....	76
3.3.3 Patient Diagnosis.....	76
3.3.4 Dengue Serology Screening method.....	77
3.3.5 Blood Film Malaria/Filaria Parasite Examination.....	79
3.3.6 The molecular analysis of Dengue Viruses and Malaria parasites in Blood Samples	80
3.3.6(a) RNA extraction of dengue virus in blood samples.....	80
3.3.6(a)(i) Agarose gel electrophoresis.....	80
3.3.6(a)(ii) Polymerase Chain Reaction (PCR).....	83
3.3.6(a)(iii) Polymerase Chain Reaction (PCR) after Optimization.....	87
3.3.6(b) DNA extraction of parasites for confirmation after Blood film examination.....	90
3.3.6(b)(i)Agarose gel electrophoresis.....	91
3.3.6(b)(ii)Polymerase Chain Reaction (PCR)	91
3.3.6(b)(iii)Polymerase Chain Reaction (PCR) after Optimization	95
3.3.7 Gel extraction of PCR products.....	98

3.3.8 Optical Density (OD) Determination.....	99
3.3.9 Sequencing.....	100
3.3.10BLAST.....	101
3.3.11Statistical Analysis.....	102
3.3.12Socio-economic and Environmental Factors	103

CHAPTERS 4-RESULTS

4.1 The Prevalence of Vector Borne Disease Cases In Tampin Hospital...	104
4.2 Dengue serology and PCR screening for Dengue infection in blood samples	107
4.2.1 Major Ethnic groups involved in blood samples.....	108
4.2.2 Dengue Serology Test.....	109
4.2.3 Molecular Identification and confirmation of Dengue Virus	103
4.2.4 Confirmation of Dengue Virus Serotype	114
4.3 Malaria Microscopic Examination and PCR test.....	115
4.3.1 Microscopic Examination of Malaria.....	116
4.3.2 Molecular Identification and confirmation of Malaria parasite...	117
4.4 Filariasis Microscopic Examination and PCR test.....	120
4.5 The Clinical Symptoms in Patients.....	120
4.6 Laboratory blood analysis.....	122
4.7 Socio-economic and Enviromental Factors	124

CHAPTERS 5-DISCUSSIONS

5.1 Socio-economic and Enviromental Factors.....	131
--	-----

5.2 Full Blood Count (FBC).....	139
5.3 Dengue Serology Test.....	143
5.4 Blood Film Microscopic Examination of Malaria (BFMP).....	148
5.5 Molecular Identification of Malaria and Dengue.....	152
5.5.1 DNA identification of Malaria, <i>Plasmodium knowlesi</i>	152
5.5.2 RNA identification of Dengue Virus, DENV 4.....	154
CHAPTERS 6-CONCLUSION	
6.1 Conclusions.....	157
6.2 Recommendations for further research.....	159
REFERENCES.....	161
APPENDICES.	

LIST OF TABLES

		Page
Table 2.1	The type of diseases , prevalence and the morbidity of diseases in Malaysia	9
Table 2.2	The number of dengue cases and death(s) reported from 2013 until 2015	15
Table 2.3	Dengue cases in Negeri Sembilan according to district	16
Table 2.4	The Number of <i>Plasmodium knowlesi</i> cases and its prevalence	21
Table 3.1	The PCR Master mix for the amplification of Dengue virus sequence (cDNA synthesis before optimizing)	85
Table 3.2	The PCR parameters for cDNA amplification of the dengue virus complex	86
Table 3.3	Mixture of PCR product after optimization Optimized dengue virus complex with specific PCR master mix	88
Table 3.4	PCR (standard) amplification condition after optimization. To optimize dengue specific virus PCR condition	89
Table 3.5	Mixture of PCR product before Optimization Process to perform the <i>Plasmodium</i> spp.	93
Table 3.6	PCR (standard) amplification condition before optimization process to perform the <i>Plasmodium species</i>	94
Table 3.7	Mixture of PCR master mix after optimization for <i>Plasmodium</i> species to specific species (<i>Plasmodium knowlesi</i>) sequence amplification	96
Table 3.8	PCR (standard) amplification condition after optimization	97

	for amplification of <i>Plasmodium knowlesi</i> sequence	
Table 3.9	The specific primer used in the sequence series	100
Table 4.1	Total number of whole blood samples collected for dengue serology test and Blood Film Malaria/Filaria Parasite (BFMP) done from year 2012 until year 2014	104
Table 4.2	The number of patients who have seen by Medical Officer in Hospital Tampin to investigate infected patients by vector-borne diseases from 2012 until 2014	106
Table 4.3	The Major Ethnic groups involved and positive in dengue serology test	107
Table 4.4	Identification of strain using BLAST analysis	112
Table 4.5	The mukims affected within the number of dengue infection cases from 2012 to 2014	114
Table 4.6	Identification of strain using BLAST analysis	118
Table 4.7	The Classic symptoms occurs in Dengue Patients	121
Table 4.8	The platelet count in dengue and malaria patients after confirmed in dengue serology test and Blood Film Malaria/Filaria Parasite	122
Table 4.9	The platelet count in dengue and malaria patients after confirming with PCR	123
Table 4.10	The records of 24 hours temperature taken from Gemencheh Station as representative of the Tampin District temperature	126
Table 4.11	The records of 24 hours temperature taken from Gemencheh station as representative of the Tampin District	126

temperature

Table 4.12	The records of 24 hours mean relative humidity which have been taken from Gemencheh station to representative the Tampin District humidity	127
Table 4.13	The records of rainfall amount which have been taken from Gemencheh station to representative the Tampin District temperature	128

LIST OF FIGURES

		Page
Figure 2.1	Combined global distribution of major vector-borne diseases	7
Figure 2.2	The comparison of total number of dengue cases in Malaysia from 1995 to 2015	12
Figure 2.3	The total cases of dengue deaths in Malaysia from 1995 to 2015	13
Figure 2.4	Malaria cases by species in Malaysia from 1997 to 2011	17
Figure 2.5	The number of malaria cases and the incident rate in Malaysia from 2010 to 2014	19
Figure 2.6	The number of malaria cases in Negeri Sembilan from 2010 to 2014	20
Figure 2.7	The number of Lymphatic Filariasis cases in Malaysia in 1992 to 1996	23
Figure 2.8	The number of filariasis cases with the incidence rate from year 2010 to 2014	24
Figure 2.9	The Map of Peninsular Malaysia and Tampin	27
Figure 2.10	The map of malaria infections, worldwide	28
Figure 2.11	The <i>Anopheles</i> mosquito	29
Figure 2.12	The transmission cycle of malaria parasite in human	31
Figure 2.13	The morphology of <i>Plasmodium spp.</i> with its cycle in human peripheral blood under light microscope	40
Figure 2.14	The distribution of dengue cases in worldwide	44
Figure 2.15	The picture of (a) <i>Aedes aegypti</i> and (b) <i>Aedes albopictus</i>	45

Figure 2.16	The life cycle of <i>Aedes</i> mosquito	46
Figure 2.17	The dengue transmission process	39
Figure 2.18	Dengue virus particle and electron microscopic picture of dengue viruses	48
Figure 2.19	The circulating dengue virus serotypes from 1990 to 2014	49
Figure 2.20	Dengue virus genome structure with the structural and non-structural genes	50
Figure 2.21	The dengue virus replication in host cells	51
Figure 2.22	The guideline for clinical management of Dengue Fever / Dengue Hemorrhagic Fever / Dengue Shock Syndrome	53
Figure 2.23	The distribution of Lymphatic filariasis in endemic countries	58
Figure 2.24	The picture of <i>Culex</i> (a), <i>Mansonia</i> (b), <i>Anopheles</i> (c) and <i>Aedes</i> (d) as vector of filariasis	60
Figure 2.25	The morphology of <i>Wuchereria bancrofti</i> in human blood sample	63
Figure 2.26	The morphology of <i>Brugia malayi</i> in human blood sample	65
Figure 2.27	The morphology of <i>Brugia timori</i> in human blood sample	67
Figure 2.28	The morphology of <i>Brugia pahangi</i> in human blood sample	69
Figure 2.29	The cycle of <i>Wuchereria</i> and <i>Brugia</i>	71
Figure 3.1	Location of the sampling region in Tampin N. Sembilan	74
Figure 3.2	Pictures of the positive results of dengue screening for a)NS1, (b)Ig M,(c) Ig G and (d) IgM and IgG (Both)	78

