A STUDY ON COMMON MICROBIAL AGENTS, THEIR CHARACTERISTICS AND IMMUNOLOGICAL RESPONSE IN PATIENTS PRESENTING WITH FEVER

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MAY 2020

CERTIFICATE

This is to certify that the dissertation titled **"A STUDY ON COMMON MICROBIAL AGENTS, THEIR CHARACTERISTICS AND IMMUNOLOGICALRESPONSE IN PATIENTS PRESENTING WITH FEVER"** is a bonafide record of work done by **Dr.SAHANA. M** during the period of her Post Graduate study from 2017 to 2020 under guidance and supervision in the Institute of Microbiology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai- 600003, in partial fulfilment of the requirement of M.D MICROBIOLOGY degree Examination of The Tamilnadu Dr. M.G.R Medical University to be held in MAY 2020.

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DECLARATION

I, **Dr.SAHANA.M**, solemnly declare that this dissertation entitled **"A STUDY ON COMMON MICROBIAL AGENTS, THEIR CHARACTERISTICS AND IMMUNOLOGICAL RESPONSE IN PATIENTS PRESENTING WITH FEVER"**submitted by me for the degree of M.D. is the record work carried out by me during the period of **March 2018 to February 2019** under the guidance of **Dr.J.Euphrasia Latha, M.D,DGO.,**Director Incharge and Professor, Institute of Microbiology, Madras Medical College, Chennai. This dissertation is submitted to **The Tamil Nadu Dr.M.G.R. Medical University, Chennai,** in partial fulfilment of the University regulations for the award of degree of M.D., Branch IV (Microbiology) examination to be held in May 2020.

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INTRODUCTION

INTRODUCTION

"Humanity has, but three great enemies fever, famine and war; Of these by far the greatest, by far the most terrible is fever". William Osler[1]

HISTORY

A number of fever types were known as early as 460BC to 370 BC when Hippocrates was practising medicine including that due to malaria(tertian or every 2days / quartan or every 3 days).It also became clear that fever was a symptom of the disease rather than a disease in and of itself.[2]

SOCIETY AND CULTURE

ETYMOLOGY

Pyrexia is from a greek word 'pyr' meaning fire.Febrile is from the latin word 'febris' and archaically known as ague.

FEVER PHOBIA

It is the name given by medical experts to parents misconceptions about fever in children.Among them,many parents incorrectly believe that fever is a disease rather than a medical sign, that even low fevers are harmful,and that any temperature even briefly or slightly above the oversimplified "normal" number marked on the thermometer is a clinically significant fever.[3] They are also afraid of harmless side effects,like febrile seizures and dramatically overestimate the likelihood of permanent damage from typical fevers.The underlying problem,

according to Professor of Pediatrics Barton D Schmitt,is “as parents we tend to suspect that our children’s brain may melt”.[1]

As a result of these misconceptions parents are anxious,give the child fever-reducing medicine when the temperature is technically normal or only slightly elevated, and interfere with the child’s sleep to give the child more medicine.[3]

FEVER

A normal body temperature is maintained despite environmental variations because the hypothalamic thermoregulatory centre balances the excess heat production derived from metabolic activity in muscle and liver with heat dissipation from the skin and lungs.

According to studies of healthy individuals 18 to 40 years of age , the mean oral temperature is 36.8°±0.4°C (98.2°±0.7°F) with low levels at 6 AM and higher levels at 4-6 PM.

The maximal normal oral temperature is 37.2°C (98.9°F) at 6 AM and 37.7°C (99.9°F) at 4 PM; these values define the 99th percentile for healthy individuals. In light of these studies, an A.M. temperature of >37.2°C or a PM temperature of >37.7°C would define a fever.

The normal daily temperature variation, also called the circadian rhythm, is typically 0.5°C (0.9°F).

The daily temperature variation appears to be fixed in early childhood; in contrast, elderly individuals can exhibit a reduced ability to develop fever,with only a modest fever even in severe infections.

Fever is an elevation of body temperature that exceeds the normal daily variation and occurs in conjunction with an increase in the hypothalamic set point. This shift of the set point from "normothermic" to febrile levels very much resembles the resetting of the home thermostat to a higher level in order to raise the ambient temperature in a room.

In the pre antibiotic era, fever due to variety of infectious diseases rarely exceeded 106°F, and there has been speculation that this natural "thermal ceiling" is mediated by neuropeptides functioning as central antipyretics[(1)].

FUO=> Defined by Petersdorf and Beeson in 1961 as

1. Fever ≥38.3°c (≥101°F) on at least 2 occasions
2. Illness duration of ≥ 3 weeks
3. No known immunocompromised state
4. 4.Diagnosis that remains uncertain after a thorough history taking, physical examination and the following obligatory investigations: determination of erythrocyte sedimentation rate (ESR) and CRP level, platelet count, leukocyte count; measurement of levels of haemoglobin, electrolytes, creatinine, total proteins, alkaline phosphatase, alanine, aminotransferase, aspartate aminotransferase,lactate dehydrogenase, creatine kinase, ferritin, antinuclear antibodies, rheumatoid factor, protein electrophoresis, urinalysis,

blood cultures (n=3), urine culture, chest X ray, abdomen ultrasound and tuberculin skin test or interferon gamma release assay[1]

- CDC considers a person to have a fever when he or she has a measured temperature of 100.4^{o} F (38^{o}c) or greater or feels warm to the touch or gives a history of feeling feverish.

✓ **Other methods of detecting a possible fever**

- Self reported history of feeling feverish when the thermometer is not available or the ill person has taken the medicine that would lower the measured temperature
- The person feels warm to the touch
- Appearance of a flushed face, glassy eyes or chills if it is not feasible to touch the person or if the person doesn't expose feverish
- The presence of fever suggest an infection cause, but the fever is not always present with an infection

✓ **Skin Rash** means abnormal areas on the skins that may appear as disclosed bumps or flat spots or area or blisters or bumps containing fluids or pees that are intact or crushed over.

Rash includes insect bites or parasite lesions

Eg : Chicken pox, Measles, Rubella

✓ **Difficulty in breathing**

Eg; indicates a traveller has a respiratory infection such as Pneumonia, Diphtheria or Influenza

✓ **Persistent cough**

- Cough that is frequent and severe enough to catch the attention of the crew or another passenger
- Eg: indicates a disease of public health concern, such as Pertussis, TB. Legionellosis, Influenza

✓ **Decreased conscious or confusion of recent onset**

- Means the person is not fully aware of surroundings and may be confused about who he or she is, where he or she is going or the time of day/ week.
- Doesn't response normally to questions or painful sensations
- May appear to be sleepy, unresponsive or difficult to awaken
- Eg: Meningococcal meningitis

✓ **New unexplained bruising or bleeding (without previous injury)**

Eg: Hemmorrhagic fever

✓ **Persistent Diarrhoea**

Eg: Salmonellosis, Cholera

✓ **Persistent vomiting**

Eg: Salmonellosis, Dengue[19]

Fever is a common manifestation of various infections with a wide range of severity. Infectious diseases are the commonest and important causes of FUO and they are often curable. Severe bacterial infections if untreated may have significant morbidity and mortality as in the case of fever in Meningitis, Pneumonia and Tuberculosis. Hence more importance should be given for diagnosing the cause of any prolonged fever.

Various studies has been done on FUO in other countries, but only limited studies have been done in India. Such a study will help in finding out the etiological agents causing FUO and to define the changing pattern of the causative agents in a tertiary care hospital in Chennai. The presence of advanced diagnostic techniques have helped in finding out relatively higher percentage of infections. Hence this study was undertaken, restricting it to fever of most common infectious agents.

AIM & OBJECTIVES

AIMS AND OBJECTIVES

- The study was aimed to describe and identify the common microbial agents,risk factors and assessing outcomes in patients presenting with fever.
- Primary objective is to identify different characteristics of fever which includes acute,chronic,continuous,intermittent and remittent.
- Secondary objective is to determine the immunological response in patients presenting with fever.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Pathogenesis of fever

PYROGENS

The term pyrogen (Greek pyro - “fire”) is used to describe any substance that causes fever .Exogenous pyrogens are derived from outside the patient ; most are microbial products, microbial toxins, or whole microorganisms (including viruses).The classic example of an exogenous pyrogen is the LPS(endotoxin) produced by all Gram negative bacteria. Pyrogenic products of Gram positive organism include the enterotoxins of *Staphlyococcus aureus* and the groups A and B *Streptococcal* toxins, also called superantigens. Endotoxin is a highly pyrogenic molecule in humans; when injected intravenously into volunteers, a dose of 2-3 ng/kgproduces fever, leukocytosis, acute-phase proteins and generalized symptoms of malaise.

PYROGENIC CYTOKINES

Cytokines, are small proteins (molecular mass, 10000-20000 Da) that regulate immune, inflammatory and hematopoietic processes.

Pyrogenic cytokines include IL-1, IL-6, TNF and ciliary neurotropic factor, a member of IL-6 family. When injected into humans at low doses (10-100 ng/kg) IL-1 and TNF produce fever; in contrast for IL-6,a dose of 1-10 µg/kg is required for fever production.

FEVER WITH RASH

INFECTIONS	ETIOLOGY	EPIDEMIOLOGICAL FACTORS	DESCRIPTION	CLINICAL SYNDROME
Scrub typhus	*Orienta tsutsugamushi*	Endemic in South Pacific, Australia, Asia, transmitted by mites	Diffuse macular rash starting on trunk, eschar at the site of mite bite	Headache, myalgia, regional adenopathy, mortality rates upto 30% if untreated
Leptospirosis	*Leptospira interroggans and other Leptospira spp*	Exposure to water contaminated with animal urine	Maculopapular eruption,conjunctivitisscleral hemmorrhage in some cases	Myalgia, aseptic meningitis, fulminant form: Icterohemmorrhagic fever(Weil's disease)
Typhoid fever	*Salmonella Typhi, Salmonella Paratyphi A & B*	Ingestion of contaminated water/food	Transient, blanchable erythematous macules and papules,2-4mm usually on trunk(rose spots)	Variable abdominal pain, diarrhoea, headache, myalgia, hepatosplenomegaly
Dengue fever	*Dengue virus (4serotypes;flaviviruses)*	Occurs in tropics and subtropics,transmitted by Aedes aegypti mosquito	Rash in 50% of cases,initially diffuse flushing;midway through illness,onset of maculopapular rash, which begins on trunk and spreads centrifugally to extremities and face; pruritus, hyperesthesia in some cases; after defervescence,petechiae on extremities may occur.	Headache, musculoskeletal pain (breakbone fever) ; leukopenia, occasionally biphasic(saddle back) fever

The concept of "Fever of unknown", "undiagnosed", "unexplained origin" or "pyrexia of unknown origin" evolved in the medical literature from 1950. Fever is

defined as an elevation of core temperature above normal, i.e. > 37.8ºC due to resetting of the thermoregulatory centre in medulla. The cause can vary from minor brief illness to life threatening infections, malignancy or autoimmune disease[4].

The spectrum of FUO seems to be determined by geographic and economic factors, and it appears to change in time. Categorisation of fever including the duration and the presence of specific localising signs have been difficult because of areas of overlap.

In most patients with fever lasting one or two weeks, the underlying disorder is soon discovered or the patient recovers spontaneously. In other patients however, fever continues for two or three weeks during which time physical examination, chest x-ray films, blood tests and routine cultures do not reveal the cause of fever. In these cases the provisional diagnosis of fever of unknown origin (FUO) is made.The term "Fever of unknown origin" and pyrexia of unknown origin" are interchangeable. Immunocompetent patients were included using criteria for FUO according to Petersdorf and Beeson PB (1961) [5].The symptoms and signs may be highly variable some have trivial symptoms and others may be incapacitated by debilitating chills, rigors, sweats and dehydration. Certain diseases have been known to produce characteristic pattern of fever, notably in malaria, brucellosis, rickettsial infection and enteric fever.

Fever can be of different types such as intermittent, remittent or continuous. An exaggerated circadian rhythm that includes a period of normal

temperature on most days is termed as "intermittent fever" extremely wide fluctuations may be termed as "septic fever". "Remittent fever" varies by more than 0.5ºC during the course of the day but does not return to normal. A "sustained fever" is persistent and does not vary by more than 0.5ºC/day. Relapsing fever should be distinguished from infectious diseases with a tendency to relapse with intervals of normal temperature. A "biphasic fever" indicates a single illness with two distinct periods of fever over one or more weeks. The clinical characteristics of drug-induced fevers are highly variable, despite the common misconception that they are usually low grade fevers with relatively little variations from peak to trough and relatively low pulse rate. Individual variations and the common use of analgesics with antipyrexial effects confuse the diagnosis.

Fever is a common manifestation of various infections with a wide range of severity. Benign febrile diseases usually respond well to appropriate antibiotics and are not life threatening. The causes for most of the FUO can be included under five simple categories [(6)].

1. Infections
2. Malignancies
3. Connective tissue disease
4. Miscellaneous conditions including fictitious fever, drug induced fever and cryptic haematomas
5. Undiagnosed.

Within the first three categories infections predominate. Infectious diseases are the commonest and important causes of FUO and they are often curable. Severe bacterial infections if untreated may have significant morbidity and mortality as in the case of fever in meningitis, pneumonia and tuberculosis. Hence more importance should be given for diagnosing the cause of any prolonged fever.

Various authors all over the world, have performed studies on classical FUO from 1952 which is depicted below :

CAUSES OF CLASSICAL FUO IN ADULTS (FROM MILLER & DURACK DT 1994)[7,8]

Author and year of study	Number of cases	Infections	Neoplasm	Collagen disease	Miscellaneous	Undiagnosed
Petersdrof (1952-57)	100	36%	19%	13%	25%	7%
Jacoby (1957-71)	128	40%	20%	15%	17%	8%
Howard (1969-76)	100	37%	31%	19%	8%	5%
Larson (1970-80)	105	31%	31%	16%	10%	12%
Knockaert (1980-89)	199	22.5%	7%	21.5%	26.5%	22.5%
Sharma (1974-89)	150	50%	21%	9%	15%	5%
Kazanian (1984-90)	86	32.5%	24.4%	16.3%	17.5%	9.3%
Kejariwal D (1998-2000)	100	53%	17%	11%	5%	14%
Kucukardaly (2002)	82	59%	11%	7%	2%	21%

The largest study is by Knockaert DC (1992) spanning nine years from 1980-1989. In all the studies except in Knockaert DC (1992) [9] infection is the major cause of FUO. The spectrum of diseases found in several series examining FUO shows some variation, but overall, infections continue to be the most important cause of FUO accounting for about 53% followed by neoplastic lesions, collagen vascular disorder and other rare illness[10]. The spectrum of diseases causing FUO not only seems to be determined by geographical factors, but also appears to change with time[11]. Infections formed the majority of causes of FUO. A further breakup of the infectious causes are as follows:

LISTING OF INFECTIONS CAUSING FUO

(FROM MILLER AND DURACT DT 1994)[7,8]

Infection	Location / Year / No.of patients					
	Connecticut 1952-57 100	Washington 1970-80 105	Belgium 1980-89 199	India 1974-89 150	Rhodeid 1984-90 86	Spain 1968-81 133
Abscess	22%	20%	6%	5%	23%	3%
Mycobacterium	11%	5%	5%	25%	5%	11%
Endocarditis	5%	0%	2%	3%	5%	2%
UTI	3%	3%	1%	0%	0%	1%
Viral	0%	4%	5%	0%	5%	0%
Protozoal	0%	1%	0%	9%	2%	2%
Brucellosis	1%	0%	0%	0%	0%	3%

The commonest causes of bacterial and parasitical etiologies of classical FUO are depicted below[12]

Bacterial	Parasitical
-*Salmonella Typhi and Paratyphi A&B* - *Leptospira species* - *Mycobacterium tuberculosis* - *Brucella species* - *Klebsiella pneumoniae* - *Staphylococcus species* - *Rickettsiae species*	- *Plasmodium species* - *Filarial worms* - *Babesia microti* - *Leishmania donovani* - *Toxoplasma gondii* - *Entamoeba histolytica*

DENGUE

HISTORY:

Dr. Benjamin Rush's description of a Philadelphia epidemic in 1780 was the earliest description of Dengue, the break-bone fever. Subsequently, sporadic outbreaks were reported throughout the tropics and subtropics.Although dengue fever had been described in the 18th century, the virus was isolated only during World War II[17].

Clinical description of Dengue complicated by haemorrhages, shock and death were reported in outbreaks in Australia in 1897, Greece in 1928 and in Formosa in 1931. Mosquito borne transmission of infection by *Aedes aegypti* was demonstrated in 1903 and its viral etiology in 1906. Sabin isolated the virus in 1944 and established the existence of Dengue viral serotypes[18].

Between 1944 and 1956 it was shown that four distinct viruses, designated Dengue virus types 1-4 were responsible for the same clinical syndrome. In

1956,a severe form of the disease, Dengue hemorrhagic fever / Dengue shock syndrome were described for the first time[17]

The epidemics from India include those from Calcutta(1963), Vishakapattanam(1964), West Bengal(1968), Ajmir(1969), Kanpur (1969), Delhi (1970), Rajasthan (1985) and Delhi in 1996[20,21]

Dengue/ DHF is widely prevalent in India, and all the 4 serotypes are found in the country. It is reported from 15 states/ Union Territories since 1996. In Southern India, the disease has been reported in TamilNadu, Karnataka, Andhra Pradesh and Kerala[22].

Viral haemorrhagic fevers are becoming increasingly common in the tropics and subtropics. Dengue fever is currently the most important arthropod borne viral disease because of its widespread distribution in more than 100 countries and its potential for extensive outbreaks of life-threatening disease. Two-fifths of world's population or 2500 million people are now at risk for Dengue and every year approximately 50 million new cases occur worldwide[13].

Dengue virus was first isolated in India in the year 1945 and is endemic in both urban and semi-urban areas. Dengue fever has struck again in India and cases of dengue fever (DF)/dengue haemorrhagic fever (DHF) have been reported from various parts of the country during the last 8 decades[14] .Dengue virus, belonging to the genus *Flavivirus* and Family *Flaviviridae*, are mosquito borne viruses and the principal vector, *Aedes aegypti* is a day-biting mosquito of public importance that breeds in natural or artificial waters.

Dengue illnesses are caused by any one of the four serologically related viruses designated as DENV-1, DENV-2, DENV-3 and DENV-4. Infection with any one of these serotypes mostly causes a mild, self-limiting febrile illness (Classical dengue fever), however, a few cases develop severe life threatening Dengue haemorrhagic fever (DHF) and Dengue shock syndrome (DSS)[15].

DHF and DSS are severe forms of the disease characterized by sudden onset of fever and nonspecific signs and symptoms. The critical stage of DHF occurs 24 hrs before to 24 hrs after the temperature falls to or below normal. During this time, haemorrhagic manifestations usually occur and signs of circulatory failure may appear. Laboratory tests show thrombocytopenia and evidence of vascular leak syndrome. Hypovolemia, shock and death may occur in case of DSS [16].