Figure 4.1	The number of patients for study and infected patients after doing dengue serology, microscopic examination for malaria and filariasis.	105
Figure 4.2	The serology dengue test results obtained from patients' samples by using dengue test kits	108
Figure 4.3	The gel band for dengue virus serotype Four (DENV 4) on 1.2% Agarose gel stained with ethidium bromide (etBR). Lane 1 and 6 shows 1 kb DNA ladder and lane 2, 3 and 4 shows PCR for Dengue Virus Serotype 4 (DENV 4).The Major Ethnic groups involved and positive in dengue serology test	110
Figure 4.4	The gel shows no band on 1.2% Agarose gel stained with ethidium bromide (etBR). Lane 1 and 8 showed 1 kb DNA ladder and lane 2, 3, 4, 5, 6, and 7 showed PCR for Dengue Virus Serotype 1 (DENV 1), 2 (DENV 2) and 3 (DENV 3)	111
Figure 4.5	The gel shows no band on 1.2% Agarose gel stained with ethidium bromide (etBR). Lane 1 and 8 showed 1 kb DNA ladder and lane 2, 3, 4, 5, 6, and 7 showed PCR for Dengue Virus Serotype 1(DENV 1), 2(DENV 2) and 3 (DENV 3)	110
Figure 4.6	Dengue Virus Serotype 4 (DENV 4) strain sequences	113
Figure 4.7	The <i>Plasmodium knowlesi</i> species in stage of trophozoites which was found in patients from Johol under light	116

	microscope (x10 objective)	
Figure 4.8	The <i>Plasmodium knowlesi</i> species in stage of early schizonts which was found in patients from Johol under light microscope (x 10 objective)	116
Figure 4.9	The gel band for malaria parasite, <i>Plasmodium knowlesi</i> on 1.2% Agarose gel stained with ethidium bromide (etBR). Lane 1 showed DNA ladder and lane 2 to lane 8 showed PCR for <i>Plasmodium knowlesi</i>	117
Figure 4.10	<i>Plasmodium knowlesi</i> strain sequences	130
Figure 4.11	The graph shows the temperature is positively correlated with number of vector-borne diseases in Tampin District	
Figure 5.1	The titre of the IgM and IgG response varies, depending on whether the infection is a primary or secondary infection	144

LIST OF DIAGRAM

	Page
Diagram 1.0 The drivers of global change considered in relation to potential changes in the status of vector-borne diseases	4

LIST OF ABBREVIATIONS

Bp	Base pair
Kb	Kilobyte
ml	Millilitre
Rpm	Rotation per minutes
µm	Micrometre
µl	Microliter
BLAST	Basic Local Alignment Search Tool
BFMP	Blood Film Malaria Parasite
C	Celcius
CDC	Clinical Disease Centre
CPG	Clinical Practice Guideline
cDNA	Complementary Deoxyribonucleic Acid
DF	Dengue Fever
DENV	Dengue Virus
DHF	Dengue Haemorrhagic Fever
DSS	Dengue Shock Syndrome
DNA	Deoxyribonucleic Acid
EtBr	Ethidium Bromide
ETD	Emergency and Trauma Department
FBC	Full Blood Count
GPELF	Global Programme to eliminate Lymphatic Filariasis
HCT	Hematocrit
Ig	Immunoglobulin

JKNNS	Jabatan Kesihatan Negeri, Negeri Sembilan
L	Litre
MDA	Mass Drug Administration
MKAK	Makmal Kesihatan Awam Kebangsaan
MOH	Ministry of Health
NS1	Non-structural Protein
NCBI	National center for Biotechnology Information
PCR	Polymerase Chain Reaction
RBC	Red Blood Cell
rDNA	Ribosomal Deoxyribonucleic Acid
rRNA	Ribosomal Ribonucleic Acid
RNA	Ribonucleic Acid
RT	Reverse Transcriptase
SSU	Small Subunit
TAT	Turn Around Time
TBE	Tris-borate-EDTA
UV	Ultra Violet
VBI	Vector Borne Disease
WHO	World Health Organization

**PREVALENS JANGKITAN PENYAKIT BAWAAN VEKTOR
DI HOSPITAL TAMPIN, NEGERI SEMBILAN**

ABSTRAK

Penyakit bawaan vektor adalah dianggap sangat penting dan telah banyak memberi kesan kepada kesihatan manusia dan juga haiwan. Pada tahun 1877, limfatik filariasis merupakan penyakit bawaan vektor yang pertama dikenalpasti disebabkan nyamuk yang merebak dari manusia ke manusia. Malaysia merupakan negara subtropika yang sering dijangkiti pelbagai penyakit bawaan vektor yang dibawa oleh nyamuk seperti malaria, denggi, filariasis, dan ensefalitis. Penyakit bawaan vektor seperti malaria, filariasis, dan denggi menyebabkan morbiditi dan kematian di negara-negara tropika, termasuk Malaysia. Maka, penyakit bawaan vektor ini menjadi tumpuan utama penyelidikan dan pengurusan alam sekitar di Malaysia, terutamanya di Hospital Tampin yang menunjukkan penyakit malaria dan denggi dilaporkan meningkat setiap tahun. Dalam kajian ini, data yang dikumpul dari tahun 2012 hingga 2014 menunjukkan jumlah kes denggi dilaporkan paling tinggi di daerah Tampin iaitu seramai 199 pesakit telah dilaporkan menghidap penyakit denggi. Ujian molekul (PCR) telah dijalankan terhadap virus denggi, didapati seramai 73 pesakit iaitu 21 pesakit (2012), 31 pesakit (2013) dan 21 pesakit (2014) yang tinggal di mukim-mukim, Daerah Tampin, Negeri Sembilan telah dijangkiti virus denggi serotaip 4 (DENV 4). Tiada kes denggi yang disebabkan oleh serotaip DENV 1, DENV 2 dan DENV 3 yang dilaporkan dalam kajian ini, kemungkinan ianya disebabkan oleh faktor-faktor

seperti kestabilan virus dan kualiti sampel yang diambil dari pesakit dari segi penyimpanan dan juga masa penghantaran sampel ke makmal. Malaria dan filariasis tidak dilaporkan di Hospital Tampin semasa kajian ini dijalankan. Namun, sampel filem darah masih diambil di kalangan pesakit bagi menjalani ujian pemeriksaan mikroskopik sebelum ujian PCR dilakukan. Walaubagaimanapun, tiada insiden kes malaria dan filariasis dilaporkan sepanjang 3 tahun kajian kecuali tiga (3) pesakit telah dilaporkan positif dengan jangkitan malaria dan spesis yang dikenalpasti adalah *Plasmodium knowlesi*. Pesakit-pesakit yang dikenalpasti positif dengan ujian malaria adalah berasal dari Hutan Percha, Alor Gajah, Melaka (pesakit 1lelaki) dan Johol, Kuala Pilah, Negeri Sembilan (1 lelaki dan 1 perempuan).

**THE PREVALENCE OF VECTOR BORNE DISEASES
IN TAMPIN HOSPITAL, NEGERI SEMBILAN**

ABSTRACT

Vector-borne diseases are considered important diseases and have greatly impact on the health of humans and animals as well. It was first described in 1877 when lymphatic filariasis was found to be transmitted by mosquitoes from human to human. Malaysia lies in a tropical zone, and often invaded by various vector borne diseases especially mosquitoes which are capable of transmitting diseases like malaria, dengue, filariasis, and Japanese encaphalitis. Vector borne diseases like malaria, filariasis, and dengue are still responsible for the high incidence of morbidity and mortality in many tropical countries, including Malaysia. Therefore, the vector-borne diseases caused by mosquitoes remain as the main focus of research and environmental management in Malaysia especially in Tampin Hospital where high numbers of malaria and dengue are reported each year. In this study, the data collected from 2012 until 2014 shows the high prevalence numbers of dengue infections within the regions of Tampin. About 199 patients were detected as being dengue-infected from year 2012 until 2014. The confirmation of dengue virus serotype was finalized by patients' clinical history and dengue serology test. From the molecular study, the results showed that 73 patients, only 21 patients in 2012, 31 patients in 2013 and 21 patients in 2014 were positive with DENV 4. were infected with dengue virus serotype 4 (DENV 4), according to the mukim in Tampin, Negeri Sembilan. The absence of serotype DENV 1, DENV 2 and DENV 3 is unexpected which is due to the viability of the

virus and the quality of the sample were affected by factors such as time, storage and transportation factors. During this study, all patients' blood film samples were examined as microscopic examination before proceeding to PCR test. However, there is no incidence rate of malaria and filariasis reported over three years except 3 cases of malaria were reported as *Plasmodium knowlesi*. The positive malaria's patients were from Hutan Percha, Alor Gajah, Melaka (1 patient) and Johol, Kuala Pilah, Negeri Sembilan (1 male and 1 female).

CHAPTER-1

INTRODUCTION

Vector-borne diseases are considered important diseases and have great impact on the health of humans and animals as well. They are among the leading causes of worldwide mortality amounting to millions of cases. Approximately, half the world's population is infected with at least, one type of Vector-borne disease every year and millions of people die of this each year. Pherez (2007) reported that Vector-borne infections (VBI) were described in the year 1877 when lymphatic filariasis was transmitted by mosquitoes from human to human. However, several vector-borne infections have been described for the past 128 years, involving a variety of infectious pathogens, together with a wide range of cold-blooded (exothermic) arthropods which are sensitive to climatic factors.

Reproduction rates of vectors and weather influences survival, which in turn influencing habitat suitability, distribution and abundance of mosquitoes. Environmental factors also affect intensity and temporal pattern of vector activity (particularly biting rates) together with reproduction of pathogens within vectors throughout the year. However, climate is only one of many factors influencing vector distribution. Other important factors such as habitat destruction, land use, pesticide application, and host density could also play a major role in its distribution (Semenza and Menne, 2009).

Vector-borne diseases (VBD) have become a major health problem affecting urban and pre-urban areas in tropical and subtropical regions around the world. These diseases also cause significant economic losses in regard to animal trade, agriculture, health care, tourism, as well as the destruction of ecosystems throughout the world. Therefore, vector-borne diseases can be controlled and prevented by both the economic community and individual. However, the infectious diseases behave within the constraint of natural biological systems with the rapid change from origin and physical environments seen today. Human interactions also play the role within these large systems compare to the changes of the nature of physical systems (WHO, 2014).

The spread and emergence of vector-borne diseases in Tampin District is a complex interplay among the pathogen, the host, and the environment. One key aspect needed to be studied is the distribution of VBD cases in Tampin district population, which is considered as one of the red areas and highest number of dengue and malaria cases in Malaysia (JKNNS, 2010, Ministry Of Health, 2011). New data on VBD epidemiology studies is sorely needed as this will definitely help us to construct an effective disease management to control the spreading of the disease.

1.1 Problem Statement

Each element that plays a major role in the spreading of the VBD has equal important because each one relies on the other which is described in Diagram 1.0. A successful strategy for the control of such diseases is not through solely vaccinating and treatment of infected patients but through the reduction in the source of infection, which is often by the treatment of mosquitoes and other vectors. The ability to effectively control the vectors is only possible through extensive knowledge of biology bionomics and the behaviour of those vectors. The population in Tampin District is at risk when the vector-borne disease becomes a problem where complaints of severe illness arises and that is when the transmission is taking place.

Therefore, it is important to look at the immediate environment of the population at risk to determine how people and communities can protect themselves. There are many things that can be done at the individual level to protect oneself from this disease. Nevertheless, many people do not take personal protection from being bitten by vectors. Their chances of getting infected is increased, in addition to the pathogen establishing itself in the community. This study will examine the prevalence of vector-borne diseases in Tampin District Hospital and will specifically investigate the correlation if the infections between socio-economic, demographic variables and environmental.

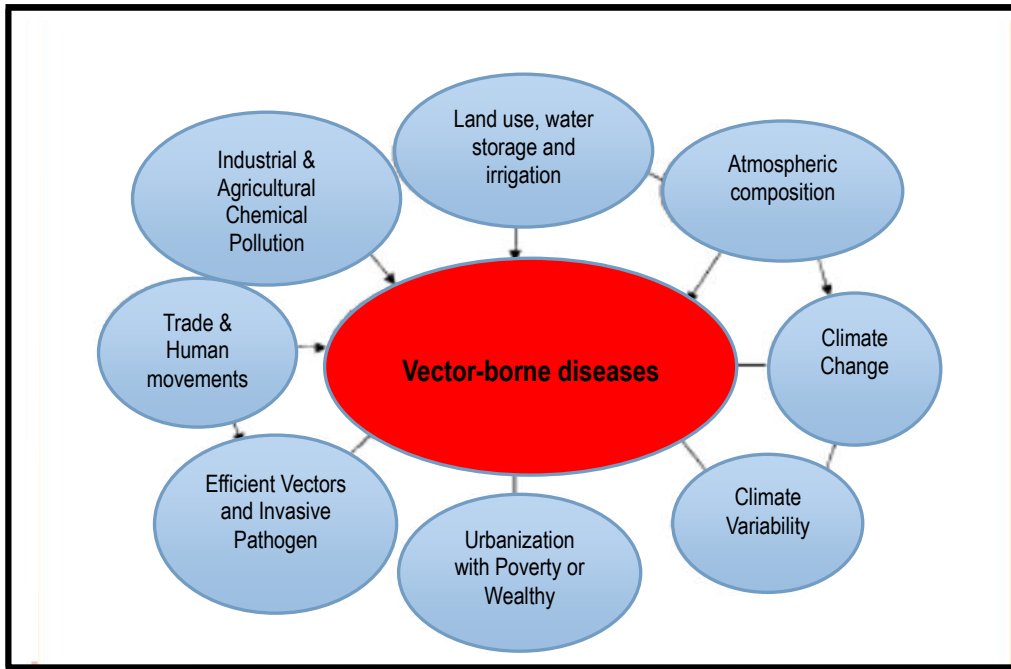


Diagram 1.0 : The drivers of global change impacting on the potential changes in the status of vector borne diseases (Ministry of Health Malaysia, 2008).

1.2 Research objectives

1.2.1 General Objective

To determine the major prevalence of vector-borne diseases in Tampin District Hospital

1.2.2 Specific Objective

1.2.2(i) To determine the high prevalence of main vector borne diseases in Tampin District Hospital

1.2.2(ii) To identify environmental factors that contribute to the prevalence of vector-borne diseases

1.2.2 (iii) To understand how specific demographic and socioeconomic status variables relate to vector-borne disease transmission

CHAPTER-2

LITERATURE REVIEW

2.1 Vector Borne Disease

2.1.1 Introduction

Vector-borne diseases are illnesses caused by pathogens and parasites carried by insects acting as vectors in the human population, causing morbidity and mortality. Most tropical and subtropical areas are represented with vector-borne diseases which is regarded as a major public health concern but the threat is more serious in developing countries. There are more than 1 billion cases and over 1 million deaths from at least one type of vector-borne disease every year (WHO, 2005). This is because nearly 82 % of the global population live in areas at risk from one vector-borne disease with over half living in areas at risk of two or more of the major vector-borne diseases. Some parts of sub-Saharan Africa, South Asia, and the Americas are at risk from five or more major vector-borne diseases and shows in the geographic distribution of the major vector-borne diseases (Figure 2.1) (Golding *et al.*, 2015).