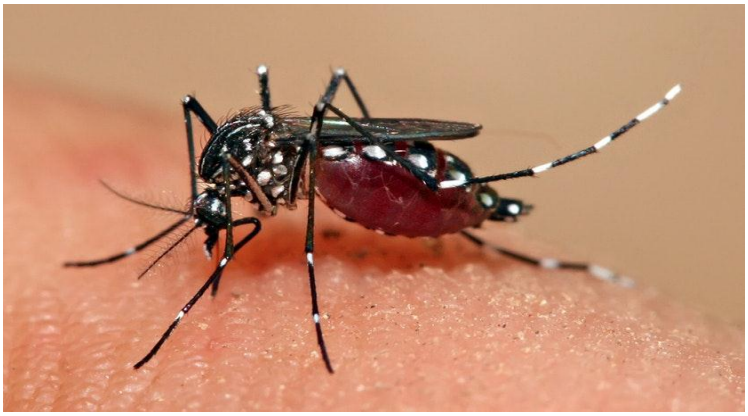
The diagnosis of DF and DHF is made on clinical and epidemiological grounds. In some areas, DHF overlaps with the distribution of other viral haemorrhagic fevers, thereby causing a confusion in the diagnosis. Therefore, serological diagnosis by detection of IgM and IgG antibodies to dengue in the serum is essential for monitoring the treatment. Commercial kits are available, which can help in differentiating between primary and secondary Dengue infections. ELISA tests are very useful in Dengue serology. They detect IgM and IgG in the serum and thus are able to distinguish primary and secondary infection.

MORPHOLOGY

Dengue virus particles are 40 to 50 nm in diameter and have a spherical nucleocapsid surrounded by a lipid bilayer envelope with small surface projections representing E glycoprotein dimers anchored to virus membrane. The

lipid envelope is covered densely with surface projections comprising 180 copies of the membrane and 180 copies of the envelope glycoproteins[23].

VECTOR



The vector for Dengue virus is *Aedes* mosquito, which is not affected by the disease, although an infected mosquito may infect others. *Aedes* mosquitoes are easily distinguished by white stripes on a black body, therefore referred to as "Tiger mosquitoes"[24].

Of the three Aedes mosquitoes, ie, *Aedes aegypti*, *Aedes albopictus* and *Aedes vittatus*, that are commonly collected in TamilNadu, *Aedes aegypti* is found to be the most prevalent species[25].

Feeding attempts may occur several times a day over the insectslifetime of one to four weeks. Adult mosquito shelters indoors and bite during one to two hour intervals in the morning and later afternoon. In areas with endemic transmission, one of every twenty hours may contain an infected mosquito[26].

Vertical transmission of DV has also been shown in *Aedes aegypti* which reveals that the virus may be maintained in mosquito even during inter-epidemic periods[27].

TRANSMISSION:

Dengue viruses are transmitted to humans through the bites of infective female *Aedes* mosquito[28].The period of viraemia during which humans are infectious for blood feeding adult female vectors is 3 to 5 days. After blood feeding, an extrinsic incubation period of 10 to 14 days must elapse before *Aedes aegypti* can transmit the virus upon refeeding.In rural areas and in some parts of the world *Aedes albopictus* plays a secondary role in inter-human transmission of Dengue[29] .

PATHOGENESIS AND IMMUNOLOGICAL REACTION

Most Dengue virus infections are subclinical. Self-limited Dengue fever is the usual outcome of infection but an immunopathogenic response in some patients, usually in the setting of heterologous immunity, produces a syndrome of Dengue hemorrhagic fever[30].

After an infectious mosquito bite, the virus replicates in local lymph nodes and within 2 to 3 days disseminates via the blood to various tissues. Virus circulates in the blood typically for 5 days in infected monocytes / macrophages, to a lesser extent and to lesser degree in B cells and T cells. It also replicates in skin, reactive spleen lymphoid cells, and macrophages[31].

Viral antigen can be demonstrated by nucleic acid detection methods more widely in liver kupffer cells, renal tubular cells and alveolar macrophages and endothelia. The malaise and flu-like symptoms that typify Dengue probably reflect patients' cytokine response. However myalgia, a cardinal feature of the

illness may also indicate pathological changes in muscle typified by a moderate perivascular mononuclear infiltrate with lipid accumulation[32].

Musculoskeletal pain (break-bone fever) could reflect viral infection of bone marrow elements, including mobile macrophages and dendritic cells (CD11b/CD18) and relatively non motile adventitial reticular cells[33]

Shock in Dengue shock syndrome occurs after the sudden extravasation of plasma into extravascular sites including pleural and abdominal cavities, usually with the defervescence of fever [34,35].The extensive increase in vascular permeability is associated with immune activation, as manifested by increased levels of plasma soluble tumour necrosis factor receptor (sTNFR), Interlukin (IL)-8, Interferon(IFN) gamma and other mediators and local endothelial production of IL-8, RANTES (Regulated on Activation, Normal T Expressed and Secreted)with apoptotic endothelial cell death[36].

In addition, immune complex formation activates the complement system, with increase in C3a and C5a levels of IL-6 and intercellular adhesion molecule -1 are depressed in parallel with hypoalbuminemia and the general loss of serum proteins. Reduced cardiac output may contribute further to shock[37].

ANTIBODY RESPONSE:

Anti-Dengue virus IgM antibody is produced transiently during primary and secondary infections.In patients with primary dengue virus infections , IgM antibodies develop rapidly and are detectable on days 3 to 5 of illness in half of the hospitalized patients. Studies of the dynamic antibody response showed that anti-Dengue virus IgM levels peak at about 2 weeks postinfection and then

decline to undetectable levels over 2 to 3 months . Anti-Dengue virus IgG appears shortly afterwards [38]. In contrast to primary infection, secondary infection with Dengue virus results in the earlier appearance of high titres of cross-reactive IgG antibodies before or simultaneously with the IgM responses[39].

Antibodies produced during Dengue infection provides short lived protection against infection with a heterologous serotype of Dengue virus. Neutralizing antibody levels correlate with protection against Dengue virus. The presence of measurable levels of Dengue antibody is generally protective, with the exception of low levels of cross-reacting antibodies induced by a virus of different serotype than the infecting type. In this situation, the antibody can conceivably enhance virus replication and the severity of disease manifestations (according to the immune enhancement theory of Dengue pathogenesis)[40].

Acute primary Dengue virus infection is defined as an IgM positive and IgG negative result, and acute secondary Dengue virus infection is defined as an IgM and IgG positive or IgM negative and IgG positive result[41].

CLINICAL FEATURES

Classical Dengue fever is an acute febrile disease with headache, musculoskeletal pain and rash, but the severity of illness and clinical manifestations vary with age. Infection is often asymptomatic or nonspecific, consisting of fever, malaise ,pharyngeal infection, upper respiratory symptoms and rash, particularly in children[42].

In severe illness after incubation period of four to seven days, fever often with chills, severe frontal headache and retro orbital pain develops abruptly with a

rapid progression to prostration, severe musculoskeletal sand lumbar back pain and abdominal tenderness. Anorexia, nausea, vomiting, hyperaesthesia of skin and dysgeusia are common complaints. Initially the skin appears flushed, but in three to four days and with the lysis of fever an indistinct macular and sometimes scarlatiform rash develops sparing the palms and soles. As the rash fades or desquamates, localized clusters of petechiae on the extensor surfaces of limbs may remain[18].

A second episode of fever and symptoms may ensue ("saddle back" pattern). Recovery may be followed by a prolonged period of listlessness, easy fatiguability, and even depression. Minor bleeding from mucosal surfaces is not uncommon and gastrointestinal haemorrhage and haemoptysis can occur. Hepatitis can also frequently complicate Dengue fever[43].

The platelet count declines and petechiae appear in wide spread distribution with ecchymoses. Bleeding occurs at mucosal surfaces from gastrointestinal tract and at many puncture sites. Liver is enlarged in up to 75% of cases. Pleural effusion can be detected in more than 80% of cases, which in combination with elevated hematocrit and hypoalbuminemia , reflects hemoconcentration.

Acute respiratory distress syndrome may develop with capillary alveolar leakage. In untreated patients, hypoperfusion complicated by myocardial dysfunction and reduced ejection fraction results in metabolic acidosis and organ failure[18].

LABORATORY DIAGNOSIS:

Laboratory diagnosis of Dengue infection can be made by the detection of specific virus, viral antigen, genomic sequence and / or antibodies [44,45,46].

Other common laboratory findings include pancytopenia, neutropenia, increased haemoconcentration, thrombocytopenia and prolonged bleeding time[47].

The field of molecular diagnosis has changed significantly over the past decade, leading to assays that are much more reliable for the detection and characterization of various pathogens. The Polymerase Chain Reaction(PCR) can be used to amplify and detect RNAviruses by using the enzyme reverse transcriptase(RT)[48].

Other variations on amplification techniques, such as NASBA, are becoming increasingly popular owing to their relative simplicity and the availability of standardized kits .

Among the viral infections that can be diagnosed by serology, dengue virus infection is the most challenging due to its cross-reactivity to homologous and heterologous flavivirus antigens. However, great advances in analyzing the complicated viral antigens and antibody responses have recently been made by the development of various methods that target different structural and non-structural proteins for sero-diagnosis and sero-epidemiological studies of Dengue virus infection[49].

ANTIGEN DETECTION

Recent studies have shown that ELISA ,Dot-blot assays and the NS1 antigens in the form of an immune complex could be detected in the acute phase

sera of both patients with primary Dengue virus infection and patients withsecondary infection [50].

The *Flavivirus* NS1 is a 46-50 Kilodalton glycoprotein which is expressed in both membrane-associated (mNS1) and secreted (sNS1) forms and possesses both group-specific and type-specific determinants. The procedure of capture ELISA has been developed for detection of *flavivirus* NS1 in patient's sera [51].

ANTIBODY DETECTION

Several methods have been described for the serological detection of dengue virusspecific antibodies, including ;

- Haemagglutination inhibition (HAI) test
- Neutralization test
- Indirect immunofluorescent-antibody test
- Enzyme-linked immunosorbent assay (ELISA)
- Complement fixation test
- Dot blotting
- Western blotting
- Rapid immunochromatography test

Among these, capture IgM and/or IgG ELISA, and the HI test are the most commonly used serological techniques for the routine diagnosis of Dengue virus infections, as they are simple and allow large number of samples to be tested [46].

IgM and IgG ELISA have replaced the HAI assay because it has the potential to be automated and thus can accommodate a large number of samples. In addition, no processing of the serum is required and only a few microlitres of the sample are needed[38] .

DENGUE IgM& IgG CAPTURE ELISA

Serum IgM/IgG antibodies, when present, combine with Anti-human IgM/IgG antibodies attached to the polystyrene surface of the microtitre plate. A concentrated pool of dengue 1-4 antigens is diluted to the correct working volume, with antigen diluent. The antigens are produced using an insect cell expression system and immunopurified utilizing a specific monoclonal antibody. An equal volume of the Horse Radish Peroxidase (HRP)conjugated monoclonal antibody is added to the diluted antigen, which allows the formation of Antigen-MAb (Monoclonal Antibodies) complexes. Residual serum is removed from the assay plate by washing and complexed antigen-MAb is added to the assay plate. After incubation, the microwells are washed and a colourless substrate system, tetramethylbenzidine/ hydrogen peroxide (TMB/ H2O2) is added.

The substrate is then hydrolysed by the enzyme and the chromogen changes to a blue colour. After stopping the reaction with acid, the TMB becomes yellow. Colour development is indicative of the presence of anti-Dengue antibodies in the test sample.

TREATMENT

There is no specific treatment for DF. However careful clinical management frequently saves the lives of DHF patients. With appropriate intensive supportive therapy, mortality may be reduced to < 1%. Maintenance of the circulating fluid volume is the central feature of DHF case management[(52).]

The haematocrit should be measured frequently. In severe cases blood transfusions may be required.

DENGUE VACCINE

There is no vaccine for Dengue virus although significant progress has been made in developing both live attenuated vaccine candidates and second-generation recombinant candidate vaccines using infectious clone technology in recent years [(16)].

There are three major concerns in the development of Dengue vaccine. Firstly, is the possibility that it could lead to antibody- dependent enhancement of infection and thus produce DHF/ DSS. Candidate vaccines based on live attenuated viruses should therefore contain all four serotypes to give comprehensive protection without adverse side effects.

Another concern is that possibility of virus evolution through genome recombination. The third concern is that the vaccine may produce adverse reactions, for example, recently a tetravalent live attenuated vaccine was tested in human volunteers and in children, Phase I and Phase II trials have shown mildly adverse reactions with monovalent vaccines, but more frequent and significantly more severe reactions with the tetravalent vaccine[(53).]

PREVENTION

A multi-sectoral, multifaceted and comprehensive response will be required to meet the challenges of frequently occurring outbreaks. Disease surveillance, training of health care providers in medical and paramedical schools and strengthening health infrastructure has to be implemented through innovative, client-friendly approaches throughout the year on a regular and sustainable basis[(54).]

The WHO guidelines for prevention of dengue are that all control efforts should be directed against mosquitoes. It is important to take control measures to eliminate the mosquitoes and their breeding places. Efforts should be intensified before the transmission season (during and after the rainy season) and during epidemics [55].

LEPTOSPIROSIS

HISTORY:

Leptospirosis is a zoonosis of ubiquitous distribution caused by infection with pathogenic *Leptospira species*[56]

Adolf Weil described Leptospirosis as a disease entity in 1886. His name is still attached to a serious form of Leptospirosis called Weil's disease, traditionally attributed to rat transmitted infection, caused by the serovars icterohaemorrhagiae and copenhageni. Goldsmidt first used the term Weil's disease in 1887. In 1907 Stimson demonstrated by silver staining the presence of clumps of Spirochaetes that caused Weil's disease in the kidney tubules of a patient who reportedly died of yellow fever. The Spirochaetes had hooked ends and Stimson named them *Spirochaeta interrogans* because of their resemblance to question mark [57].

The disease is caused by pathogenic *Leptospira species* and is characterized by a broad spectrum of clinical manifestations, varying from asymptomatic infection to fulminant, fatal disease. In its mild form, Leptospirosis may present as nonspecific symptoms such as fever, headache, and myalgia. Severe Leptospirosis, characterized by jaundice, renal dysfunction, and hemorrhagic diathesis, is often referred to as Weil's syndrome. With or without

jaundice, severe pulmonary hemorrhage is increasingly recognized as an important presentation of severe disease [1].

The first isolate made in 1917 from a patient in Japan with jaundice and haemorrhagic manifestations was named as *Icterohaemorrhagiae*. Subsequently other members of serogroups were isolated in various places of the world from different animals reservoir hosts. Inada identified *Leptospira hebdomadis* carried by the field mouse as the causative agent for the nonicteric syndrome the "7 day fever".

ETIOLOGIC AGENT

Leptospira species are spirochetes belonging to the order *Spirochaetales* and the family *Leptospiraceae*. Traditionally, the genus *Leptospira* comprised two species: the pathogenic *L. interrogans* and the free-living *L.biflexa*, now designated *L.interrogans sensu lato* and *L.biflexa sensu lato*, respectively. Twenty-two *Leptospira species* with pathogenic (10 species), intermediate (5 species), and nonpathogenic (7 species) status have now been described on the basis of phylogenetic and virulence analyses .

MORPHOLOGY:

Leptospires are coiled, thin, highly motile organisms that have hooked ends and two periplasmic flagella, with polar extrusions from the cytoplasmic membrane that are responsible for motility .These organisms are 6–20 μm long and ~0.1 μm wide; they stain poorly but can be seen microscopically by dark-field examination and after silver impregnation staining of tissues.

EPIDEMIOLOGY

Leptospirosis has a worldwide distribution but occurs most commonly in the tropics and subtropics because the climate and occasionally poor hygienic conditions favour the pathogen's survival and distribution. Rodents, especially rats, are the most important reservoir, although other wild mammals as well as domestic and farm animals may also harbour these microorganisms. Leptospires establish a symbiotic relationship with their host and can persist in the urogenital tract for years [(1)].

TRANSMISSION:

Transmission of Leptospires may follow direct contact with urine, blood, or tissue from an infected animal or, more commonly, exposure to environmental contamination. The dogma that human-to-human transmission is very rare is challenged by recent findings on household clustering, asymptomatic renal colonization, and prolonged excretion of Leptospires. Outbreaks may result from exposure to flood waters contaminated by urine from infected animals, as has been reported from several countries. For example, an outbreak took place in 1998 among athletes after a triathlon in Springfield, Illinois. Ingestion of one or more swallows of lake water during the swimming leg of the triathlon was a prominent risk factor for illness. Heavy rains that preceded the triathlon, with consequent agricultural runoff, are likely to have increased the level of Leptospiral contamination in the lake water.

In another outbreak, 42% of participants contracted Leptospirosis during the 2000 Eco-Challenge- Sabah multisport endurance race in Malaysian Borneo. Swimming in the Segama River was shown to be an independent risk factor. In addition, Leptospirosis is a traveler's disease. Large proportions of patients acquire the infection while traveling in tropical countries, usually during adventurous activities such as whitewater rafting, jungle trekking, and caving. New data indicate that Leptospirosis may develop after unanticipated immersion in contaminated water (e.g., in an automobile accident) more frequently than has generally been thought and can also result from an animal bite.

PATHOGENESIS

Transmission occurs through cuts, abraded skin, or mucous membranes, especially the conjunctival and oral mucosa. After entry, the organisms proliferate, cross tissue barriers, and disseminate hematogenously to all organs (Leptospiremic phase). During this initial incubation period, Leptospires can be isolated from the bloodstream .The organisms are able to survive in the nonimmune host: they evade complement-mediated killing by binding factor H, a strong inhibitor of the complement system, on their surface.

During the immune phase, the appearance of antibodies coincides with the disappearance of Leptospires from the blood. Renal pathology shows both acute tubular damage and interstitial nephritis. Acute tubular lesions progress in time to interstitial edema and acute tubular necrosis. The reported deregulation of the expression of several transporters along the nephron contributes to impaired sodium absorption, tubular potassium wasting, and polyuria.

Histopathology of the liver shows focal necrosis (widespread hepatocellular necrosis usually is not found), foci of inflammation, and plugging of bile canaliculi. Hepatocyte apoptosis has also been documented. Experimental work showed infiltration of Leptospira in Disse's space and migration between hepatocytes with detachment of the intercellular junctions and disruption of bile canaliculi leading to bile leakage. Petechiae and hemorrhages are observed in the heart, lungs ,kidneys, pancreas, liver, gastrointestinal tract (including retroperitoneal fat, mesentery, and omentum), muscles, prostate, testis, and brain (subarachnoid bleeding). A consumptive coagulopathy may occur, with elevated markers of coagulation activation (thrombin–antithrombin complexes, prothrombin fragments 1 and 2, d-dimer), diminished anticoagulant markers (antithrombin, protein C), and deregulated fibrinolytic activity. Overt disseminated intravascular coagulation (DIC) has been documented in several studies.