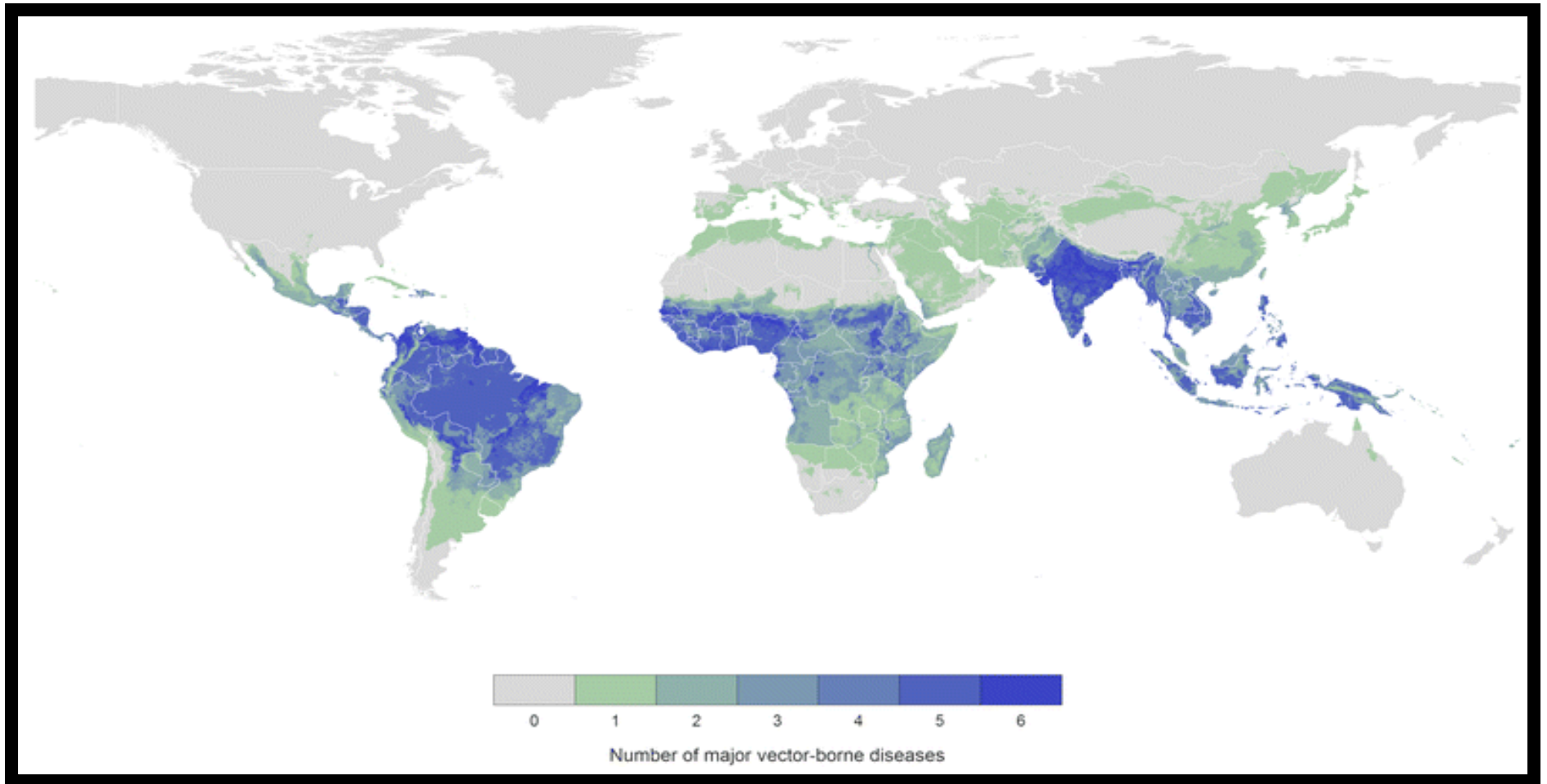


Figure 2.1: Combined global distribution of major vector-borne diseases (Golding *et al.*, 2015)

Vector-borne diseases account for over 17% of all globally infectious diseases such as malaria, dengue, yellow fever, and filariasis. In 2014, the WHO or the World Health Organization in Geneva, highlighted the serious and increasing threat of vector-borne diseases, with the slogan “Small bite, big threat” (United Nations in Loa PDR, 2014). These disease outbreak are determined by the complex dynamics of environmental factors such as climate, temperature, rainfall and humidity as well as social factors such as community, movement of people, housing and others (Huang *et.al*, 2012).

Malaria is the most deadly vector-borne disease which has caused around 627,000 deaths in 2012, mostly African children under the age of five. An estimated 90% of annual global malaria deaths occur especially in sub-Saharan Africa. Approximately, 3.4 billion people at risk and the transmission occurs in 97 countries, around the world (WHO, 2013). Whereas, dengue is the world’s fastest growing vector-borne disease especially when it’s in the form of dengue hemorrhagic fever (DHF) (WHO, 2012). Lately, dengue is endemic in more than a hundred countries in five out of the six WHO regions and about 2.5 billion people living in dengue-endemic countries (Su *et al.*, 2016). Currently, estimates there may be 50–100 million dengue infections worldwide every year which reported by WHO in 2013.

Despite malaria and dengue infections, lymphatic filariasis is another common vector-borne disease which has affected about 120 million people worldwide in 80 countries. About 40 million of them are disfigured and incapacitated by the disease. Approximately, 65% of those infected live in the WHO South-East Asia

Region, 30% in the African Region, and the rest in other tropical areas (WHO, 2013).

2.1.2 Transmission of Vector-borne diseases in Malaysia

Malaysia lies in a tropical climate area, and thus often has vectors (especially mosquitoes) which are capable of transmitting serious diseases like malaria, dengue, filariasis, Japanese Encephalitis and others. The strategy to control these diseases is not by chemotherapeutic, but through the reduction in the source of infection of the disease (WHO, 2014). The ability to control the vectors effectively is only possible through extensive knowledge in biology and the behavior of those vectors. Vector-borne diseases are still responsible for the high incidence of morbidity and mortality in many tropical countries, including Malaysia. The burden of main vector borne diseases is shown in Table 2.1. (MOH, 2014).

Table 2.1 : The type of diseases , prevalence and the morbidity of diseases in Malaysia (MOH, 2016 and WHO, 2016)

TYPE OF DISEASE/ POPULATION OF 100,000	PREVELANCE/INCIDENCE							
	2012		2013		2014		2015	
	Incidence Rate	Mortality Rate	Incidence Rate	Mortality Rate	Incidence Rate	Mortality Rate	Incidence Rate	Mortality Rate
Dengue	76.0	0.16	145.9	0.21	361.1	0.20	396.4	0.28
Malaria	16.11	0.05	1.30	0.01	13.03	0.03	7.58	0.03
Filariasis	0.27	0	0.60	0	0.047	0	0.17	0

The transmission of vector-borne disease is a challenging task to control because the diseases show complex dynamics impacted by a wide range of ecological factors (Xue, 2013). In Malaysia, dengue is the highest infected disease among the population and causes high mortality compared to malaria and filariasis (MOH, 2012).

The data from Table 2.1 shows the highest incidence rate and mortality rate of vector-borne disease within 4 years from the year 2012 to 2015 was dengue. Malaysia also experienced the global increase of dengue incidence. A total of 45,466 cases were reported which is equivalent to an incident rate of 145.9 cases per 100,000 populations in year 2013 whereas the incident rate was inclined in year 2014 and 2015 from 361.1 to 396.4 (cases per 100,000 populations) and the mortality rate were 0.20 to 0.28. Therefore, dengue is the most common endemic vector-borne disease which is known as an endemic infective disease in Malaysia.

The first case of dengue fever outbreak in Malaysia was reported in 1962 from Penang. Eventually, the first major outbreak of dengue hemorrhagic fever (DHF) in Malaysia occurred in 1973 and the country experienced a large epidemic with 3006 notified cases with 35 deaths in 1982 (Rose, 2015). Dengue infection poses a great threat to the local inhabitants in Malaysia due to rapid increase in population and industrialization in the past few decades (Nadeem and Shamala, 2006). According to Jihoo *et al.*, (2015), dengue cases recorded increased from 7,103 cases in 2000 to 108,698 in 2014, with 215 deaths, and not less than 31,500 notified cases in any given year. The dengue incidence in Malaysia continues to increase from 32 cases per

100,000 population to 361 cases per 100,000 population in 2014 and declined in 2015. This shows that Malaysia is one of the worstly affected country which has witnessed the highest number of dengue infection cases with significant raise from 2014 to 2015 (Figure 2.2 and Figure 2.3).