Pathogenic Leptospires contain a variety of genes coding for proteins involved in motility and in cell and tissue adhesion and invasion that represent potential virulence factors. Many of these are surface-exposed outer-membrane proteins (OMPs). To date, the only Leptospiral virulence factor shown to satisfy Koch's molecular postulates is loa22 encoding a surface-exposed protein with an unknown function. In recent work, the whole-blood transcriptome of patients from Brazil with severe Leptospirosis (13 who survived and 3 who died) were studied. In fatal cases, expression of chemokines and the antimicrobial peptide cathelicidin was decreased, whereas transcription of proinflammatory cytokine pathways was more abundant.

CLINICAL MANIFESTATIONS

The incubation period is usually 1–2 weeks but ranges from 1 to 30 days. Leptospirosis is classically described as biphasic. The acute Leptospiremic phase is characterized by fever of 3–10 days' duration, during which time the organism can be cultured from blood and detected by polymerase chain reaction (PCR). During the immune phase, resolution of symptoms may coincide with the appearance of antibodies, and Leptospires can be cultured from the urine. The distinction between the first and second phases is not always clear: milder cases do not always include the second phase, and severe disease may be monophasic and fulminant.

Mild symptomatic Leptospirosis usually presents as a flu-like illness of sudden onset, with fever, chills, headache, nausea, vomiting, abdominal pain, conjunctival suffusion (redness without exudate), and myalgia. Muscle pain is intense and especially affects the calves, back, and abdomen. The headache is intense, localized to the frontal or retroorbital region (resembling that occurring in dengue), and sometimes accompanied by photophobia. Aseptic meningitis may be present and is more common among children than among adults. Although Leptospira can be cultured from the cerebrospinal fluid (CSF) in the early phase, the majority of cases follow a benign course with regard to the central nervous system; symptoms usually disappear within a few days but may persist for weeks. Physical examination may include any of the following findings, none of which is pathognomonic for Leptospirosis: fever, conjunctival suffusion, pharyngeal injection, muscle tenderness, lymphadenopathy, rash, meningismus, hepatomegaly, and splenomegaly. If present, the rash is often transient; may be macular, maculopapular, erythematous, or hemorrhagic (petechial or ecchymotic);

and may be misdiagnosed as due to scrub typhus or viral infection. Lung auscultation may reveal crackles. Mild jaundice may be present.

The natural course of mild Leptospirosis usually involves spontaneous resolution within 7–10 days, but persistent symptoms have been documented.Severe Leptospirosis is often rapidly progressive and is associated with a case–fatality rate ranging from 1 to 50%. Patients die of septic shock with multiorgan failure and/or severe bleeding complications that most commonly involve the lungs (pulmonary hemorrhage), gastrointestinal tract (melena, haemoptysis), urogenital tract (hematuria), and skin (petechiae, ecchymosis, and bleeding from venipuncture sites).

Other syndromes include (necrotizing) pancreatitis, cholecystitis, skeletal muscle involvement, and rhabdomyolysis with moderately elevated levels of serum creatine kinase. Cardiac involvement is commonly reflected on the electrocardiogram as nonspecific ST- and T-wave changes. Repolarization abnormalities and arrhythmias are considered poor prognostic factors. Rare hematologic complications include hemolysis, thrombotic thrombocytopenic purpura, and haemolytic-uremic syndrome.

DIAGNOSIS

Laboratory results usually show signs of a bacterial infection, including leukocytosis with a left shift and elevated markers of inflammation (C-reactive protein level, procalcitonin level, and erythrocyte sedimentation rate)., a single antibody titer of 1:200–1:800 (depending on whether the case occurs in a low- or high-endemic area) in the microscopic agglutination test (MAT) is required. Preferably, a fourfold or greater rise in titer is detected between acute- and

convalescent-phase serum specimens. Antibodies generally do not reach detectable levels until the second week of illness.

Rapid tests available are lateral flow, (latex) agglutination, or ELISA methodology and are reasonably sensitive and specific, although results reported in the literature vary, probably as a consequence of differences in test interpretation, (re)exposure risks, serovar distribution, and the use of biased serum panels. PCR methodologies, notably real-time PCR, have become increasingly widely implemented. Compared with serology, PCR offers a great advantage, its capacity to confirm the diagnosis of Leptospirosis with a high degree of accuracy during the first 5 days of illness.

TREATMENT :

Severe Leptospirosis should be treated with IV penicillin as soon as the diagnosis is considered. Leptospires are highly susceptible to a broad range of antibiotics, including the β-lactam antibiotics, Cephalosporins, Aminoglycosides, and Macrolides. In mild cases, oral treatment with Doxycycline, Azithromycin, Ampicillin, or Amoxicillin is recommended. In regions where rickettsial diseases are coendemic, Doxycycline or Azithromycin is the drug of choice. Patients with nonoliguric renal dysfunction require aggressive fluid and electrolyte resuscitation to prevent dehydration and precipitation of oliguric renal failure. Peritoneal dialysis or haemodialysis should be provided to patients with oliguric renal failure.

PREVENTION

Measures for controlling Leptospirosis include avoidance of exposure to urine and tissues from infected animals through proper eyewear, footwear, and

other protective equipment. Targeted rodent-control strategies could be considered. Vaccines for agricultural and companion animals are generally available, and their use should be encouraged. The veterinary vaccine used in a given area should contain the serovars known to be present in that area. The efficacy of chemoprophylaxis with Doxycycline (200 mg once a week) or Azithromycin (in pregnant women and children) is being disputed, but focused pre- and postexposure administration is indicated in instances of well-defined short-term exposure[1].

SCRUB TYPHUS

Scrub typhus, tsutsugamushi disease or chigger borne rickettsiosis is an acute febrile illness among humans that is caused by infection with the bacterium *Orientia tsutsugamushi* following the bite of infected mite vectors [58].

The term tsutsugamushi is derived from two Japanese words *tsutsuga* (something small and dangerous) and *mushi* (creature)[59]. This organism was formerly known as *Rickettsia tsutsugamushi*, but then it was found to be different genetically and in cell wall structure and was reclassified as *Orientia*[60].The word ‘typhus‘ has been derived from the Greek word ‘Typos’ for fever which means ‘fever with stupor‘ or smoke [61].

HISTORY

The term ‘akamushi’ from which originates the Japanese term for this rickettsiosis means red chigger [62].Medical accounts of typhus were written as early as 1536 by Cardano and in 1546 by Fracastroin. Coyttarus in 1578 was the

first to suggest that typhoid and 9 typhus were different diseases. The illness was then later described by Hashimoto in 1810.

In 1916 Weil and Felix described the heterophile antibody agglutination of OX – 2 and OX – 19 strains of *Proteus vulgaris* by typhus sera. This was extended to scrub typhus by Fletcher and Lesslar in 1926. They named another agglutinated variant OX – K in honor of their friend Kingbury. The first identification of Scrub typhus was by Nagayo and coworkers in 1930. They called this organism as *Rickettsia orientalis* but this was then renamed as *Rickettsia tsutsugamushi* in 1948 and then finally *Orientia tsutsugamushi* in 1998. Other names for Scrub typhus include chigger borne rickettsiosis, kedani (hairy mite) fever, akamushi (red mite) fever , flood fever, Japanese river fever, tropical typhus and Bush typhus[(61)].

EPIDEMIOLOGY

O. tsutsugamushi is maintained by transovarial transmission in trombiculid mites. After hatching, infected larval mites (chiggers, the only stage that feeds on a host) inoculate organisms into the skin. Infected chiggers are particularly likely to be found in areas of heavy scrub vegetation during the wet season, when mites lay eggs. Scrub typhus is endemic and reemerging in eastern and southern Asia, northern Australia, and islands of the western Pacific and Indian Oceans. Immunity wanes over 1–3 years, and the organism exhibits remarkable antigenic diversity. After an incubation period of 6–21 days, onset is characterized by fever, headache, myalgia, cough, and gastrointestinal symptoms. Some patients recover spontaneously after a few days. The classic case description includes an eschar where the chigger has fed, regional lymphadenopathy, and a maculopapular

rash—signs that are seldom seen in indigenous patients. Severe cases typically manifest with encephalitis and interstitial pneumonia due to vascular injury. The case–fatality rate for untreated classic cases is 7% but would probably be lower if all mild cases were diagnosed [(1).]

DIAGNOSIS & TREATMENT

Serologic assays (indirect fluorescent antibody, indirect immunoperoxidase, and enzyme immunoassays) are the mainstays of laboratory diagnosis. PCR amplification of *Orientia* genes from eschars and blood also is effective. Patients are treated with oral Doxycycline (100 mg twice daily for 7–15 days), Azithromycin (500 mg for 3 days), or Chloramphenicol (500 mg four times daily for 7–15 days)[(1)]

TYPHOID FEVER

HISTORY

Before the 19th century, typhus and typhoid fever thought to be same disease. Many clinical distinctions were proposed,butnone reliably distinguished these syndromes. In 1829 in Paris, P. Ch. A. Louis distinguished typhoid fever from other fevers on thebasis of intestinal lymph node and spleen pathology[(63)]. He described the clinical phenomena of rose spots, intestinal perforation, and haemorrhage**.**

William Jenner in 1850 settled the dispute between typhus and typhoid fever [(63)]. He differentiated typhoid fever based on the pathologic evidence of enlargement of the Peyer's patches and mesenteric lymph nodes. He also noted that prior attacks of typhoid protected against subsequent attacks, this was not the

case in fever due to typhus. In 1869, Wilson proposed the term “Enteric fever”, given the anatomic site of infection[64].

Karl Joseph Eberth(1879) first observed the typhoid bacillus in mesenteric lymph nodes and spleen ; Gaffkey(1884) in Germany isolated the bacillus .Hence,typhoid bacillus was then called *Eberth-Gaffky bacillus* or *Eberthella typhi*[65]

Enteric (typhoid) fever is a systemic disease characterized by fever and abdominal pain and caused by dissemination of *S. Typhi* or *S. Paratyphi*. The disease was initially called typhoid fever because of its clinical similarity to typhus. In the early 1800s, typhoid fever was clearly defined pathologically as a unique illness on the basis of its association with enlarged Peyer’s patches and mesenteric lymph nodes.

EPIDEMIOLOGY

Most commonly, food-borne or waterborne transmission results from fecal contamination by ill or asymptomatic chronic carriers. Sexual transmission between male partners has been described. Health care workers occasionally acquire enteric fever after exposure to infected patients or during processing of clinical specimens and cultures. Worldwide, however, there are an estimated 21–27 million cases of enteric fever, with 200,000–600,000 deaths annually. The annual incidence is highest (>100 cases/100,000 population) in South-Central and Southeast Asia; medium (10–100 cases/100,000) in the rest of Asia, Africa, Latin America, and Oceania (excluding Australia and New Zealand); and low in other parts of the world . A high incidence of enteric fever correlates with poor sanitation and lack of access to clean drinking water. In endemic regions, enteric

fever is more common in urban than rural areas and among young children and adolescents than among other age groups. *S. Typhi* –associated enteric fever reported to the Centre for Disease Control and Prevention in 1999–2010, 82% were associated with recent international travel, most commonly to India, Pakistan, and Bangladesh, and occurred predominantly in young to middle-aged adults. Only 6% of travellers diagnosed with enteric fever had received *S. Typhi* vaccine.

PATHOGENESIS

All Salmonella infections begin with ingestion of organisms, most commonly in contaminated food or water. The infectious dose ranges from 200 colony-forming units (CFU) to 106 CFU, and the ingested dose is an important determinant of incubation period and disease severity. Conditions that decrease either stomach acidity (an age of <1 year, acid suppression therapy, or achlorhydric disease) or intestinal integrity (inflammatory bowel disease, cytotoxic chemotherapy, prior gastrointestinal surgery, or alteration of the intestinal microbiome by antibiotic administration) increase susceptibility to Salmonella infection.

Once *S. Typhi* and *S. Paratyphi* reach the small intestine, they penetrate the mucus layer of the gut and traverse the intestinal layer through phagocytic microfold (M) cells that reside within Peyer's patches. Salmonellae can trigger the formation of membrane ruffles in normally nonphagocytic epithelial cells. These ruffles reach out and enclose adherent bacteria within large vesicles by bacterium-mediated endocytosis. This process is dependent on the direct delivery of Salmonella proteins into the cytoplasm of epithelial cells by the specialized bacterial type III secretion system. These bacterial proteins mediate alterations in the actin cytoskeleton that are required for Salmonella uptake. After crossing the

epithelial layer of the small intestine, *S. Typhi* and *S. Paratyphi*, which cause enteric (typhoid) fever, are phagocytosed by macrophages. These Salmonellae survive the antimicrobial environment of the macrophage by sensing environmental signals that trigger alterations in regulatory systems of the phagocytosed bacteria.

For example, PhoP/PhoQ (the best-characterized regulatory system) triggers the alteration of the outer membrane by increasing the synthesis and transport of different outer-membrane proteins, lipopolysaccharides, and glycerophospholipids, so that the altered bacterial surface can resist microbicidal activities and potentially alter host cell signalling. In addition, salmonellae encode a second type III secretion system that directly delivers bacterial proteins across the phagosome membrane into the macrophage cytoplasm. This secretion system functions to remodel the Salmonella-containing vacuole, promoting bacterial survival and replication.

Once phagocytosed, typhoidal Salmonellae disseminate throughout the body in macrophages via the lymphatics and colonize reticuloendothelial tissues (liver, spleen, lymph nodes, and bone marrow). Patients have relatively few or no signs and symptoms during this initial incubation stage. Signs and symptoms, including fever and abdominal pain, probably result from secretion of cytokines by macrophages and epithelial cells in response to bacterial products that are recognized by innate immune receptors when a critical number of organisms have replicated. Over time, the development of hepatosplenomegaly is likely to be related to the recruitment of mononuclear cells and the development of a specific acquired cell-mediated immune response to *S. Typhi* colonization.

The recruitment of additional mononuclear cells and lymphocytes to Peyer’s patches during the several weeks after initial colonization/infection can

result in marked enlargement and necrosis of the Peyer's patches, which may be mediated by bacterial products that promote cell death as well as the inflammatory response. In the case of *S.Typhi*, many strains produce a toxin, which probably contributes to systemic symptoms as well as the unusual neuropsychiatric states that can be seen in severe typhoidal illness. In contrast to enteric fever, which is characterized by an infiltration of mononuclear cells into the small-bowel mucosa, NTS gastroenteritis is characterized by massive polymorphonuclear leukocyte infiltration into both the large- and small-bowel mucosa. This response appears to depend on the induction of Interleukin 8, a strong neutrophil chemotactic factor, which is secreted by intestinal cells as a result of nontyphoidal Salmonella colonization and translocation of bacterial proteins into host cell cytoplasm. The degranulation and release of toxic substances by neutrophils may result in damage to the intestinal mucosa, causing the inflammatory diarrhoea observed with nontyphoidal gastroenteritis.

CLINICAL COURSE

Enteric fever is a misnomer, in that the hallmark features of this disease—fever and abdominal pain—are variable. While fever is documented at presentation in >75% of cases, abdominal pain is reported in only 30–40%.The incubation period for *S. Typhi* averages 10–14 days but ranges from 5 to 21 days, depending on the inoculum size and the host's health and immune status. The most prominent symptom is prolonged fever (38.8°–40.5°C; 101.8°– 104.9°F), which can continue for up to 4 weeks if untreated.

S. Paratyphi A is thought to cause milder disease than *S. Typhi*, with predominantly gastrointestinal symptoms. However, a prospective study of 669 consecutive cases of enteric fever in Kathmandu, Nepal, found that the infections

caused by these organisms were clinically indistinguishable.Physical findings included coated tongue (51–56%), splenomegaly (5–6%), and abdominal tenderness (4–5%). Early physical findings of enteric fever include rash (“rose spots”; 30%), hepatosplenomegaly (3–6%), epistaxis, and relative bradycardia at the peak of high fever (<50%). Rose spots make up a faint, salmon-colored, blanching, maculopapular rash located primarily on the trunk and chest. The rash is evident in ~30% of patients at the end of the first week and resolves without a trace after 2–5 days. Patients can have two or three crops of lesions, and Salmonella can be cultured from punch biopsies of these lesions.

Gastrointestinal bleeding (10–20%) and intestinal perforation (1–3%) most commonly occur in the third and fourth weeks of illness and result from hyperplasia, ulceration, and necrosis of the ileocecal Peyer’s patches at the initial site of Salmonella infiltration .Neurologic manifestations occur in 2–40% of patients and include meningitis, Guillain-Barré syndrome, neuritis, and neuropsychiatric symptoms (described as “muttering delirium” or “coma vigil”), with picking at bedclothes or imaginary objects.

Rare complications include disseminated intravascular coagulation, haematophagocytic syndrome, pancreatitis, hepatic and splenic abscesses and granulomas, endocarditis, pericarditis, myocarditis, orchitis, hepatitis, glomerulonephritis, pyelonephritis and haemolytic-uremic syndrome, severe pneumonia, arthritis, osteomyelitis, endophthalmitis, and parotitis.

Up to 10% of patients develop mild relapse, usually within 2–3 weeks of fever resolution and in association with the same strain type and susceptibility profile. Up to 10% of untreated patients with typhoid fever excrete *S. Typhi* in the feces for up to 3 months, and 2–5% develop chronic asymptomatic carriage, shedding *S. Typhi* in either urine or stool for >1 year. *S. Typhi* and other

salmonellae are adapted to survive in the gallbladder environment by forming biofilms on gallstones and invading gallbladder epithelial cells.

Chronic carriage is associated with an increased risk of gallbladder cancer, which is much more common in locales where *S. Typhi* is common, such as the Indian subcontinent.

DIAGNOSIS

Because the clinical presentation of enteric fever is relatively nonspecific, the diagnosis needs to be considered in any febrile traveller returning from a developing region, especially the Indian subcontinent, the Philippines, or Latin America. Other than a positive culture, no specific laboratory test is diagnostic for enteric fever.

In 15–25% of cases, leukopenia and neutropenia are detectable. Leukocytosis is more common among children, during the first 10 days of illness, and in cases complicated by intestinal perforation or secondary infection. Other nonspecific laboratory findings include moderately elevated values in liver function tests and muscle enzyme levels.