However, the current status of dengue infections in Malaysia until October, 2016 is 87,890 cases with 202 deaths compared to 21900 cases with 35 deaths in 2012, 43346 cases with 92 deaths in 2013, 108,698 cases with 215 deaths in 2014 and 120,836 cases with 336 deaths in 2015 as shown in Figure 2.2 (Ministry of health, 2016). A recent increase in dengue incidents is a significant cause for concern, especially given the hyperendemicity of serotypes. According to the Ministry of Health (2015), the reason for the rise in the number of cases and deaths is the dengue serotype shift in August, 2014. There was a shift in the dominant serotype from DENV 2 to DENV 1. Other factors contributing to the increase in the number of dengue cases were environmental factors, uncontrolled human movements especially those humans carrying the virus, the weather and unhealthy human behavior. Most of the dengue cases reported were from urban areas (70%–80%) where factors such as high density population and rapid development favour dengue transmission

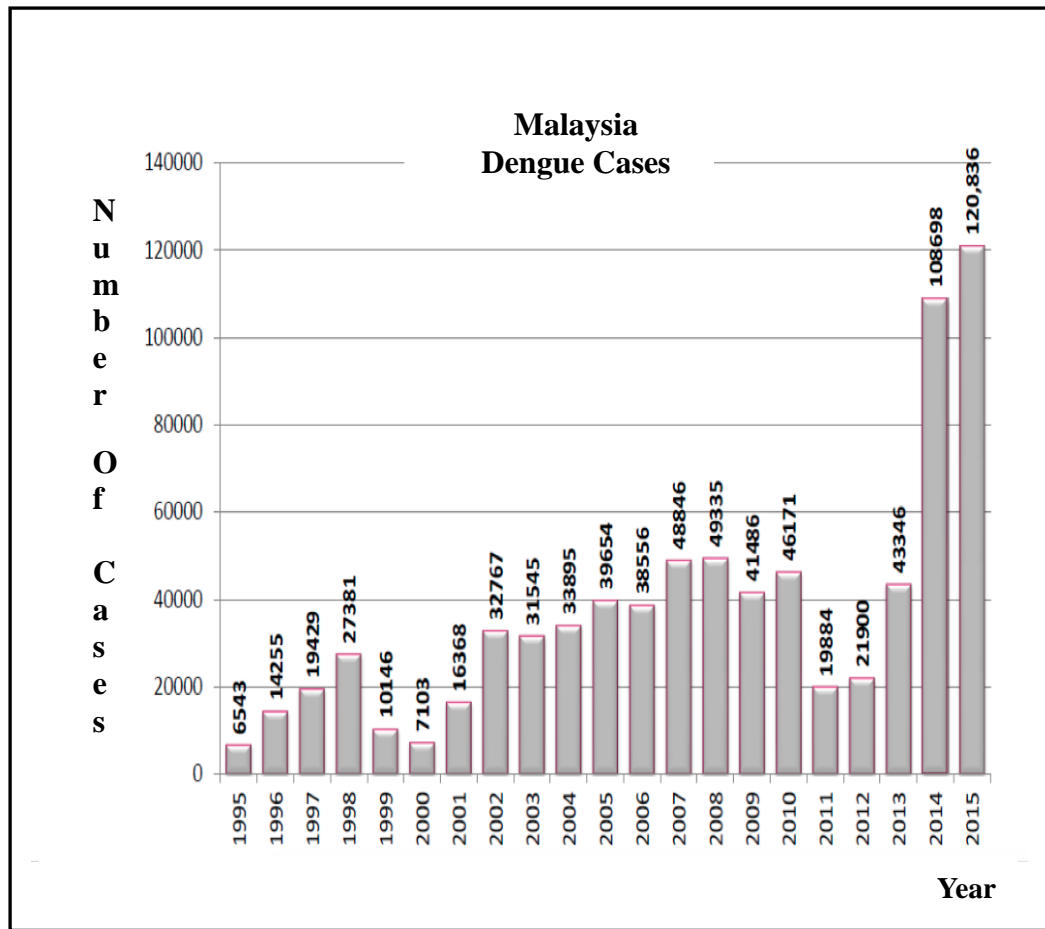


Figure 2.2 : The comparison of total number of dengue cases in Malaysia from 1995 to 2015 (MOH, 2016)

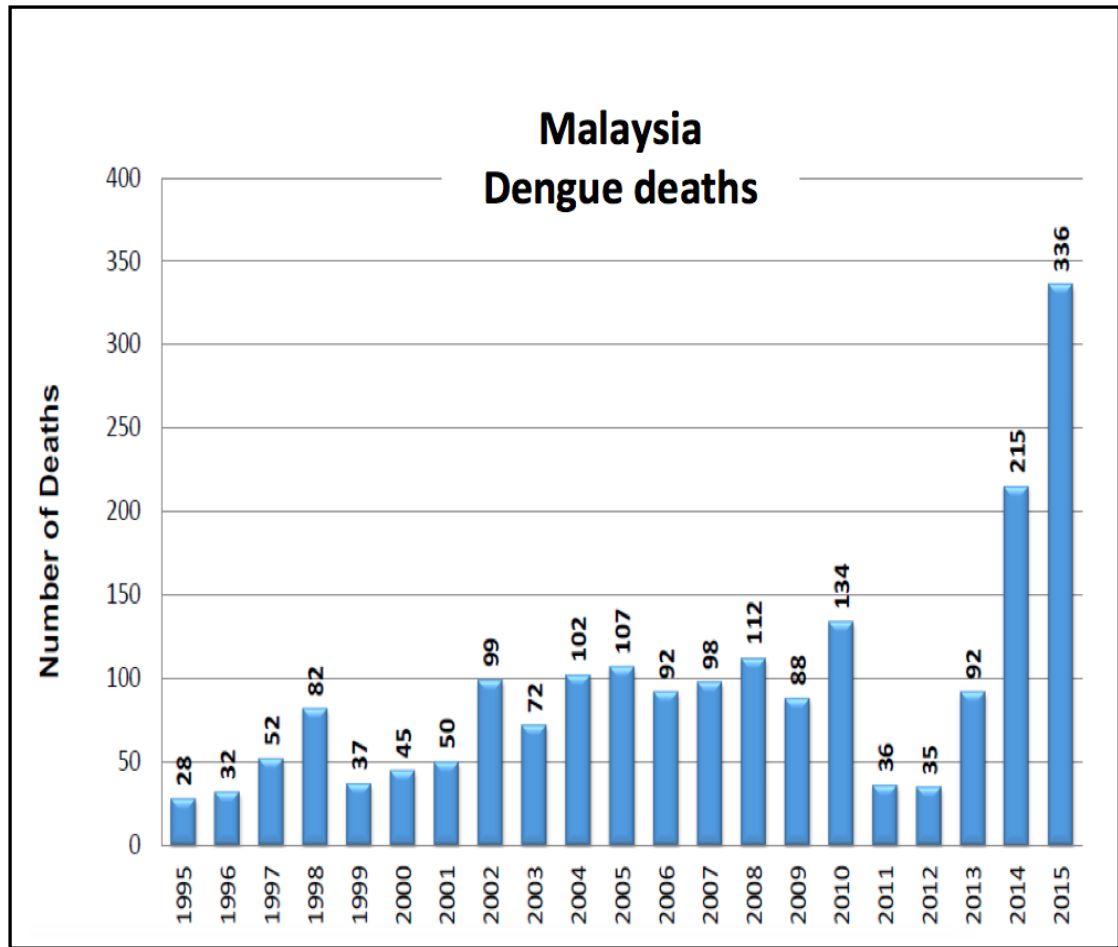


Figure 2.3 : The total cases of dengue deaths in Malaysia from 1995 to 2015 (MOH, 2016)

Table 2.2 shows the number of dengue cases and mortality which was reported according to states from 2013 to 2015 (Ministry of Health, 2016). The recent data shows Selangor has the highest number of dengue cases, followed by Johor, WP Kuala Lumpur & Putra Jaya, and Perak compared to other states. Other states such as Sabah, Kedah, Pahang and Penang also showed increasing in the dengue cases as well as death cases.