The definitive diagnosis of enteric fever requires the isolation of *S. Typhi* or *S. Paratyphi* from blood, bone marrow, other sterile sites, rose spots, stool, or intestinal secretions. The classic Widal serologic test for “febrile agglutinins” is simple and rapid but has limited sensitivity and specificity, especially in endemic regions. Rapid point-of-care tests that detect antibodies to outer-membrane proteins or to Vi or O:9 antigen are available for detection of *S. Typhi*; they are moderately sensitive and specific, but their cost and accuracy have limited their routine use in developing countries.

TREATMENT

For treatment of drug-susceptible typhoid fever, Fluoroquinolones are the most effective class of agents, with cure rates of ~98% and relapse and fecal carriage rates of <2%. Experience is most extensive with Ciprofloxacin. Short-course Ofloxacin therapy is similarly successful against infection caused by Quinolone-susceptible strains. However, the 1177 high prevalence of DSC and ciprofloxacin-resistant *S. Typhi* and *S. Paratyphi* on the Indian subcontinent, in Nepal, and in some locales in Africa suggests that Fluoroquinolones should no longer be used for empirical treatment of enteric fever in these regions.

Patients infected with DSC strains of *S. Typhi* or *S. Paratyphi* should be treated with Ceftriaxone or Azithromycin. Alternatively, high-dose ciprofloxacin (750 mg twice daily for 10–14 days) can be used to treat DSC strains but should not be used to treat Ciprofloxacin-resistant enteric fever (MIC, ≥1 μg/mL) because of high failure rates. Ceftriaxone, Cefotaxime, and (oral) Cefixime are effective for treatment of MDR enteric fever, including that caused by DSC and Fluoroquinolone-resistant strains.

Most patients with uncomplicated enteric fever can be managed at home with oral antibiotics and antipyretics. Patients with persistent vomiting, diarrhoea, and/or abdominal distension should be hospitalized and given supportive therapy as well as a parenteral third-generation Cephalosporin or a Fluoroquinolone, depending on the susceptibility profile. Therapy should be administered for at least 10 days or for 5 days after fever resolution.

PREVENTION AND CONTROL

Thus, travelers to developing countries should be advised to monitor their food and water intake carefully and to strongly consider immunization against *S. Typhi.* Two typhoid vaccines are commercially available:

(1) Ty21a, an oral live attenuated S. Typhi vaccine (given on days 1, 3, 5, and 7, with revaccination with a full 4-dose series every 5 years)

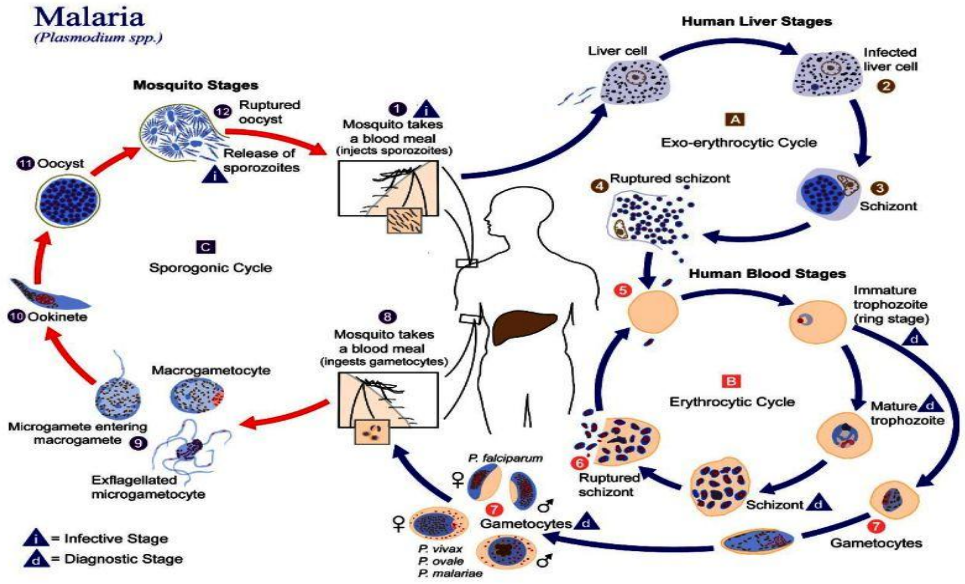
(2) Vi CPS, a parenteral vaccine consisting of purified Vi polysaccharide from the bacterial capsule (given in a single dose, with a booster every 2 years). The old parenteral whole-cell typhoid/paratyphoid A and B vaccine is no longer licensed, largely because of significant side effects, especially fever[(1)]

MALARIA

HISTORY

Human malaria is a febrile illness caused by species belonging to the genus *Plasmodium.* Malaria has always been a major public health concern, probably representing the most important parasitic disease in human.It has been infecting humankind for millennia. Earliest recordings of this disease are available from description of the Chinese and Egyptian civilization between 1700 & 1500 B.C. Recordings can also be found in the Vedic writings of 1600 BC in India. Charaka and Sushrutha gave vivid descriptions of malaria and even associated it with the bite of mosquitoes. Malaria was also a scourge of the western civilization even at the beginning of this century[(66)].Malaria is a protozoan (*Coccidian-Apicomplexa*) disease transmitted by the bite of infected female Anopheles mosquitoes, which breed in fresh water[(67)].

LIFE CYCLE OF MALARIAL PARASITE



ETIOLOGY AND PATHOGENESIS

Six species of the genus Plasmodium cause nearly all malarial infections in humans. These are *P. falciparum*, *P. vivax*, two morphologically identical sympatric species of *P. ovale (curtisi and wallikeri)*, *P. malariae*, and—in Southeast Asia—the monkey malaria parasite *P. knowlesi* . Human infection begins when a female anopheles mosquito inoculates plasmodial sporozoites from its salivary glands during a blood meal .These microscopic motile forms of the malaria parasite are carried rapidly via the bloodstream to the liver, where they invade hepatic parenchymal cells and begin a period of asexual reproduction.

By this amplification process (known as intrahepatic or pre erythrocytic schizogony), a single sporozoite may produce from 10,000 to >30,000 daughter merozoites. The swollen infected liver cells eventually burst, discharging motile merozoites into the bloodstream. These merozoites then invade red blood cells (RBCs) to become trophozoites and multiply six- to twentyfold every 48 h (*P. knowlesi*, 24 h; *P. malariae*, 72 h).

When the parasites reach densities of ~50/μL of blood (~100 million parasites in the blood of an adult), the symptomatic stage of the infection begins. In *P. vivax* and *P. ovale* infections, a proportion of the intrahepatic forms do not divide immediately but remain inert for a period ranging from 2 weeks to ≥1 year. These dormant forms, or hypnozoites, are the cause of the relapses that characterize infection with these species. Attachment of merozoites to erythrocytes is mediated via a complex interaction with several specific erythrocyte surface receptors. *P. falciparum* merozoites bind to erythrocyte binding antigen 175 and glycophorin A.

During the first few hours of intraerythrocytic development, the small "ring forms" of the different malaria species appear similar under light microscopy. As the trophozoites enlarge, species-specific characteristics become evident, malaria pigment (haemozoin) becomes visible, and the parasite assumes an irregular or amoeboid shape. By the end of the intraerythrocytic life cycle, the parasite has consumed two-thirds of the RBC's haemoglobin and has grown to occupy most of the cell. It is now called a schizont. Multiple nuclear divisions have taken place (schizogony). The infected RBC then ruptures to release 6–30 daughter merozoites, each potentially capable of invading a new RBC and repeating the cycle.

The disease in human beings is caused by the direct effects of the asexual parasite—RBC invasion and destruction—and by the host's reaction. Some of the blood-stage parasites develop into morphologically distinct, longer-lived sexual forms (gametocytes) that can transmit malaria. In falciparum malaria, a delay of several asexual cycles precedes this switch to gametocytogenesis. Female gametocytes typically outnumber males by 4:1. After being ingested in the blood meal of a biting female anopheles mosquito, the male and female gametocytes

fuse to form a zygote in the insect's midgut. This zygote matures into an ookinete, which penetrates and encysts in the mosquito's gut wall. The resulting oocyst expands by asexual division until it bursts to liberate myriad motile sporozoites, which then migrate in the hemolymph to the salivary gland of the mosquito to await inoculation into another human at the next feed, thus completing the life cycle.

EPIDEMIOLOGY

Malaria occurs throughout most of the tropical regions of the world.*P. falciparum* predominates in Africa, New Guinea, and Hispaniola (i.e., the Dominican Republic and Haiti); *P. vivax* is more common in Central and South America. The prevalence of these two species is approximately equal on the Indian subcontinent and in eastern Asia and Oceania. *P. malariae* is found in most endemic areas, especially throughout sub-Saharan Africa, but is much less common. *P.ovale* is relatively unusual outside of Africa and, where it is found, comprises <1% of isolates. *P. knowlesi* causes human infections commonly on the island of Borneo and, to a lesser extent, elsewhere in Southeast Asia, where the main hosts, long-tailed and pig-tailed macaques, are found.

CLINICAL FEATURES

The first symptoms of malaria are nonspecific; the lack of a sense of well-being, headache, fatigue, abdominal discomfort, and muscle aches followed by fever are all similar to the symptoms of a minor viral illness. The fever is usually irregular at first (that of falciparum malaria may never become regular). The temperature of nonimmune individuals and children often rises above 40°C (104°F), with accompanying tachycardia and sometimes delirium. Anaemia is common among young children living in areas with stable

transmission,particularly where resistance has compromised the efficacy of antimalarial drugs. Slight enlargement of the liver and spleen is also common, particularly among young children. Mild jaundice is common among adults; it may develop in patients with otherwise uncomplicated malaria and usually resolves over 1–3 weeks.

DIAGNOSIS

When a patient in or from a malaria prevalent area presents with fever, thick and thin blood smears should be prepared and examined immediately to confirm the diagnosis and identify the species of infecting parasite .

DEMONSTRATION OF THE PARASITE

The diagnosis of malaria rests on the demonstration of asexual forms of the parasite in stained peripheral-blood smears. Of the Romanowsky stains, Giemsa at pH 7.2 is preferred; Field's, Wright's, or Leishman's stain can also be used. Staining of parasites with the fluorescent dye Acridine orange allows more rapid diagnosis of malaria in patients with low-level parasitemia. Both thin and thick blood smears should be examined. The thin blood smear should be air-dried, fixed in anhydrous methanol, and stained; the RBCs in the tail of the film should then be examined under oil immersion (×1000 magnification).

The density of parasitemia is expressed as the number of parasitized erythrocytes per 1000 RBCs. The thick blood film should be of uneven thickness. The smear should be dried thoroughly and stained without fixing. As many layers of erythrocytes overlie one another and are lysed during the staining procedure, the thick film has the advantage of concentrating the parasites (by 40- to 100-fold compared with a thin blood film) and thus increasing diagnostic sensitivity. Both

parasites and white blood cells (WBCs) are counted, and the number of parasites per unit volume is calculated from the total leukocyte count.

A minimum of 200 WBCs should be counted under oil immersion. In high-transmission areas, the presence of up to 10,000 parasites/μL of blood may be tolerated without symptoms or signs in partially immune individuals. Thus, in these areas, the detection of low-density malaria parasitemia is sensitive but has low specificity in identifying malaria as the cause of illness. Rapid, simple, sensitive, and specific antibody-based diagnostic stick or card tests that detect P. falciparum–specific, histidine-rich protein 2 (PfHRP2), lactate dehydrogenase, or aldolase antigens in finger-prick blood samples are now being used widely in control programs .

Molecular diagnosis by polymerase chain reaction (PCR) amplification of parasite nucleic acid is more sensitive than microscopy or rapid diagnostic tests for detecting malaria parasites and defining malarial species. While currently impractical in the standard clinical setting, PCR is used in reference centre in endemic areas. Serologic diagnosis with either indirect fluorescent antibody or enzyme-linked immunosorbent assays is useful for screening of prospective blood donors and may prove useful as a measure of transmission intensity in future epidemiologic studies.

TREATMENT

Patients with severe malaria and those unable to take oral drugs should receive parenteral antimalarial therapy immediately . The World Health Organization (WHO) recommends artemisinin- based combination therapy (ACT) as first-line treatment for uncomplicated falciparum malaria in malaria-endemic areas. ACT is also the recommended first-line treatment for *P. knowlesi* infections

and is highly effective against the other malarias as wellfrom other malaria-endemic regions[1].

INTERLEUKIN-6

- Multifunctional cytokine belonging to IL-6 family
- Human IL-6 consists of 184 amino acids with 2 potential N-glycosylation sites and cysteine residues
- It is produced by various cells such as T cells,B cells,monocytes,endothelial cells,fibroblasts,mesangial cells,keratinocytes,several tumour cells,astrocytes,bone marrow stroma cells.
- IL-6 receptors exists in 2 forms- a soluble IL-6 receptor(s IL-6 R) and a membrane bound IL-6 receptor(m IL-6 R).
- IL-6 trans-signalling is mediated through s IL-6R by activating cells that express gp130.
- Classic signalling is mediated through m IL-6R.

MECHANISM OF ACTION

- IL-6 on binding IL-6 R results in either homo or heterodimerization of gp130 subunit and leads to the formation of IL-6/gp 130 complex.
- This complex in turn activates Janus tyrosine kinase/signal transducer and activator of transcription pathway(JAK-STAT Pathway)
- IL-6 has various pleiotropic functions, of which salient ones are as follows-
  - ✓ B cells-Immunoglobulin production
  - ✓ T cells – proliferation and differentiation
  - ✓ Hematopoietic progenitor cells-enhancement of multipotential hematopoietic colony formation.

- ✓ Hepatocytes- acute phase protein synthesis
- ✓ Blood vessels-proliferation of vascular smooth muscle cells.
- ✓ Bone metabolism-stimulation of osteoclast formation and induction of bone resorption.
- ✓ Heart muscle cells-negative ionotrophic effect on heart
- ✓ Placenta-secretion of chorionic gonadotropin from trophoblasts[68]

- IL-6 and acute phase response- Acute phase response is the response exhibited by the organism to disturbances in homeostasis resulting from infection,tissue damage,immunological disorders or any neoplastic growth,trauma or surgery[69]
- IL-6 and CRP- IL 6 is the main mediator stimulating CRP production,but other cytokines like IL-1 and TNF are also involved.

MATERIALS & METHODS

MATERIALS AND METHODOLOGY

ETHICAL CONSIDERATION

The study was conducted after obtaining approval from the Institutional Ethical Committee of Madras Medical College, RGGGH, Chennai. Informed Consent was obtained from the patients before their Participation in the study.

STUDY PERIOD

One Year from March 2018 to February 2019.

STUDY SETTING

Institute of Microbiology, Madras Medical College in association with Institute of Internal Medicine and hospitals attached to Madras Medical College, Rajiv Gandhi Government General Hospital, Chennai-3.

STUDY DESIGN

Prospective study

STUDY GROUP

250 patients with symptoms of fever

INCLUSION CRITERIA

Patients presenting with 1-15 days of fever

EXCLUSION CRITERIA

Patients presenting with more than 15 days of fever and those who have not given consent to participate

SPECIMEN COLLECTION:

Under aseptic precautions, samples were collected from the patients presenting with fever.

1.Blood & Serum

Preparation of site :

1. Peripheral vein to be drawn was chosen and disinfected using 70% alcohol.
2. Skin over the venipuncture site was cleansed with 70 % alcohol in a circular fashion, approximately 5 cm in diameter , rubbed vigorously and allowed to air-dry.
3. Starting in the centre of the circle , 2% tincture of iodine was applied in ever-widening circles until the entire circle has been saturated with iodine, it was then allowed to dry for 1minute.
4. Sterile needle was inserted into the vein and 10ml of blood sample was collected in adult patients, and in children according to the body weight , transferred to 50 ml of BHI broth, making 1: 5 or 1:10 dilution of blood in broth.
5. After the sample was collected , the site should be cleansed again with 70% alcohol.

Time of collection :

Blood was collected from patients during febrile episodes, and before the antibiotic therapy was initiated.

SAMPLE PROCESSING :

Incubation Conditions :

Blood culture bottles was incubated aerobically at 37ºC for 18-24 hours. All the blood culture bottles were examined for evidence of growth (hemolysis , turbidity) during 6 - 18 hours of incubation. Blind subcultures were done on Nutrient agar plate, Mac Conkey agar plate,5% Sheep Blood agar plate, after 24 hours of incubation .Then further subcultures were done after 48 hours, 72 hours and 1 week of incubation.

DENGUE ANTIBODY ELISA REQUIREMENTS

1. Anti-human IgM / IgG coated microwells (Assay plate)
2. Dengue 1-4 antigens (Recombinant)
3. Wash buffer concentrate-20X concentrate of phosphate buffered saline (PBS) ,pH 7.2-7.6 with Tween 20 and 0.1% proclin as preservative.
4. Serum diluent-Tris buffered saline with preservatives and additives.
5. Antigen diluent- PBS with preservative and 0.005% gentamycin.
6. Horse Radish Peroxidase(HRP) conjugated Monoclonal Antibody Tracer
7. Tetramethyl benzidine (TMB)- 3,3',5,5'-the substrate, tetramethyl benzidine, hydrogen peroxide in a citric-acid citrate buffer (pH 3.5-3.8)
8. Positive control serum,Negative control serum, and cut-off calibrator - Human serum with 0.1 % sodium azide and 0.005% Gentamycin sulphate.
9. Stop solution-1Mole Phosphoric acid.

DENGUE IgM CAPTURE ELISA PROCEDURE

Serum predilution

1. The microwells are inserted into the strip holder. 5 microwells arerequired for positive control (PC), negative control(NC) and cut-off calibrator (CO) in triplicate.
2. The PC,NC& CO & patient samples are diluted using suitable test tubes or microtitre plate.
3. 1000 µl or 1ml of serum diluent is added to 10µl of serum and mixed well.

ELISA procedure

1. Antigen is diluted 1/250 using the antigen diluent. ie, 10µl of antigen + 2.5 ml of antigen diluent. A volume of 0.5 ml of diluted antigen is required per strip.
2. Required volume of diluted antigen is mixed with equal volume of MAb tracer (Horse Radish Peroxidase conjugated Monoclonal antibody tracer) in a test tube and kept at room temperature (20- 25˚C) until required.
3. 100µl of diluted patient sample and controls (one positive control, one negative control and three cut-off calibrators) are pipetted into their respective microwells of the assay plate.
4. The plate is covered and incubated for 1 hour at 37˚C.
5. After incubation , the plate is washed 6 times with diluted wash buffer.
6. The antigen- MAb tracer solution is mixed well and 100µl is transferred to microtitre wells.
7. The plate is covered and incubated for 1 hour at 37˚ C.
8. The plates are washed 6 times with diluted wash buffer after incubation.

9. 100µl of TMB(Tetra methyl benzidine) is pipetted into each well and a blue colour develops. The plate is incubated for 10 min at room temperature.
10. At the end of 10min, 100µl of stop solution is pipetted into all wells. The blue colour will change into yellow.
11. The absorbance of each well is read at a wavelength of 450nm with a reference filter of 600-650nm, using a dual wavelength spectrophotometer.