The number of dengue cases in Negeri Sembilan in 2013 was lowest compared in year 2014 and 2015. During this period, there were 1323 cases of dengue infections reported from Negeri Sembilan compared to 3781 cases in year 2014 and 2454 cases in 2015. But the number of death cases was the highest in 2015 and shows increasing from 2013 to 2015 in Negeri Sembilan if compare in year 2009 (5 deaths) and 2010 (7 deaths) (JKNNS, 2010). Table 2.3 shows the number dengue cases according to districts in Negeri Sembilan. The number of cases of Dengue Hemorrhagic Fever was the highest in 2010 compared to subsequent years. After the year 2010, the dengue cases were decreasing in Negeri Sembilan compared to others states in Malaysia (MOH, 2015).

Table 2.2 : The number of dengue cases and death(s) reported from 2013 until 2015 (MOH, 2016).

STATE	2013		2014		2015	
	CASES	DEATH	CASES	DEATH	CASES	DEATH
PERLIS	230	1	317	0	258	1
KEDAH	833	1	1014	7	1000	14
PENANG	1094	7	3141	11	5830	19
PERAK	7525	21	2648	4	9466	25
SELANGOR	26260	24	54290	77	63,198	127
WP KL & PUTRAJAYA	2664	8	7185	21	8332	34
N.SEMBILAN	1323	1	3781	10	2454	16
MELAKA	1549	9	2770	6	2420	8
JOHOR	4977	27	6323	25	15,743	51
PAHANG	744	2	2170	6	3001	16
TERENGGANU	1688	2	621	0	1455	5
KELANTAN	1454	2	14456	17	2850	7
SARAWAK	1311	4	2571	6	1923	3
SABAH	744	6	1456	6	2904	10
WP LABUAN	14	0	11	0	2	0
TOTAL	45466	96	108698	215	120836	336

Table 2.3 : Dengue cases in Negeri Sembilan according to districts (JKNNS, 2010)

District	2009	2010	(+/-)	
			Cases	%
SEREMBAN	524(5)	1132(5)	608	+160
KUALA PILAH	18	22	4	+22.2
PORT DICKSON	67	82(2)	14	+20.9
JEMPOL	28	53	25	+89.3
JELEBU	19	11	-8	-42.1
TAMPIN	14	48	34	+242.9
REMBAU	26	31	5	+19.2
NEGERI SEMBILAN	696(DF:619, DHF:77) 5 DEATH	1378(DF:1266, DHF:112) 7 DEATH	+682	+98.0%

Even though dengue is the highest prevalence of vector-borne diseases in Malaysia, but currently, malaria is also shows the most important vector-borne diseases, primarily in Malaysian Borneo (Sarawak and Sabah states), although only 4% of the population is living within active malaria transmission foci areas. Malaysia has battled malaria for most of its recent history. Post-World War II reports show upwards trend of 300,000 cases treated annually (inpatient and outpatient) in West Malaysia alone (WHO, 2015). Infection rates remained high through the 1950s and 1960s with more than 200,000 reported cases in 1961.

The Global Health Group and WHO (2014) reported that *Plasmodium vivax* (2,422 cases, 45.6%) and *P. falciparum* (973 cases, 18.3%) were responsible for the majority of malaria cases in Malaysia, closely followed by *P. malariae* (903 cases, 17.0%) and *P. knowlesi* (854 cases, 16.1%), which together represent a substantial proportion of cases in Sabah and Sarawak in 2011. However, the incident rate of

malaria declined to 18.6 per 100,000 population in 2011 from 318.6 per 100,000 in 1980.

Figure 2.4 shows the number of malaria cases by species in Malaysia from 1997 until 2011. In 2011, *Plasmodium vivax* (2 422 cases, 45.6%) and *P. falciparum* (973 cases, 18.3%) were responsible for the majority of malaria cases in Malaysia, closely followed by *P. malariae* (903 cases, 17.0%) and *P. knowlesi* (854 cases, 16.1%), which together represent a substantial proportion of cases in Sabah and Sarawak. This is in contrast to parasitological trends in 1992, at which time *P. falciparum* made up 65.1% of reported cases, while *P. vivax* contributed 31.6%. As a result, *Plasmodium falciparum* cases were declining from 1997 until 2011, whereas *Plasmodium knowlesi* cases were first reported in 2008 (WHO, 2015).

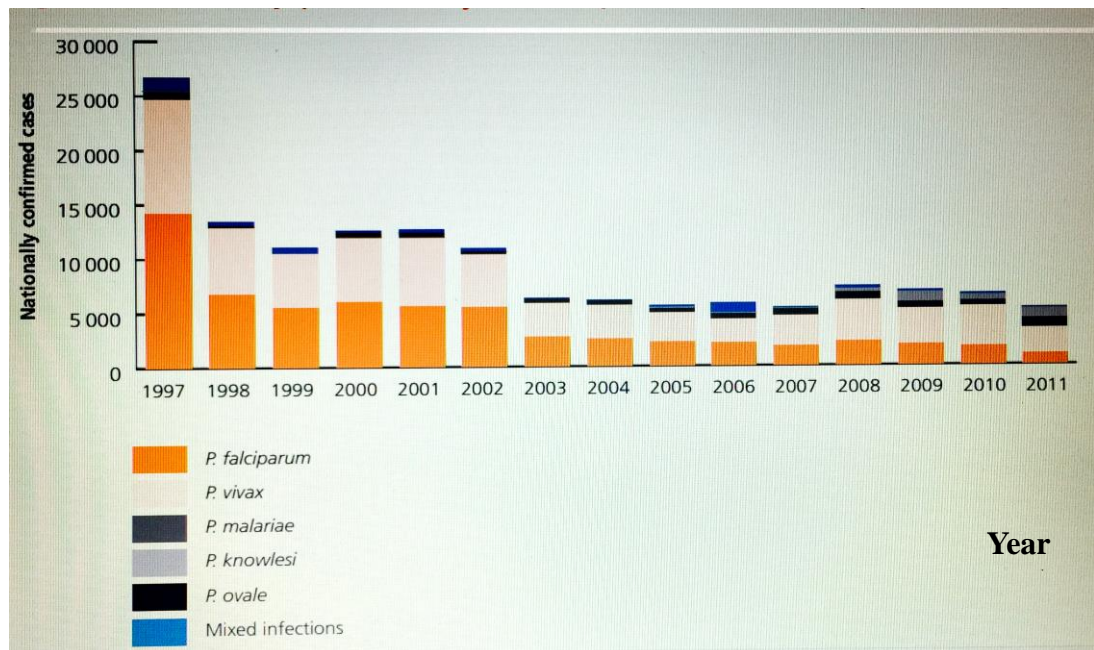


Figure 2.4 : Malaria cases by species in Malaysia from 1997 to 2011 (WHO,2015)

One of the main contributing factors for higher infection of malaria in Malaysia is the presence of the large number of migrant workers. About 21.9 per cent of malaria cases in Malaysia were imported which was reported in 2011 (MOH, 2011). Most of these foreigners came from malaria-endemic countries, a majority from Indonesia (68.9%), followed by Nepal (9.9%), India (6.9%) and Myanmar (4.6%) since 2005 (WHO, 2015).

Lately, Malaysia's National Strategic Plan for the Elimination of Malaria (NSPEM) is pursuing spatially-progressive malaria elimination and has set a goal of nationwide elimination by 2020. The Ministry of Health (2016) has reported that the potential threats and challenges to the elimination includes the importation of cases from malaria-endemic neighboring countries, especially the multi-drug resistant strains from Myanmar, Indonesia and Thailand. Figure 2.5 and Figure 2.6 show the number of malaria cases in Malaysia and Negeri Sembilan. From year 2010 to 2012 is showing declined in number of malaria cases accept 2014 showed slightly increased but number of death cases are decreased from year to year. A total of 9 deaths were reported in year 2014, which is a reduction of 74% compared to year 2000 (35 deaths) (MOH, 2015).