Calculations

- The cut-off value was determined by calculating the average absorbance of the triplicate of the cut-off calibrator.
- The index value was calculated by dividing the sample absorbance by the cut-off value.
- Panbio units can be calculated by multiplying the index value by 10.

Index value = Sample absorbance/cut-off value

Panbio units= Index value x 10.

Test validity:

Calibrator mean ≥ 1.5 x Negative absorbance.

Positive control/cut-off= 1.1-6.0

Negative control < 0.350

INTERPRETATION OF RESULTS

INDEX	PANBIO UNITS	RESULTS
<0.9	<9	Negative
0.9-1.1	9-11	Equivocal
>1.1	>11	Positive

Sensitivity of this test is 94.7%, Specificity is 100%.

LEPTOSPIROSIS

- MEDIUM- EMJH (Ellinghausen – Mccullough – Johnson – Harris) medium was used for subculturing the organism for maintenance and antigen preparation.
- MACROSCOPIC SLIDE AGGLUTINATION TEST (MSAT)

A rapid macroscopic slide agglutination test can be used to screen serum samples. These tests are carried out with a dense suspension of leptospires, which agglutinate into clumps visible to the naked eye. The best method is Galton's macroscopic slide agglutination test, in which 12 antigens were originally proposed, and later supplementary antigens were suggested MSAT [(70)]is found to be a simple, rapid, and sensitive diagnostic test for active Leptospirosis; the sensitivity of the test can be improved by the addition of locally prevalent serovars[(71).] This test is slightly less specific than MAT, but it gives a positive reaction earlier in disease.

PROCEDURE

- 8µl of PBS was added to all the depressions of the slide
- Then 11µl of the prepared antigen was added to all the depressions of the slide
- Negative serum added with antigen and PBS was used as negative control
- Positive serum added with antigen and PBS was used as positive control
- The last depression containing saline and antigen was used as antigen control
- 4ml of patients serum was added to the depressions in the slide
- The slide was placed in a rotator (180rpm) for 8 minutes
- The slide was viewed macroscopically for the presence of any agglutination clumps and was confirmed in DFM

Interpretation of results

1.Clumps of agglutination with complete clearing of Leptospiral antigen	4+
2.Obvious Agglutination with partial clearing of antigen suspension	3+
3. 50% agglutination	2+
4. 25% agglutination	1+

No agglutination and uniformity of serum antigen mixture-Negative

SCRUB TYPHUS IgM ELISA

TEST PROCEDURE:

Bring all kit reagents and specimens to room temperature (25ºc) before use.Thorughly mix the reagents and samples before use by gentle invasion.

Assay Procedure:

1) Determine number of sera to be tested.
2) Organize sera according to the "Example for Sera application" provided below or any preferred arrangement dilutions can be made either in tubes or in ELISA-type plastic wells
3) Dilute test sera to 1/100 by using the provided Sample dilution buffer for scrub typhus.
4) Apply 100µL per well of the 1/100 diluted test sera and controls to marked scrub typhus ELISA plate.
5) Cover the plate with parafilm or plate covers just on the well opening surface, so the bottom of the plate is not covered.
6) After the incubation is complete, wash the strips six times with the 1x wash buffer using an automatic plate washer. Use 300µL per well of 1x wash buffer in each wash cycle for all plate washing.

7) Add 100µl per well of ready to use enzyme-HRP conjugate for scrub typhus IgM into all wells by multi-channel pipettor.
8) Cover the plate with parafilm just on the well opening surface, so the bottom of the plate is not covered
9) Incubate the plate at 37ºc for 30 minutes in an incubator.
10) After the incubation, wash the plate 6 times with an automatic plate washer using 1x wash buffer, 300µl per well.
11) Add 150µL per well of Enwash into all wells by a multi channel pipettor.
12) Incubate the plate at room temperature for 5 minutes without any cover on the plate.
13) After the incubation, wash the plate 6 times with an automatic plate washer using 1x wash buffer, 300µL per well.
14) Add 100µL per well of liquid TMB substrate into all wells by multichannel pipettor.
15) Incubate the plate at room temperature (20-25ºc) in a dark place for 10 minutes without any cover on the plate.
16) After the incubation ,add 50µL per well off stop solution into all wells by multi-channel pipettor and incubate at room temperature (20-25ºc) for 1 minute without any cover on the plate.
17) After the incubation, read the optical density at 450nm with a Microtiter plate reader.

ENTERIC FEVER

IDENTIFICATION OF *SALMONELLA* :[72,73]

COLONY MORPHOLOGY :

On Nutrient agar plate colonies of *Salmonella species* were large 2- 3 mm , moist, translucent, low convex, discrete colonies with smooth surface with entire edges.

On Blood agar, *Salmonella species* form moist greyish non haemolytic colonies and on MacConkey agar plate produce lactose non fermenting colonies.

Colonies morphologically resembling Salmonella species were subjected to preliminary test- Gram stain , Motility by Hanging drop method, Catalase and Oxidase test.

GRAM STAIN :

Salmonella was gram negative bacilli measuring approximately 2-4 x 0.6 µm, uniformly stained with parallel sides and rounded ends, non capsulated, non-sporing.

Presumptive identification of the isolates were done using standard biochemical tests such as Hugh Leifson's oxidative fermentative test, Nitrate reduction test, Indole production, Methyl red and Voges Proskaeur reaction, Citrate utilization ,Urease production, Phenylpyruvic acid test, 1 % carbohydrate fermentation test for Glucose, Lactose, Xylose, Arabinose andMueller's Decarboxylation test [Table 3,4].

SLIDE AGGLUTINATION TEST :[(72)]

Confirmation of the isolates were done by Slide agglutination test using specific antisera- Polyvalent 'O' antisera, and *Salmonella Typhi* 'H' ,*Salmonella Paratyphi* 'AH' and 'BH'

Procedure :

1) A sterile, grease free glass slide was taken and an identification linewas drawn in the upper surface of the slide, and two circles measuring 2 x 1 cm were drawn underneath, and labelled as Control and Test.

2) Using a sterile inoculating loop portion of pure growth from a fresh subculture in a non-selective medium (Nutrient agar plate) was taken and emulsified in a drop of physiological saline (20 µL) and mixed thoroughly in a 'Control' ring.

3) Rocked the slide back and forth and observed for any autoagglutination under a bright light and over a black background .

4) The saline suspension was carefully examined to ensure that it is even and does not show any clumping . If still autoagglutination occurs ,the culture is cannot be serotyped.

5) Test was further proceeded if there is no autoagglutination .

6) Emulsified a portion of pure growth in a drop of physiological saline in 'Test' ring and a drop of (equal volume) of Polyvalent 'O' antisera was added and mixed well.

7) Tilt the slide back and forth and observed for agglutination .Clumping was seen within 30 seconds to 1 minute, if the reaction was positive, .

8) Similarly the test was proceeded for flagellar antigens , using polyvalent 'H' antisera for *S.Typhi* isolates, 'AH' for *S.Paratyphi* A and 'BH' for *S.Paratyphi B.*

ANTIBIOTIC SUSCEPTIBILITY TESTING :[73]

KIRBY-BAUER DISC DIFFUSION METHOD :

Antibiotic susceptibility testing of the isolates was done by KirbyBauer disc diffusion method according to Clinical Laboratory Standards Institute (CLSI

-2019) guidelines for the following drugs - Ampicillin (10 µg), Chloramphenicol (30µg), Cotrimoxazo (1.25/23.75 µg),Ciprofloxacin (5µg), Nalidixic acid(30 µg),Pefloxacin(5 µg),Cefotaxime (30 µg),Ceftriaxone (30 µg), Azithromycin(15 µg).

3-4 well isolated , morphologically similar colonies were taken with a sterile loop and inoculated into peptone water and incubated at 370 C for 2 hours. Turbidity was adjusted to 0.5 McFarland standards and a lawn culture was made on Muller-Hinton agar and appropriate antibiotic discs were placed. Plates were incubated at 370 C for 16-18 hours.The zones of inhibition were measured and interpreted according to CLSI 2019guidelines-M100 document. Quality control was done using ATCC E.coli 25922 strain[(74)].

TABLE : KIRBY-BAUER DISC DIFFUSION METHOD

ANTIBIOTIC	DISK CONTENT µg	Diameter of zone of inhibition (mm)		
		Susceptible	Intermediate	Resistant
Ampicillin	10	≥17	14-16	≤13
Chloramphenicol	30	≥18	13-17	≤12
Cotrimoxazole	1.25/23.75	≥16	11-15	≤10
Nalidixic acid	30	≥19	14-18	≤13
Ciprofloxacin	5	≥31	21-30	≤20
Pefloxacin	5	≥24	-	≤23
Cefotaxime	30	≥26	23-25	≤22
Ceftriaxone	30	≥23	20-22	≤19
Azithromycin	15	≥13	-	≤12

DETECTION METHODS AND POSITIVITY RATE DURING DIFFERENT STAGE OF ILLNESS

STAGE OF ILLNESS	METHODS	RESULTS (%Positivity)
1st week	Blood culture	95
2nd week	Blood culture	40-50
	Widal test	Low antibody titre
3rd week	Blood culture	15-20
	Stool and Urine culture	80
	Widal test	100
4th week	Blood culture	5-10
	Stool and Urine culture	90
	Widal test	100

BIOCHEMICAL REACTIONS [73]

Salmonella enterica subspecies enterica can be phenotypically identified by the following biochemical reactions include

1. Fermentation of glucose, maltose, mannitol and sorbitol with the production of acid and gas.(*S.Typhi, Gallinarium*-anaerogenic).
2. Absence of fermentation of sucrose, lactose, salicin, and adonitol.
3. Failure to produce indole, hydrolyse urea, deaminate phenylalanine.
4. Positive methyl red reaction and a negative Voges-Proskauer reaction

BIOCHEMICAL REACTIONS OF *Salmonella enterica subspecies enterica* (72,73)

BIOCHEMICAL REACTIONS	INTERPRETATION
Cytochrome oxidase	Negative
Catalase	Positive
Nitrate reduction	Reduces nitrates to nitrites
Phenylalanine deaminase test	Fails to deaminate phenylalanine
Hugh Leifson's OF media	Shows both oxidative and fermentative pattern
Fermentation of glucose	Produces acid only or acid and gas
KCN	Sensitive
Indole	Not produced
Methyl red	Positive
Voges proskauer	Acetoin not produced
Simmon's citrate	Utilized
Urease	Not produced
Triple Sugar Iron (TSI)	Alkaline/Acid with speck of H2S-S.Typhi Alkaline/acid with gas and no H2S- S.Paratyphi A Alkaline/acid with plenty of H2S- S.Paratyphi B

BIOCHEMICAL DIFFERENCES BETWEEN *S.Typhi* and *S.Paratyphi A*

Biochemical Test	*S.Typhi*	*S.Paratyphi A*
Glucose fermentation	Production of acid only	Acid with gas
Xylose fermentation	±	-
Arabinose fermentation	-	+
Dulcitol fermentation	-	+
Rhamnose fermentation	-	+
d-tartarate	Acid only	Does not ferment
Lysine	+	_
Arginine	+	+
Ornithine	-	+

IL- 6 ELISA (DIACLONE)

PROCEDURE :

1) Add 100µl of each sample, control and zero (Standard dilution) in duplicate to appropriate number of wells
2) Add 50µl of diluted biotinylated anti- IL-6 to all wells
3) Cover with a plastic plate cover and incubate at room temperature (18 to 25ºc) for 1 hour
4) Remove the cover and wash the plate as follows :
    a. Aspirate the liquid from each well
    b. Dispense 0.3ml of 1x washing solution into each well
    c. Aspirate the contents of each well
    d. Repeat step b and c another two times
5) Add 100µl of Streptavidin- HRP solution into all wells
6) Cover with a plastic plate cover and incubate at room temperature (18 to 25ºc) for 30 minutes
7) Repeat wash step 5
8) Add 100µl of ready-to-use TMB substrate solution into all wells
9) Incubate in the dark for 12-15minutes at room temperature. Avoid direct exposure to light by wrapping the plate in aluminium foil.
10) Add 100µl of H_2SO_4 : Stop reagent into all wells

RESULTS

RESULTS

TOTAL NUMBER OF FEVER CASES TAKEN UP FOR STUDY-250

TABLE-1 : AETIOLOGICAL CAUSES OF FEVER (n=250)

INFECTIONS	NUMBER OF POSITIVES	PERCENTAGE (%)
Dengue	**47**	**18.8**
Leptospirosis	**31**	**12.4**
Scrub typhus	**26**	**10.4**
Enteric fever	**9**	**3.6**

From the above table it is evident that among infectious diseases the commonest cause of fever was found to be Dengue followed by Leptospirosis, Scrub typhus, Enteric fever. The other causes of fever were three cases of Malaria,and few cases of Pneumonia, Bacteremia, Urinary tract infection, and undiagnosed causes of fever.

Statistically significant with a p value of < 0.001

TABLE-2A : GENDER DISTRIBUTION OF FEVER CASES(n=250)

Gender	No of patients (n= 250)	Percentage (%)
Male	157	62.8
Female	93	37.2

The above table shows a increased distribution of male preponderance**.**

TABLE- 2 B : GENDER DISTRIBUTION OF FEVER CASES (n = 113)

INFECTIONS	No of males affected	No of females affected
DENGUE(n=47)	**28 (59.5%)**	**19 (40.4%)**
LEPTOSPIROSIS(n=31)	**21(67.7%)**	**10(32.2%)**
SCRUB TYPHUS(n=26)	**18(69.2%)**	**8 (30.7%)**
ENTERIC FEVER(n=9)	**7 (77.7%)**	**2 (22.2%)**

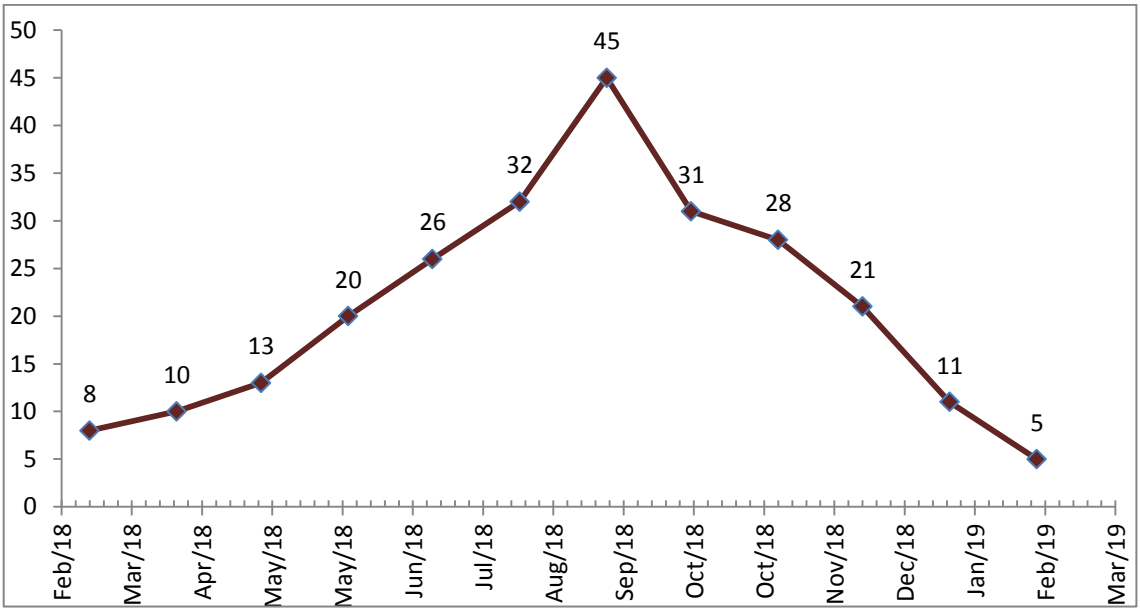
The above table shows that all the positive cases also showed a male preponderance

TABLE-3: AGE-WISE DISTRIBUTION OF FEVER CASES (n =113)

INFECTIONS	**<15yrs**	**16-25yrs**	**26-40yrs**	**41-60yrs**	**>60yrs**
DENGUE(n=47)	**5**	**9**	**20**	**9**	**4**
LEPTOSPIROSIS (n=31)	**3**	**7**	**14**	**6**	**1**
SCRUB TYPHUS (n=26)	**3**	**5**	**11**	**5**	**2**
ENTERIC FEVER (n=9)	**2**	**1**	**4**	**1**	**1**

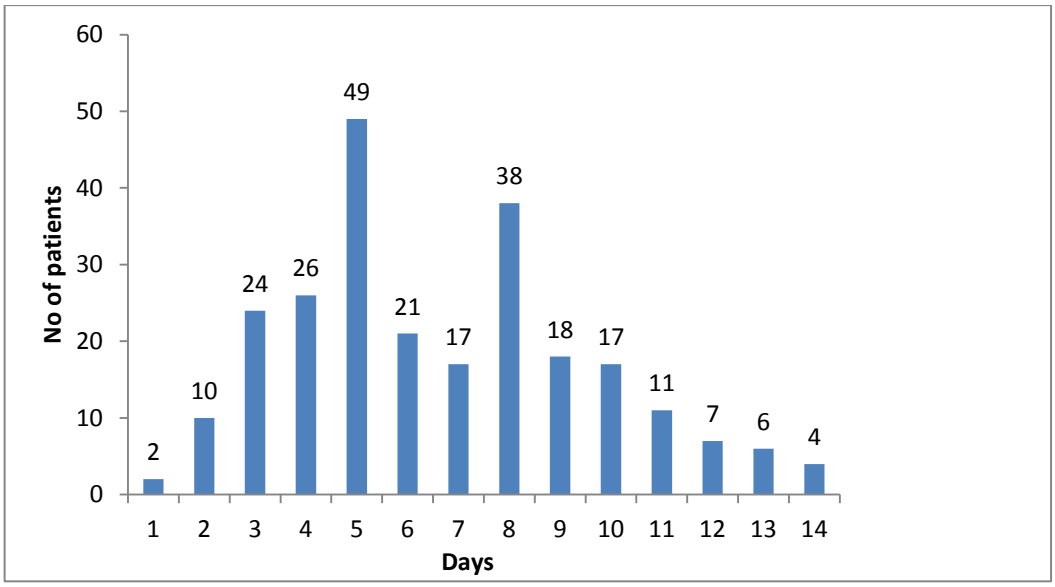
From the above table, it is evident that majority of the fever cases fall betweenthe age group of 21-40 yrs

FIGURE 1- MONTH WISE DISTRIBUTION OF CASES (n=250)



The above graph shows that most of the fever cases taken up for the study presented during the month of October

FIGURE 2 : DURATION OF FEVER CASES (n= 250)



From the above chart, it is evident that most of the fever cases presented during the period of 5 – 10 days

TABLE 4 – DISTRIBUTION OF CASES IN MIXED INFECTIONS & THEIR OUTCOME (n= 15)

Mixed Infection	Dengue & Leptospirosis	Dengue & Scrub typhus
No of cases	9	6
Cases recovered	8	2
Cases expired	1	4

Among the 15 mixed infections, 9 cases presented with Dengue and Leptospirosis & 6 cases presented with Dengue and Scrub typhus. 5 cases expired , out of which 4 were Dengue and Scrub typhus and 1 case was with Dengue and Leptospirosis.