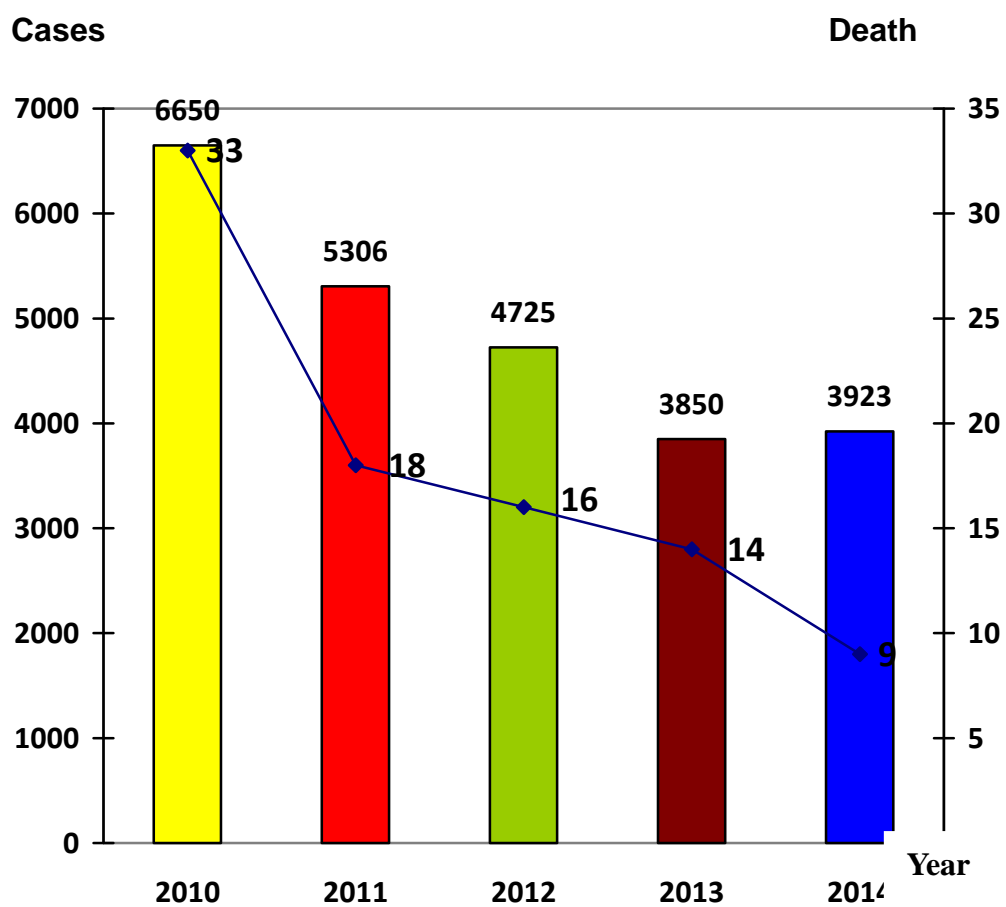


Figure 2.5 : The number of malaria cases and the incident rate in Malaysia from 2010 to 2014 (MOH, 2016)

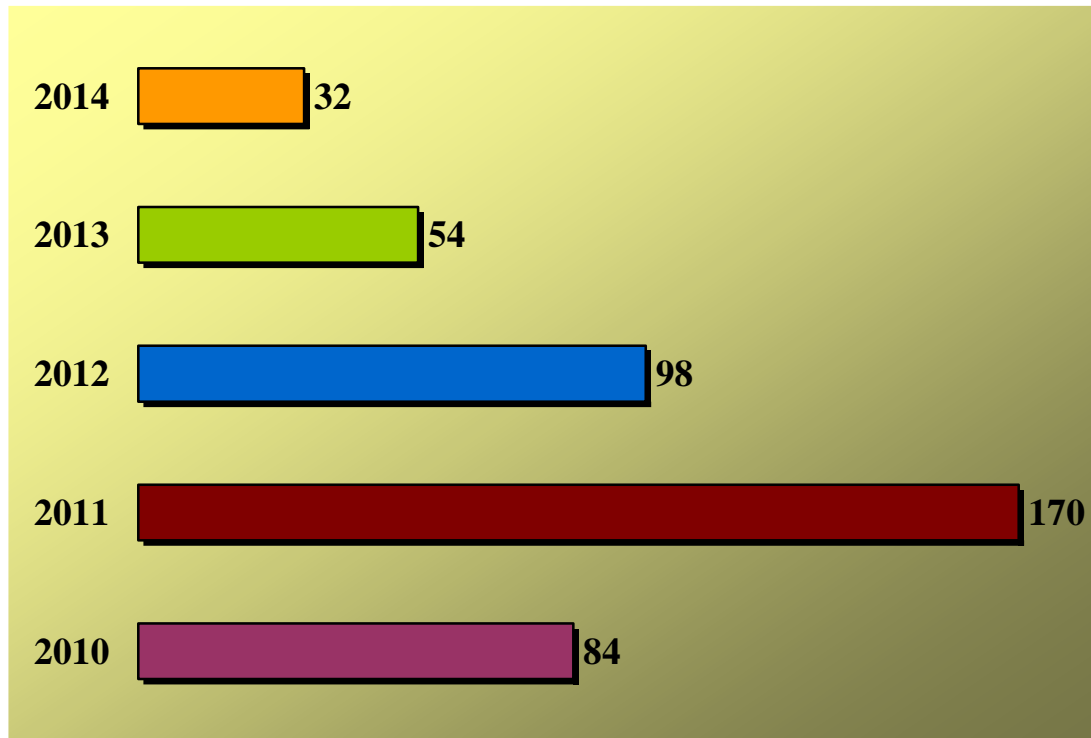


Figure 2.6 : The number of malaria cases in Negeri Sembilan from 2010 to 2014 (MOH, 2016)

A study done by Timothy and Jayaram (2014) between September, 2012 and December, 2013, has shown that *P. knowlesi* was identified in 256 (56.5%) cases, followed by 133 (29.4%) cases of *P. vivax*, 49 (10.8%) cases of *P. falciparum*, two (0.4%) cases of *P. ovale* and one (0.2%) case of *P. malariae*. Twelve mixed infections were detected, including *P. knowlesi* and *P. vivax* (10 cases), *P. knowlesi* and *P. falciparum* (1 case), and *P. falciparum* and *P. vivax* (1 case). *P. knowlesi* (including mixed infections involving *P. knowlesi* (*P. knowlesi/P. vivax* and *P. knowlesi/P. falciparum*)) showed the highest proportion in Sabah (84/115 cases, prevalence of 73.0%), Sarawak (83/120, 69.2%), Kelantan (42/56, 75.0%), Pahang (24/25, 96.0%), Johor (7/9, 77.8%), and Terengganu (4/5, 80.0%). However, *P. knowlesi* infections in

Selangor and Negeri Sembilan were found to be 16.2% (18/111 cases) and 50.0% (5/10 cases) of national figures respectively and shown in Table 2.4.

Table 2.4 : The Number of *Plasmodium knowlesi* cases and its prevalence

No.	States	Cases	Plasmodium knowlesi or mixed infection	Prevalance (%)
1.	Sabah	115	84	73.0
2.	Sarawak	120	83	69.2
3.	Kelantan	56	42	75.0
4.	Pahang	25	24	96.0
5.	Johor	9	7	77.8
6.	Terengganu	5	4	80.0

Lendrum *et al.*, (2016) reported that approximately, more than one billion people are infected and more than one million deaths from malaria and dengue every year. In addition, lymphatic filariasis also cause significant debilitation and suffering in most infected people. During the years 1988 to 1990, there appeared to be a decreasing trend in the number of filariasis cases detected countrywide that every year. In 1991, Brugian filariasis accounted for 92% of the cases detected (Marzuki *et al.*, 1993).

In Malaysia, the prevalence of lymphatic filariasis has decreased by 41.3% since 1990. This was reported annually with an average of 1.8% a year (WHO, 2015). According to Nazeh *et.al.*, (2014), the WHO organized the ‘Global Programme’ in 1997, to eliminate the Lymphatic Filariasis as a public health crisis by the year 2020, mainly through the institution of annual mass drug administration (MDA) programs for people living in endemic areas. In addition to interrupting the transmission, mass drug administration (MDA) such as diethylcarbamazine and albendazole, provides

significant collateral health benefits, to reduce morbidity from intestinal worms and ecto-parasites (WHO, 2010).

Filariasis infestation is endemic in 8 states such as Kedah, Perak, Johor, Pahang, Terengganu, Kelantan, Sabah and Sarawak. The National Lymphatic Filariasis Elimination Program under the Ministry of Health with the collaboration of the World Health Organization has given special attention to all these states by stopping the transmission of filariasis and controlling the morbidity of lymphatic filariasis patients (MOH, 2016). The number of filariasis infected cases raised in 1996 and is shown in Figure 2.6 (MOH, 1996). Five local Malaysian patients with clinical manifestations consistent with lymphatic filariasis were found between 2003 and 2006 (Lian *et al.*, 2010).

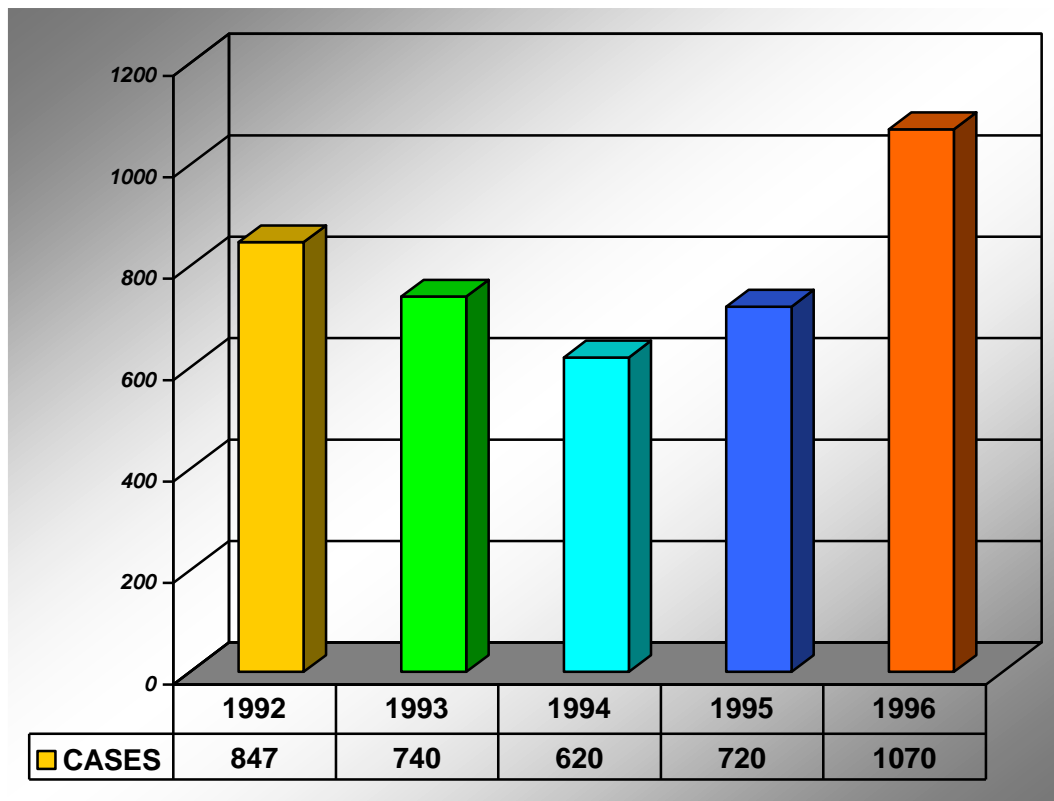


Figure 2.7 : The number of Lymphatic Filariasis cases in Malaysia in 1992 to 1996 (MOH, 1996)

Nevertheless, in 2011, the total number of filariasis were 387 cases which was increased number of cases (148%) compared to the previous year (156 cases). Filariasis cases increased in 2011 was influenced by increased activity in active case detection in which total of night blood sample slides were increased by 30% over 2010. In 2011, the incidence rate of filariasis was 1.36 per 100,000 population. However, the microfilaria rate for the last 5 years ranges from 2.14 to 1.41 per 1000 people. Out of 387 total cases, 201 cases (52%) are detected among local and 186 cases (48%) are detected among immigrant.

In 2012, the prevalence rate of filariasis was 0.93 per 100,000 populations. The number of cases noted increase in year 2011 and 2012 as compared to 2010 due to increase detection of cases from survey activities in elimination programme. A total of 136 filariasis cases were reported in 2014, showing a 58% decrease from 321 cases in 2013. In 2014, the prevalence rate of filariasis was 0.11 per 100,000 populations. Most cases (96%) were detected through Active Case Detection (ACD) from survey activities in elimination programmes. Out of 136 total cases, 18 cases (13%) are detected among locals and 118 cases (87%) are detected among immigrants.

The predominant parasite species are *Wuchereria bancrofti* which contributes the highest if compare to *Brugia malayi* (periodic) and *Brugia malayi* (subperiodic) in those years.

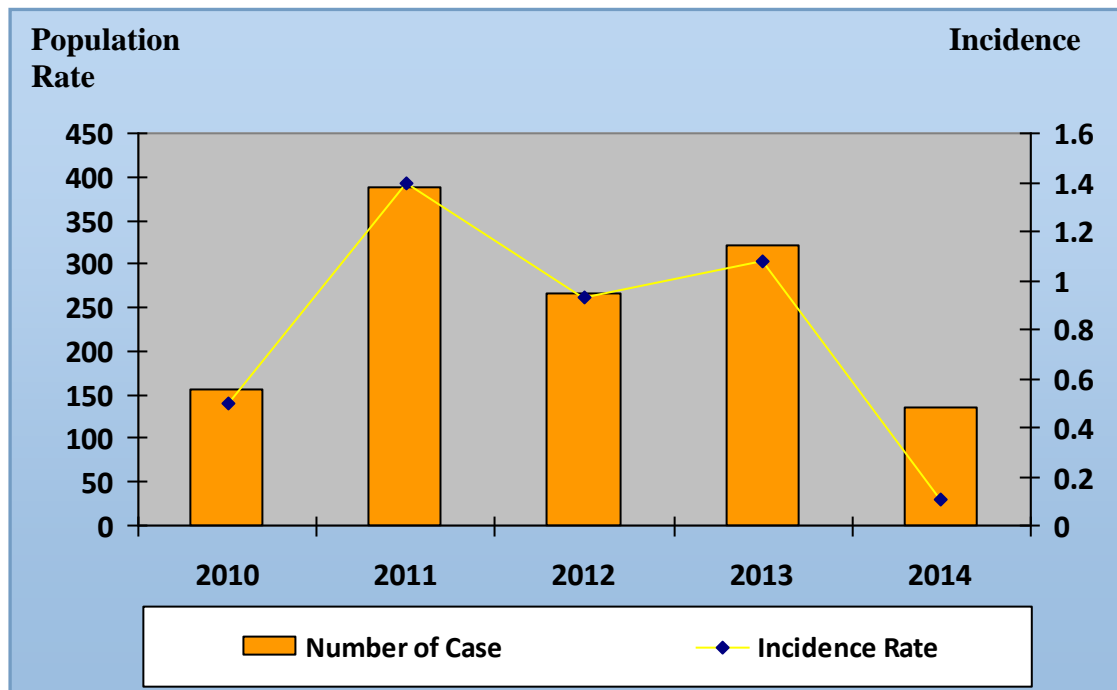


Figure 2.8 – The number of filariasis cases with the incidence rate from year 2010 to 2014 (MOH, 2014)