FIGURE 3 – DISTRIBUTION OF CASES IN MIXED INFECTIONS (n = 15)

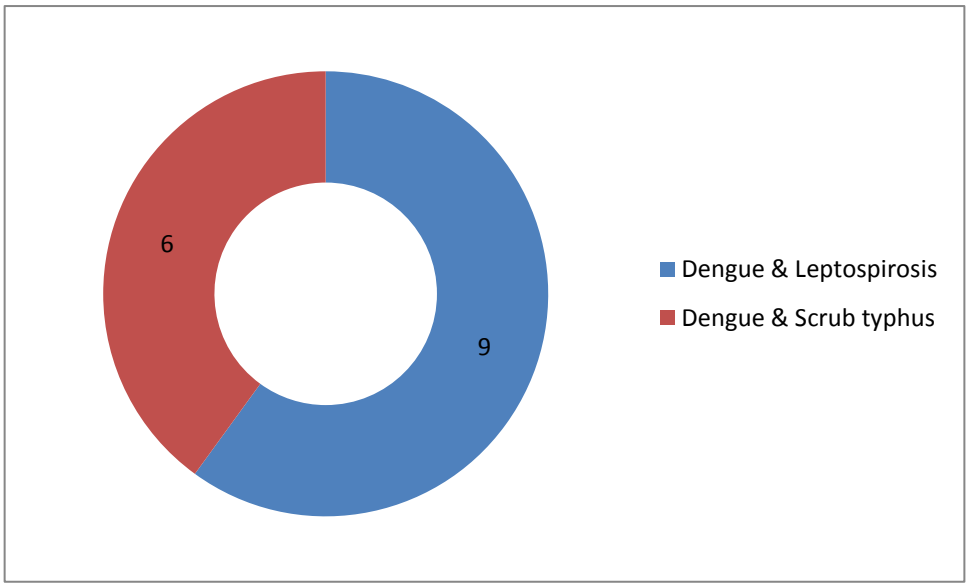


FIGURE 4 – SEX DISTRIBUTION OF DENGUE CASES

(n = 47)

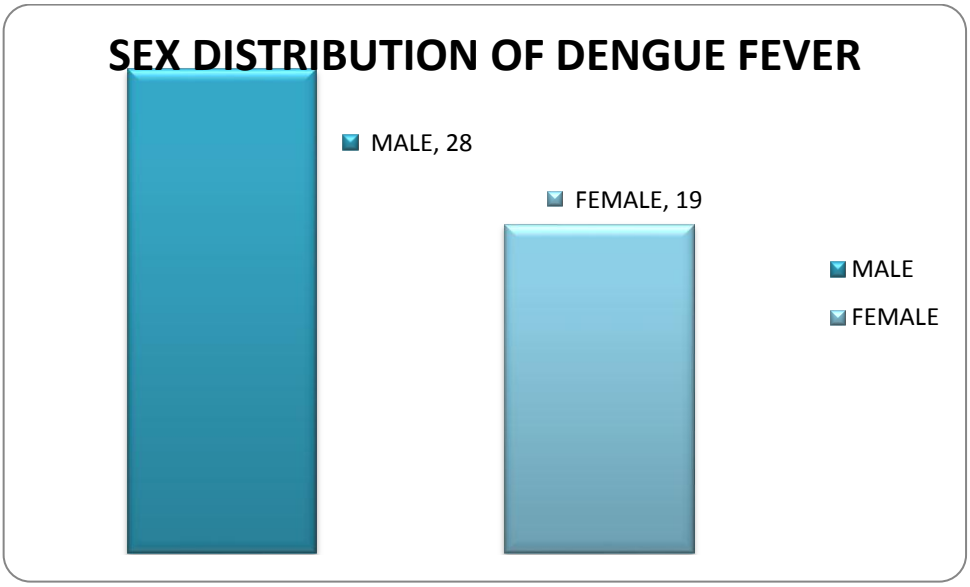


TABLE-5: DISTRIBUTION OF SYMPTOMS IN DENGUE CASES (n=47)

SYMPTOMS	NO OF PATIENTS	PERCENTAGE (%)
FEVER	47	100
MYALGIA	39	82.9
RASHES	19	40.4
HAEMORRHAGIC MANIFESTATIONS	21	44.6
GI SYMPTOMS	17	36.1
HEPATOMEGALY	12	25.5
RETRO – ORBITAL PAIN	7	14.8

All the Dengue positive cases presented with fever followed by myalgia, haemorrhagic manifestations, rashes, Gastrointestinal symptoms, hepatomegaly and retro orbital pain.

TABLE-6 : PLATELET COUNT IN DENGUE CASES (n=47)

PLATELET COUNT (lakh /cu.mm))	TOTAL CASES	PERCENTAGE (%)
<20000	5	10.6
21000-40000	9	19.1
41000-50000	5	10.6
50000-100000	19	40.4
>1 lakh	9	19.1

The above table shows most of the Dengue positive cases had a platelet count range between 50,000 – 1 lakh/ cu.mm

TABLE-7 : DISTRIBUTION OF HAEMORRHAGIC MANIFESTATIONS IN DENGUE CASES (n=47)

SYMPTOMS	NUMBER OF CASES	PERCENTAGE
BLEEDING GUMS	8	17
PETECHIAE	5	10.6
HAEMATEMESIS	3	6.4
MELENA	2	4.3
EPISTAXIS	2	4.3
VAGINAL BLEEDING	1	2.1

From the above table, it is evident that most common haemorrhagic manifestation was bleeding gums, followed by petechiae , hematemesis, melena, epistaxis and vaginal bleeding.

TABLE-8: ULTRASOUND FINDINGS IN DENGUE CASES

Category	Normal %	GB thickening %	Pleural effusion %	Ascites %	Hepatomegaly %
Dengue with/without warning signs (33)	17 (51.1%)	7 (21.2%)	4 (12.1%)	3 (9%)	3 (9%)
Severe Dengue (14)	2 (14.2%)	5 (35.7%)	3 (21.4%)	1 (7.1%)	3 (21.4%)

The above table shows that gall bladder wall thickening was the most common ultrasound finding in Dengue patients.

TABLE-9 :CASE FATALITY RATE(CFR) IN DENGUE CASES

Dengue positive cases	Number of deaths	CFR
47	1	2.1 %

Range: 1-9% (Based on Odds Ratio)

FIGURE 5 :CASE FATALITY RATE IN DENGUE

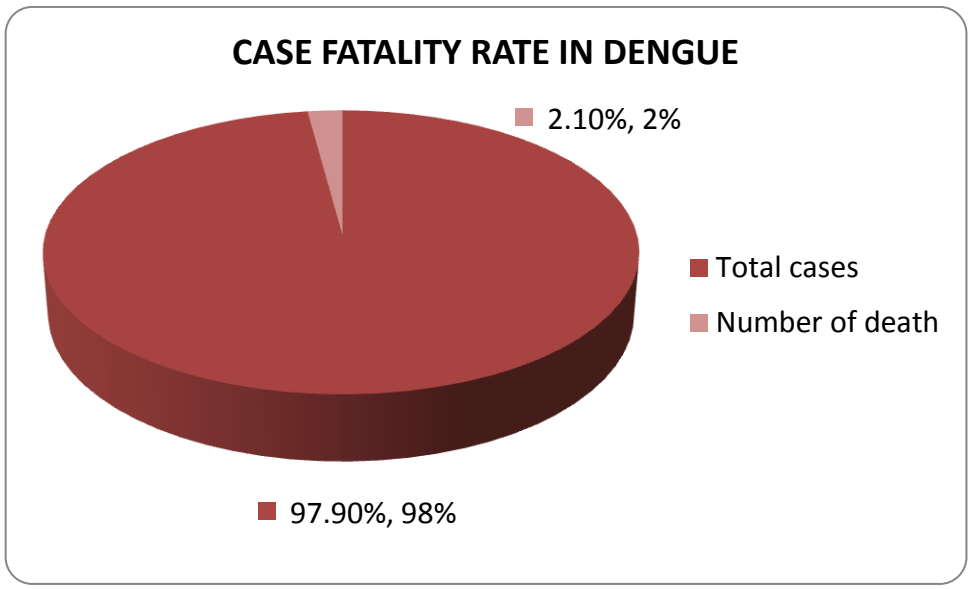


TABLE-10:CLINICAL PRESENTATION OF FATAL CASES

S. No	Age/Sex	Underlying condition	Presentation of symptoms	Diagnosis	Hospital stay	Cause of death
1	29/M	Alcoholic	Fever,bleeding gums,melena	DSS/Leptospirosis	4	Septic shock with acute pulmonary edema
2	F/21	Nil	Fever, Hemetemesis, Renal failure, Peritoneal dialysis	DSS/Scrub typhus	3	Profound shock, HF, ARF, brainstem dysfunction, ICH, CardioPulmonary arrest
3	23/F	Antenatal	Fever, Pallor, Rashes, Dyspnea, Peripheral cyanosis, Purpura	DSS/Scrub typhus	4	Profound shock, Cardiopulmonary arrest.
4	32/F	Nil	High grade fever*5days, vomiting, abdominal pain	DSS/Scrub typhus	4	ARDS/ Pulmonary oedema
5	65/M	Renal failure ,on haemodialysis	Fever*4days, breathlessness, abdominal pain	Dengue hemmorrhagic fever/ SHTN/ Type II-DM	3	Acute pulmonary oedema/ Bronchopneumonia
6	48/F	Nil	Fever*5days, bleeding gums	DSS	5	Cardiopulmonary arrest

TABLE- 11 : CLASSIFICATION OF DENGUE CASES BASED ON WHO GUIDELINES (n= 47)

CLASSIFICATION OF DENGUE CASES	No of cases	Percentage (%)
DENGUE WITH/WITHOUT WARNING SIGNS*	33	70.2
SEVERE DENGUE$^{\infty}$	14	29.8

*Warning signs- Abdominal pain/tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleed, lethargy and restlessness, liver enlargement >2cm, increase in hematocrit with rapid decrease in platelet count

∞Severe Dengue-Shock, fluid accumulation with respiratory distress, severe bleeding, AST/ALT ≥1000, Impaired consciousness

FIGURE6 : PERCENTAGE OF BLOOD TRANSFUSION IN DENGUE CASES

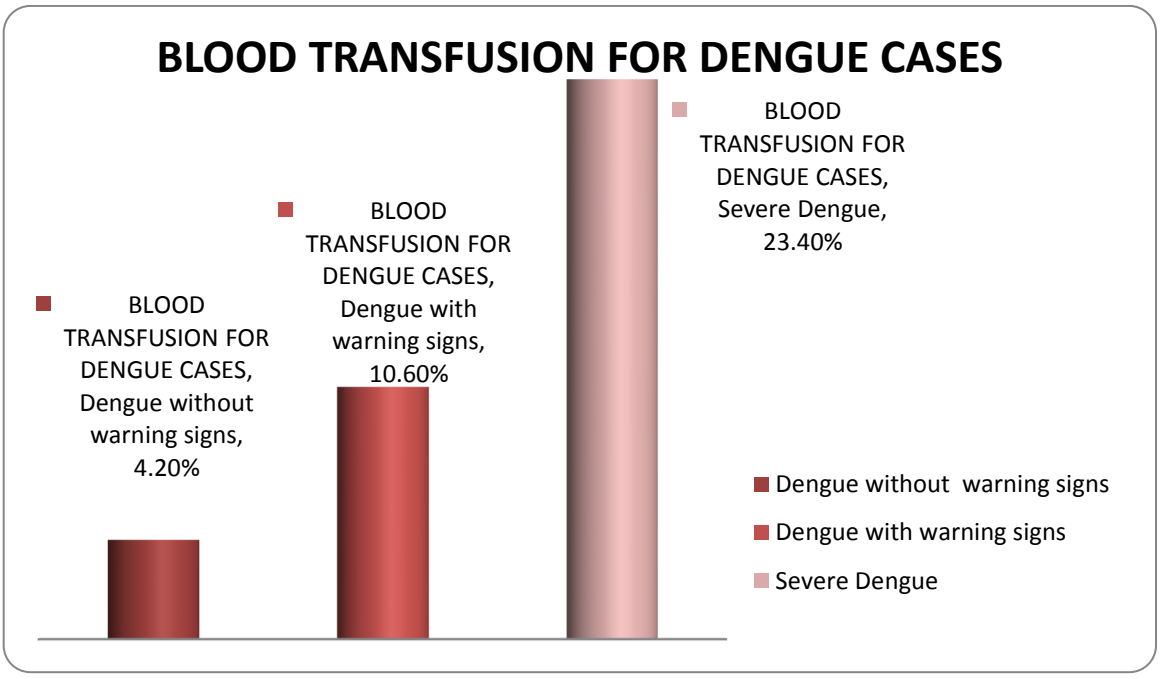


TABLE-12:DISTRIBUTION OF SYMPTOMS IN CASES WITH LEPTOSPIROSIS(n = 31)

SYMPTOMS	NUMBER	PERCENTAGE (%)
Fever	31	100
Myalgia	21	67.7
Conjunctival suffusion	17	54.8
Jaundice	13	41.9
CNS dysfunction	4	12.9
Renal failure	3	9.7

The above table shows most common presenting feature in Leptospirosis is fever followed by myalgia, conjunctival suffusion, jaundice, CNS dysfunction, Renal failure.

TABLE- 13 : LABORATORY PARAMETERS IN PATIENTS WITH LEPTOSPIROSIS (n=31)

INVESTIGATIONS	NO OF CASES	PERCENTAGE
ELEVATION OF ESR	19(20-50mm/hr) 11 (>50mm/hr)	61.3 35.4
ABNORMAL LFT	23	74.2
THROMBOCYTOPENIA	16	51.6
ABNORMAL RFT	9	29
ABNORMAL RFT AND LFT	8	25.9

From the above table, it is evident that abnormal liver function tests are more common than the abnormal renal function tests. In 25.9% of the cases both renal and liver function tests abnormalities were seen.

TABLE-14: RENAL FUNCTION TESTS IN LEPTOSPIROSIS(n = 31)

Renal parameters	Range	No of cases(n=31)	Percentage (%)
Creatinine mg/dl	<1.5	22	71
	1.5 -2.0	4	12.9
	2.0 – 2.5	2	6.4
	2.5 – 3.0	1	3.2
	>3.0	2	6.4
Urea mg/dl	20 -40	22	71
	40 – 50	5	16.1
	50 – 100	2	6.4
	>100	2	6.4

The above table shows that most of the Leptospirosis positive patients presented with increased urea and creatinine levels

TABLE- 15 : CORRELATION OF INCREASED RENAL PARAMETERS WITH PLATELET COUNT (n = 31)

Parameters	Platelet count	No. of cases (n=31)	Percentage (%)
Increased Blood Urea and Serum Creatinine	< 1,50,000	26	23.8
	1,50,000 – 2,50,000	5	16.1

The above table shows that most of the patients who had raised blood urea and creatinine levels presented with a platelet count range of <1,50,000lakh/cu.mm

FIGURE 7 : DISTRIBUTION OF CASES IN CO-INFECTIONS WITH LEPTOSPIROSIS (n=31)

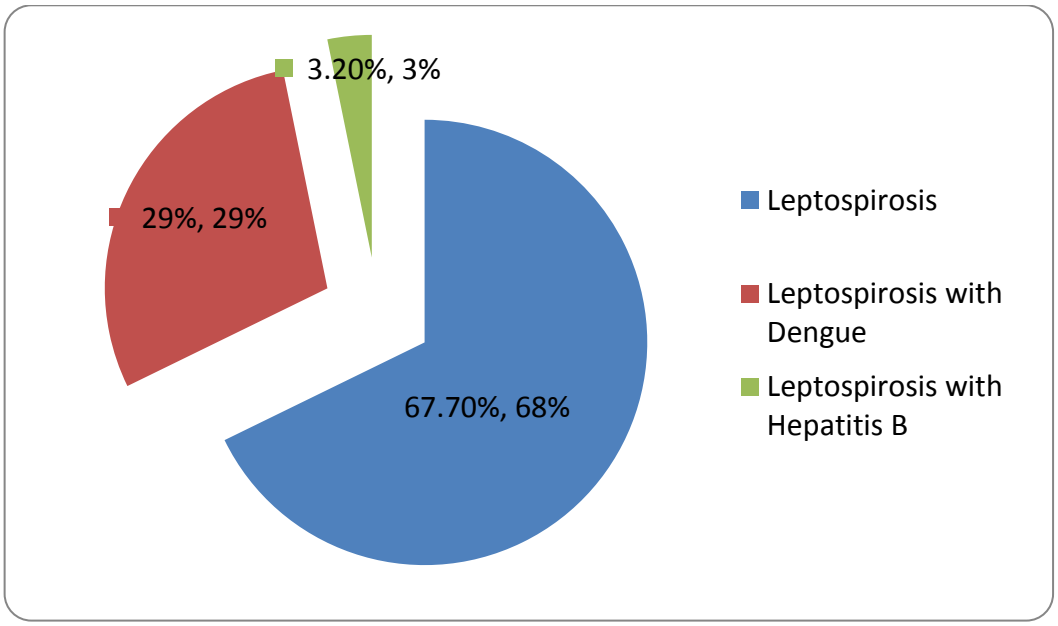


TABLE- 16 : DISTRIBUTION OF SYMPTOMS IN CASES WITH SCRUB TYPHUS (n=26)

SYMPTOMS	NO OF CASES (n=26)	PERCENTAGE (%)
FEVER	26	100
MYALGIA	17	65.3
BREATHLESSNESS	10	38.4
ALTERED MENTAL STATUS	3	11.5
VOMITING	9	34.6

The above table shows most common presenting symptom in Scrub typhus positive cases were fever, followed by myalgia, breathlessness, vomiting and altered mental status

FIGURE 8 :PERCENTAGE OF ESCHAR IN SCRUB TYPHUS (n=26)

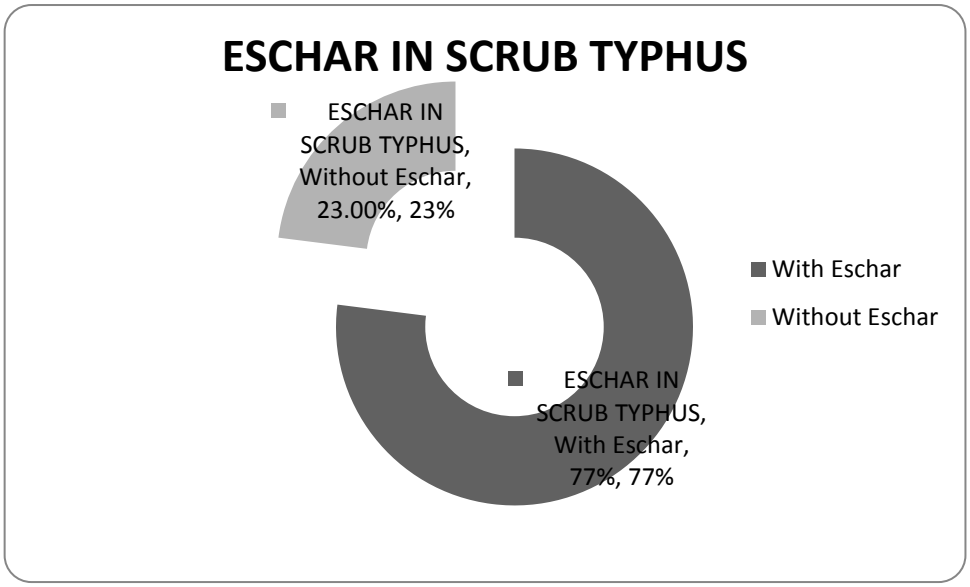


TABLE- 17 : DISTRIBUTION OF SYMPTOMS IN CASES WITHENTERIC FEVER (n = 9)

SYMPTOMS	NUMBER	PERCENTAGE (%)
Fever	9	100
Myalgia	7	77.7
Diarrhoea	4	44.4
Hepatosplenomegaly	3	33.3
Coated tongue	2	22.2

From the above table, it is evident that most common presenting symptom in Enteric fever positive cases was fever, followed by myalgia, diarrhea , hepatosplenomegaly, and coated tongue.

TABLE- 18 :DISTRIBUTION OF CARDINAL SIGNS IN CASES WITH ENTERIC FEVER (n=9)

CARDINAL SIGNS	No of cases (n=9)	Percentage (%)
Pyrexia,toxic look , pallor	1	11.1
Pyrexia, toxic look, coated tongue	3	33.3
Pyrexia, toxic look, coated tongue,hepatomegaly	1	11.1
Pyrexia, toxic look, coated tongue,Splenomegaly	3	33.3
Pyrexia, toxic look, coated tongue,hepatosplenomegaly	1	11.1

The above table shows that the cardinal signs of Enteric fever most commonly encountered were pyrexia, toxic look, coated tongue and splenomegaly.

TABLE- 19 : INVESTIGATIONS OF ENTERIC FEVER(n=250)

BLOOD CULTURE	ANTIBODY DETECTION		URINE CULTURE	STOOL CULTURE
Total no of positive cases	Slide agglutination test positive cases	Tube agglutination test positive cases	Positive cases	Positive cases
2	9	9	Nil	Nil

The above table infers that two cases of Salmonella Typhi was grown in culture. Nine cases of enteric fever were detected by serological method. The rapid method was equally effective as conventional Widal test. Urine and stool cultures were negative for Salmonella sp. All the 9 cases positive for antibodies to enteric fever showed rise in titre when repeated after 1 week for S. Typhi .

The above table is Statistically significant with Pearson Chi- Square Value- 250.01 and p value of < 0.001

TABLE-20: ANTIBIOTIC SUSCEPTIBILITY PATTERN OF SALMONELLA TYPHI BY DISK DIFFUSION METHOD(n =2)

ANTIBIOTIC DISK	PERCENTAGE(%)OF SUSCEPTIBILITY
AMPICILLIN 10µg	100
COTRIMOXAZOLE 25µg	100
CHLORAMPHENICOL 30µg	100
CEFOTAXIME 30µg	100
CEFTRIAXONE 30µg	100
AZITHROMYCIN 15µg	100
PEFLOXACIN 5µg	0

The above table shows that the 2 isolates of Salmonella Typhi were sensitive to Ampicillin, Cotrimoxazole, Chloramphenicol, Cefotaxime, Cetriaxone and Azithromycin

FIGURE 9 : MORTALITY OF THE PATIENTS PRESENTED WITH FEVER (n=250)

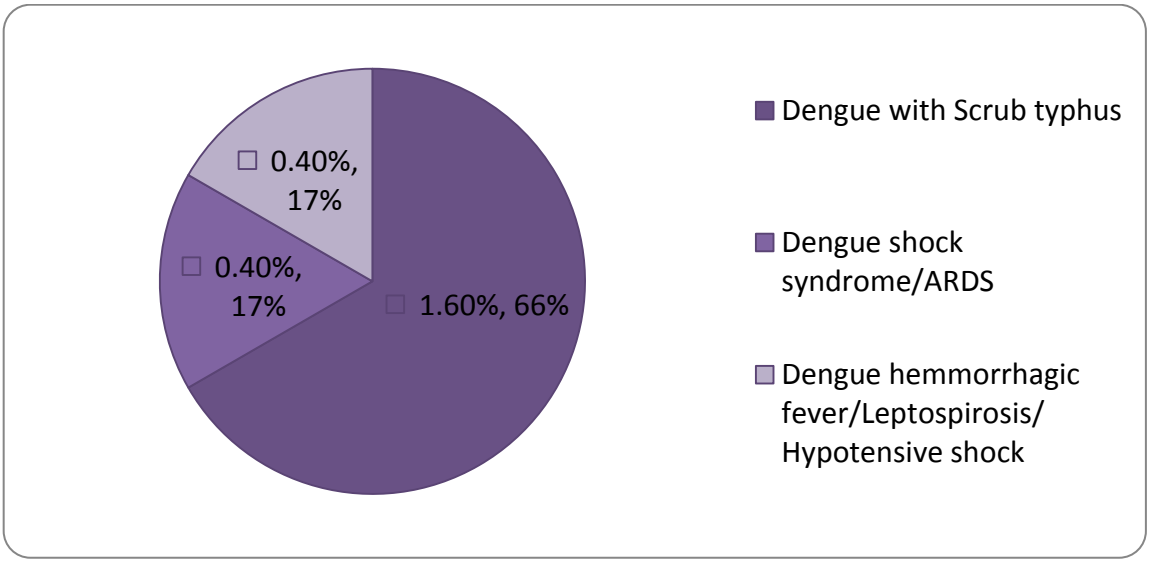


TABLE- 21 : INTERLEUKIN-6 ASSAY IN PATIENTS WITH FEVER (n=250)

IL-6 Concentration range	3-11 pg/ml	12-60pg/ml	70-120 pg/ml	200pg/ml & above
IL-6(n= 250)	81(32.4%)	45(18%)	91(36.4%)	33(13.2%)
Dengue(n=47)	6 (12.7%)	16 (34%)	18 (38.2%)	7 (14.8%)
Leptospirosis(n=31)	3 (9.6%)	7 (22.5%)	15 (48.3%)	6 (19.3%)
Scrub typhus(n=26)	3 (11.5%)	6 (23%)	13(50%)	4 (15.3%)
Enteric fever(n=9)	1 (11.1%)	3 (33.3%)	3 (33.3%)	2 (22.2%)

From the above table, it is evident that raised Interleukin-6 levels were more commonly seen among patients with Scrub typhus followed by Leptospirosis, Dengue and Enteric fever.

FIGURE 10 :GRAPHICAL REPRESENTATION OF IL-6 CONCENTRATION VS OD VALUE

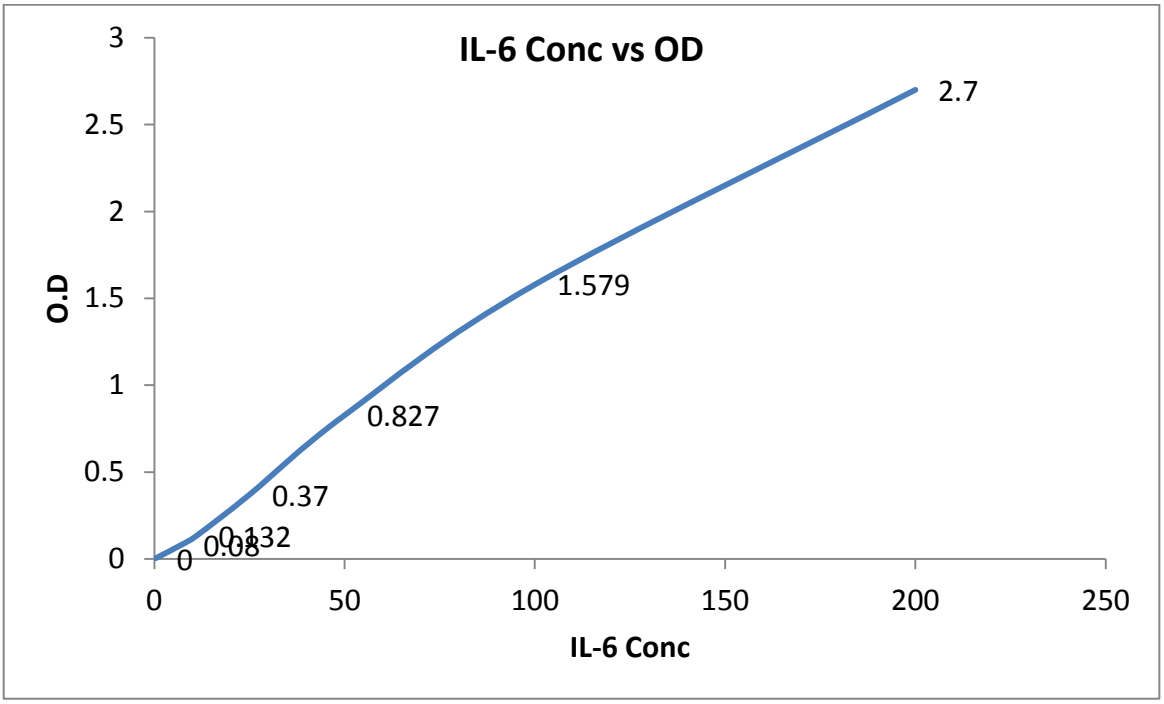


TABLE- 22 : ANALYSIS OF ASSOCIATION BETWEEN DIFFERENT VARIABLES

S.NO	VARIABLES	ASSOCIATED VARIABLE	CHI-SQUARE VALUE	P- VALUE
1.	AGE	DENGUE	58.13	0.41
2.	SEX	DENGUE	4.61	0.202
3.	PLATELET COUNT	DENGUE	85.649	0.000*
4.	HEMOGLOBIN	DENGUE	146.24	0.000*
5.	BLOOD CULTURE	SCRUB TYPHUS	60.282	0.000*
6.	DENGUE	DIAGNOSIS	250	0.000*
7.	WIDAL TEST	DIAGNOSIS	250.01	0.000*
8.	SCRUB TYPHUS	DIAGNOSIS	401.04	0.000*
9.	MSAT-LEPTOSPIROSIS	DIAGNOSIS	250.0	0.000*
10.	PLATELET COUNT	HEMATOCRIT	289.8	0.000*

DISCUSSION

DISCUSSION

Two hundred and fifty cases of fever with 1- 14 days duration were taken up for this study. It included 157 males and 93 females. Patients from 2-70 years age group were included in this study.

Among the etiologies, Infectious disease formed the largest group (44.4%) (Table 1). This was low when compared to other Indian studies by Sharma and Kumari [6] and Kejariwal D.[77] where infectious disease formed 50% and 53% respectively. In other studies it was 30% (Larson & Featherstone, 1982)[78], 36% (Petersdorf & Beeson 1961)[5] 40% (Jacoby & Schwartz 1973)[79], 37% (Howard et al.)[80]and 22.5% (Knockaert,) [9]. In an Indian study of FUO by Kucukardaly Y. [81] in 2002 infectious disease formed 59%.

Among infectious disease Dengue tops the list forming 18.8 %. The other causes of Infections in this study were Leptospirosis 14.4 %, Scrub typhus 12.4 % , Enteric fever 3.6% , Malaria 1.2% ,Urinary tract infection 8 %, followed by Pneumonia, Bacteremia (Table 1), 15 cases presented with mixed infections which included 9 cases of Dengue and Leptospirosis and 6 cases of Dengue and Scrub typhus (Figure 3). Among these mixed infections, 4 cases which presented with diagnosis of Dengue and Scrub typhus expired, and the most common cause of death being Acute Respiratory Distress Syndrome and Hypotensive shock.

The characteristic fever patterns were namely, continuous, remittent, intermittent and recurrent. It was associated with chills in a few cases. A study in Wardha, India by Jung A[82], showed intermittent type of fever more commonly recorded in infectious disease. Most of the cases had fever lasting between 5-10

days in this study(Figure 2).General systemic complaints like myalgia,vomiting, abdominal pain occurred in over two-thirds of patients and one quarter experienced chills and rigors. But these symptoms were not of any diagnostic significance.

Infectious etiology was detected in 80 males and 49 females in this study. The number of males was slightly higher than the number of females (Table 2). In Kejariwal D. (2001) [76] study there were 59 males and 41 females out of 100 cases. In the present study most of the patients fall between the age group 21-40 years (Table 3). An Indian study by Kucukardaly[81] 2002 showed the mean age of the patients to be 39 years which correlates with the present study.

DENGUE

Dengue has been increasingly recognized as an emerging infectious disease for the last four decades. The global burden of Dengue has grown dramatically in recent years. The high prevalence of Dengue cases at Chennai in the recent years, makes it necessary to evaluate the incidence of dengue and to find out the seropositivity of Dengue cases. Rapid diagnosis of dengue is crucial for proper patient care. As IgM antibody appears early during the disease course, its detection is a valuable tool for rapid diagnosis.

According to the WHO guidelines 2009,patients were classified on the basis of severity were 20 patients in DNWS,13 patients in DWWS,14 patients in SD (Table 11)

The predominant symptoms with which the patients presented in the present study (Table 5) were fever(100%), myalgia/ arthralgia (82.9%), haemorrhagic manifestations (44.6%), rashes (40.4%),gastro-intestinal symptoms (36.1%), hepatomegaly (25.5%) and retro-orbital pain(14.8%).In the studyconducted by Min-Shen Lee et al in 2005, a one year study involving 1551patients in Taiwan, fever was the most common symptom (96.1) , followed by myalgia (68.5%), skin rash (53.7%) and retro-orbital pain (15.8%), which correlated well with the present study [83]. In a 16 months study by Shahid Ahamed et al in2008[84], involving 5200 fever cases, they showed that fever was the commonest symptom (100%), followed by, myalgia (67%), and rash (28%).

Haemorrhagic manifestations (Table 7) were seen in 21 cases (44.6%), in the present study, which included petechiae in 5 cases(10.6%), bleeding gums in 8 cases(17%), epistaxis in 2 cases(4.3%), hemetemesis in 3 cases (6.4%), melena in 2 cases (4.3%), and vaginal bleeding in 1 case(2.1%).

Leukopenia was seen in 33 (70.2%) patients, thrombocytopenia (Table 6) with platelet count of less than 1 lakh was seen in 38 cases (80.8%) and more than 1 lakh in 9(19.9%)cases. In a study by Shahid Ahmed et al, in 2008, gum bleeding & epistaxis were seen in 40%, hemetemesis in 22%, melena in 14%, leucopenia in 73% and thrombocytopenia in 84% of cases[83]. In the study done by Min-Sheng Lee et al, in 2005 at Taiwan, they observed that haemorrhagic manifestations were present in 73% of patients, with bleeding from skin and mucosal sites of 70.6%, leucopenia sin 55% and thrombocytopenia in 78.9% of patients[52].

The incidence of Dengue is higher following rainfall. True to this, in the present study, a clear cut increase in incidence of Dengue cases was seen between August to December when Tamilnadu receives rainfall from North East monsoon. In a Laboratory based study on Dengue fever surveillance conducted by John Victor et al in 2007, the data on month wise incidence of Dengue in Tamilnadu for the past nine years revealed that the number of cases increased from June to December, confirming that the active transmission period is during monsoon and post–monsoon period every year[85]. Early diagnosis may be challenging as Dengue infection presents with non-specific signs and symptoms which may not be easily differentiated from other febrile illnesses. In our study, peak incidence of Dengue occurred in the month of October which correlates with other Indian studies [4,5] .

In this study 40% were females and 60% were males. And the mean age was 34 years. Among the 47 Dengue patients studied 32(68%) had thrombocytopenia but only 21 had bleeding manifestations. PCV rise was seen in 34 % and a fall in pulse pressure was seen in 33 %.

Most common ultrasound finding was thickened gall bladder that was present in 50% of the study population. Next common finding was pleural effusion 14.8 % followed by hepatomegaly 12.7 % and ascites 8.5 %.In a similar study conducted during the epidemic in 1997 by Joshi et al., the most common age group affected was 20 to 40 years and right sided pleural effusion was the most common finding, like .In their study, ascites was seen in only 50% of cases;

Thickened gall bladder wall was first reported as a finding of Dengue Fever by Pramuljo et al[15]. It has been found in a lot of studies to be a consistent and common ultrasound finding of Dengue Fever. Venkata Sai et al.[1] had found it in hundred percent patients in their study as the most common first ultrasound finding. In fact, it has been propagated to be used in children as a reliable criterion to predict the onset. Javed et al. found hepatomegaly in 35.5% patients and splenomegaly in 28.9% patients. In our study hepatomegaly and splenomegaly was seen only in 12.7 % and 6.3 % respectively. That was the least common among the ultrasound parameters studied.

SGOT (Aspartate Transaminase) of normal value of 12-38 U/L, of which 12 (25.5%) patients had high value ,remaining normal. SGPT(Alanine Transaminase) of normal value of 7-41 U/L,of which 11 (23.4%) patients had high value remaining normal. Laboratory investigations reported, apart from thrombocytopenia gross leucopenia and transaminitis were significant derangements consistent with several studies across India (Prafulla et al., 2012)[86].

Case fatality rate seen in the present study was 2.1%(Table 9). This was similar to the study conducted by Nazish Butt et al, in 2007, who observed a case fatality rate of 2.88% [89]. The WHO fact sheet 2002 also shows a statistics of 2.5% case fatality rate each year among dengue cases, which coincides well with the present study [90].

LEPTOSPIROSIS

Leptospirosis (12.4 %) was the second most common cause of infections in the present study(Table 1). An Indian study by Ratnam et al. [91] at Pondicherry in 1983 showed 24% of Leptospirosis among FUO cases which was slightly higher than the present study. The study done at Nagpur, India by R. Angnani 2003 showed 32.73% among FUO patient, which was slightly higher than the present study. The age and sex distribution of patients in this study indicates that Leptospirosis is the disease of middle age adults with male preponderance. There were 21 males and 10 females among the 31 patients.

Myalgia was present in 67.7% (Table 12) of cases in the present study. Sumathi G 108 (1995) at Madras showed myalgia as a clinical symptoms in 56% cases which was slightly lower than the present study. Conjunctival suffusion was present in 54.8 % of cases which was higher as compared to 33%, noted by Sumathi G, in Madras. The study conducted by Sumathi, showed 55% of cases with jaundice,[92] where as the present gave only 41.9% positive for jaundice. CNS dysfunction were present in 12.9% of cases which was lower as compared to 28% in Muthusethupathy [93] study . 18 patients (58%) had anicteric Leptospirosis. Among the 13 (41.9%) icteric patients, 3 (23%) patients had renal failure, 4 (30.7%) patients had CNS dysfunction (Table 14).

Serological test MSAT (a widely accepted screening test for Leptospirosis) was positive in 31 cases (100%) . Galton et al. [94] (1958) found that Patoc strain (killed antigen) used for MSAT was more sensitive, Sumathi et al.[92] (1997)

found that MSAT was positive in 39.8% in the year 1996 when they investigated 1461 samples. But the Gold standard serological test for the diagnosis of leptospirosis is taken as MAT.

Other laboratory parameters were done for all patients in which ESR was raised in all cases (100%), followed by abnormal LFT in 74.2%, thrombocytopenia in 51.6%, abnormal RFT in 29 % and both abnormal LFT and RFT in 25.9% of patients (Table 13). In Sritharan M et al study abnormal RFT was seen in 52% and abnormal LFT in 44%of patients [(95)]. In Gancheva et al study (2005) ESR was elevated in 86.90%, thrombocytopenia 42.86%, abnormal RFT in 72.62%, abnormal LFT in 70.24% which was slightly lower than the present study [(96)] . Differential Count shows percentage of polymorphs were increased in 66.66% of patients in the present study. In Gancheva G et al study polymorphs % were increased in 95.12%[(96)..] ESR was moderately raised (less than 50mm/hr) in 61.3% and extremely raised (more than 50mm/hr) in 35.4% (Table 13) in this study. This is in accordance with Gancheva G et al* (2007) study in which moderate rise in ESR was present in 74.39% and extreme rise in 20.73%[(96).]

Blood urea, serum creatinine were increased in 26.92% of cases (Table 14) in this study.This is in contrary to Marcial M R et al study in which blood urea and serum creatinine were increased in 73.1% of patients [(97)] and with Margarita R et al study in which blood urea and serum creatinine were increased in 92.3% of patients[(98).]

Only two cases (6.4%) went in for Acute Renal Failure . Both the cases after appropriate treatment recovered. In Margarita R et al study, Acute renal failure was seen in 30.7%of patients[98]. In Marcial M R et al study Acute Renal Failure was seen in 74%[97] and in De A et al study it was seen in 16.2% of patients[99]. In Muthusethupathi MA et al (1994) study in Madras city during 1987-91 there were 120[100] cases of Acute Renal Failure due to leptospirosis, but in the last two years there were only 15 cases of leptospiral ARF.53 In the present study there were only 2 cases which indicates a decline in the severity of the disease and now more number of milder form of disease occurs.

Blood urea, serum creatinine were increased in most patients of decreased platelet count (90.47%) than in patients with normal platelet count (9.52%). This correlates well with Ramon Peces study in which it was concluded that there exists a significant inverse correlation between platelet count and the renal parameters[101].

Concomitant infection with Hepatitis B was seen in one patient (3.2%) (Figure 7).In Singapore, Kaushik et al reported one case of Weil syndrome and concomitant Hepatitis B infection[102]

SCRUB TYPHUS

Scrub typhus is a re-emerging zoonosis. In the pre-antibiotic era methods to prevent the spread of Scrub typhus included spraying and dusting clothes with insecticides, and burning areas at the fringe of forests.

In this study, the predominant clinical feature was fever with an average of 8 days followed by myalgia, vomiting, cough, breathlessness, loose stools, reduced urine output and abdominal pain . These findings correlated with the other studies from Goa and Pondicherry [103,104].

Eschar was observed in 20 out of the 26 patients (77 %)(Figure 8) in this study. The percentage of patients with scrub typhus having Eschar are variable with different studies citing different results. A study from Korea showed that as much as 92.04% of the patients presented with eschar[105] which almost correlated with this study. It has been reported that the eschars were more frequently detectable in the fair skinned Japanese children than the dark skinned Thai children .It's also reported that in dark skinned patients the early eschar lesions were atypical and could be easily overlooked. A retrospective study on dark skinned Thai pediatric patients showed that only in 7% was the eschar detectable. Another reason for variable reports could be because the presence of an eschar could be easily missed on routine physical examination and the vector bite is painless so the patients wouldn't notice it either[106].

Out of the 26 cases, 18(69.2%) were males and 8(30.7 %) were females in this study. In a study from Andhra Pradesh, the males constituted 59.3% and females 40.7%[107]. About 50% of the patients were agricultural workers showing an increased risk among those involved in this occupation. Literature also reports

Scrub typhus is generally seen among those whose occupation or recreational activities bring them in contact with the scrub vegetation[108].

In this study, the seasonal variation was from September to December and noticed an increased number of cases from September to February, which coincided with the cooler months of the year. It has been reported that outbreaks of scrub typhus in some areas are seen more often in the cooler months [109].This could be due to the growth of secondary scrub vegetation (mite islands commonly seen in the post monsoon season from September to early months of next year) which is the habitat of the trombiculid mites[110].

Platelet count less than 1.5 lakh/cu.mm was seen in 47.6% of those suffering from Scrub typhus alone and in patient with Scrub typhus and Dengue, thrombocytopenia was seen in 85% of the patients in the present study. Thus correlating with study stating that the platelet levels (<1.4 lakh/cu.mm) were found to be much lower in those suffering from Dengue as compared to scrub typhus infection[111]. Suputtamongkol et al from Thailand showed that thrombocytopenia was associated in 20.9% of the patients suffering from scrub typhus[112].

ENTERIC FEVER

Out of the 250 fever cases taken up for study, 9 cases were positive by Widal test and 2 cases were positive by Blood culture (Table 20). The predominant symptoms observed were fever(100%) ,chills, abdominal pain and diarrhoea (44.4%) (Table 18). The predominant signs were pyrexia, toxic look and coated tongue (22.2%) (Table 19) .Most common age group affected was between 7- 25yrs. Authors from various parts of the world have done

similar studies among enteric fever patients .Stuart et al., found that school aged children or young adults between 5-25 years of age were the most commonly affected age group in the areas of endemicity [113,114,115] . He also observed that the predominant symptom was fever (75%) followed by abdominal pain (40%). Scragg et al., observed that diarrhoea was the predominant symptom in children .

Conventional blood culture was done for all the 9 patients who were positive by Widal test and antimicrobial susceptibility testing was done. Among these 2 Salmonella Typhi were isolated (Table19) In India, varying prevalence of typhoid fever has been reported over a period of time and geographical distribution. The systematic review and meta analysis study done in 2016 reported the prevalence of Salmonella Typhi to be about 9.7 % [116] .

The World Health Organisation , in 2008 , reported the prevalence of typhoid fever as 28.1 per 1000 febrile episodes in India. Blood culture positivity is usually high during the first week of illness but can also be isolated from subsequent weeks also if there is no prior antibiotic therapy [76,117] . The low isolation rate of Salmonella species from blood culture could be attributed to many factors- prior antibiotic therapy, low bacterial count (sometimes as low as one) ,poor selection of cases, volume of blood sampled [76] .In this study ,the isolation rate in blood culture of Salmonella species, with isolation of S.Typhi about 18.1% (n=2). In the present study, all the 2 isolates were susceptible to Ampicillin (100%), Chloramphenicol (100%)and Trimethoprim sulphamethoxazole (100%), and none of the isolates were Multidrug resistant (Table 20).

Typhoid fever is known to show seasonal variation and is mainlyassociated with hot summer months. Many studies worldwide and Indian studies showed peak incidence around the end of dry season .Mohanty et al, observed peak incidence of enteric fever occurs between April and June followed by July-September .In this study the peak isolation was between June-August [(118)] .

INTERLEUKIN- 6

Interleukin-6 assays were performed for all the 250 cases who presented with fever.It was performed by ELISA method using Diaclone Human IL-6 kit. Immunological response in patients presenting with fever were tested using IL-6 assay and it is correlated with the infectious diseases detected in the study (Statistically significant with p value < 0.001).Most of the infectious causes of fever has been associated with a strong activation of acute phase response (IL-6, TNF- α, IL-1β) and TH1 cytokines (IFN-γ, IL-12).

Among the infectious causes of fever higher positivity of IL-6 with values > 200ng/dL were seen among patients with Scrub typhus, followed by Leptospirosis, Dengue and Enteric fever. Monoinfection of Dengue showed higher levels of IL-6 than the co-infections of Dengue with other infectious causes of fever. The levels of IL-6 was found to be elevated in Severe form of Dengue than Dengue with/ without warning signs according to WHO classification (2009).

SUMMARY

SUMMARY

- A total of 250 fever cases were taken up for the study. Microbial infections were seen in 44.4 % of fever cases.
- Dengue (18.8%) was the most common infection followed by Leptospirosis (12.4 %) ,Scrub typhus (10.4 %) and Enteric fever (3.6 %).
- Mixed infections were seen in 15 cases, which includes 9 cases of Dengue and Leptospirosis and 6 cases of Dengue and Scrub typhus . Among these mixed infections, four patients expired who presented with Dengue and Scrub typhus.
- Most of the cases had fever lasting for 5-10 days
- Males were infected more than the female population .
- Majority of the cases fell into the age group of 21 to 40 years.
- Increased incidence of all the fever cases was found during August to December months, during monsoon and post monsoon period.
- Fever was the most common presenting symptom (100%) in almost all the cases followed by myalgia/arthralgia
- In Dengue, haemorrhagic manifestations (44.6%) and the most common haemorrhagic manifestations among dengue patients were gum bleeding and petechiae.
- Thrombocytopenia was seen in all the dengue cases and most of the cases had a platelet count of 50,000 to 1 lakh/cu.mm

- Dengue cases were categorized according to WHO criteria into Dengue with/without warning signs (70.2 %), Severe Dengue (29.7 %)
- WBC count of <4000, elevated hematocrit> 41, elevated AST and ALT, was more commonly associated with DHF and DSS
- Of the USG findings, Gall bladder wall thickening, pleural effusion and ascites were seen in majority of Dengue positive cases.
- Myalgia and conjuctival suffusion were the common clinical features seen in the Leptospirosis cases. Antibodies were detected by MSAT in 28 cases Leptospirosis occured throughout the year although the number of cases increased after rainy season.
- Blood urea, serum creatinine were raised in 26.92% of patients. 2 cases out of 31 went in for Acute Renal Failure. Serum total bilirubin was elevated in 71.7% and normal in 28.2% of patients. Serum total bilirubin was elevated in all the cases of leptospirosis except in a patient with the Hepatitis B concomitant infection whose serum total bilirubin in this patient was 21.8mgm/dl showing marked elevation. All the patients recovered with appropriate drug and supportive therapy.
- In Scrub typhus, Eschar was observed in 20 (76.9%) out of the 26 cases in our study. The percentages of patients with Scrub typhus having eschars were variable with different studies citing different results.
- Scrub Typhus diagnosis is made more complex by the presence of dual infections. Dual infections should be suspected when the patients present

with atypical clinical features of either disease or when patient responds poorly to treatment.

- The platelet levels were within the range of 50,000- 1,50,000 lakh/cu.mm in Scrub typhus, but it was lower when the patient was infected with both Scrub typhus and Dengue infection.
- Main stay of Scrub typhus diagnosis remains serology. All the 26 cases were positive by Scrub typhus IgM ELISA.
- Scrub typhus responds well to treatment and if not treated in time the patient can go in for complications emphasizing the need for early diagnosis and treatment.
- In Enteric fever, most common symptoms were fever followed by myalgia, diarrhoea, hepatosplenomegaly and coated tongue. Nine cases were picked up by the tube agglutination test, out of which two cases were positive by blood culture.
- Interleukin-6 assays showed higher positivity in cases of Scrub typhus followed by Leptospirosis , Dengue and Enteric fever.

CONCLUSION

CONCLUSION

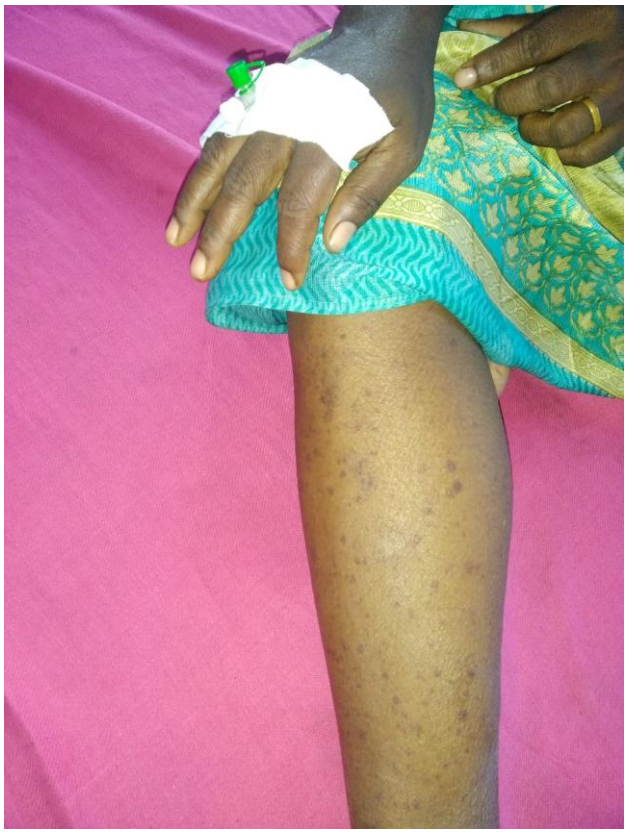
- It was proven in our study that majority of the causes of fever could be reliably predicted using proper history, good physical examination and laboratory tests.
- Despite of all limitations, our study clearly revealed that predominant infectious cause of fever was Dengue followed by Leptospirosis, Scrub typhus and Enteric fever , most commonly presenting during the post-monsoon period.
- It is also revealed from our study that if proper protocol was used for fever cases, it helps in the proper use of antibiotics as well as investigations. This reduces cost and resistance to antibiotics
- Infections (44.4%) remain the most important cause of fever in India, confirming the trends found earlier in other studies.
- The role of other less common viruses like Influenza virus, Chikungunya virus have not been touched upon in this study. Further studies of other etiological agents will help in diagnosing the other causes of infectious fever.
- Ultrasound abdomen supported with lab parameters like rising haematocrit and decreasing platelet count predicts the progression to severe form of the disease.
- Serological diagnosis should be done in all clinically suspected dengue cases for early initiation of treatment and thereby to minimize the mortality.

- By correlating the biochemical and haematological parameters a quick clinical suspicion of leptospirosis can be made out and diagnosed early, for initiating appropriate treatment.
- Scrub typhus is a prevalent disease in this part of the country therefore it should be kept in mind as a possible diagnosis in fever even if an eschar is not found. Scrub typhus was found to constitute 10.4 % of the fever cases taken up for study. This being a treatable disease further emphasizes the need for its timely and accurate diagnosis.
- Interleukin – 6 being a pyrogenic cytokine, was very useful tool in detecting the immunological response of patients presenting with fever.
- Correlation of Interleukin-6 levels with the infectious causes of fever were statistically significant with a p value of < 0.001.

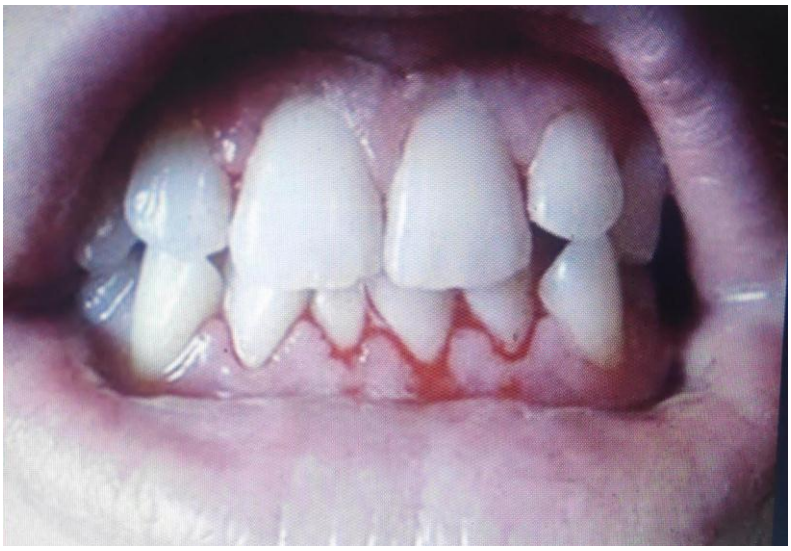
COLOUR PLATES

COLOUR PLATES

1. A CASE OF DENGUE WITH PETECHIAE

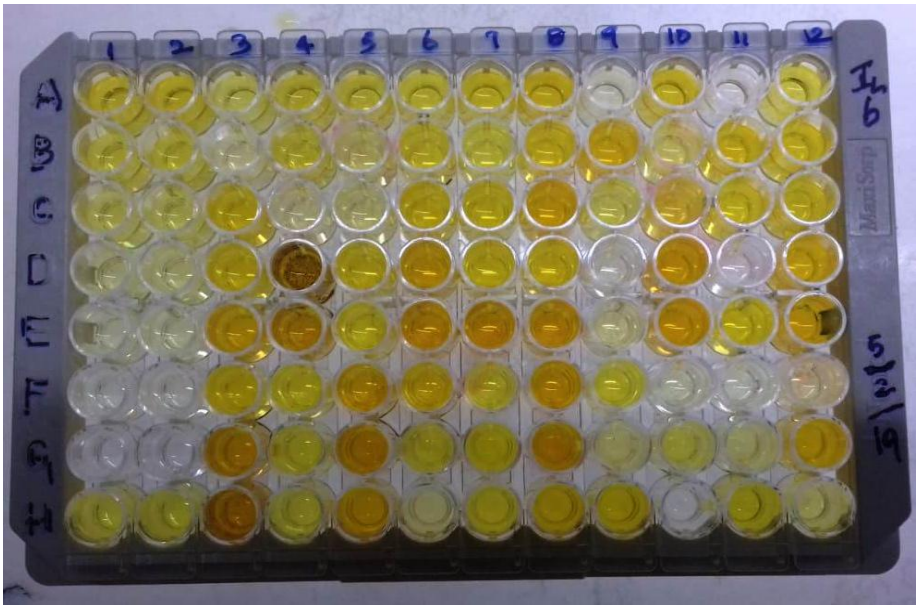


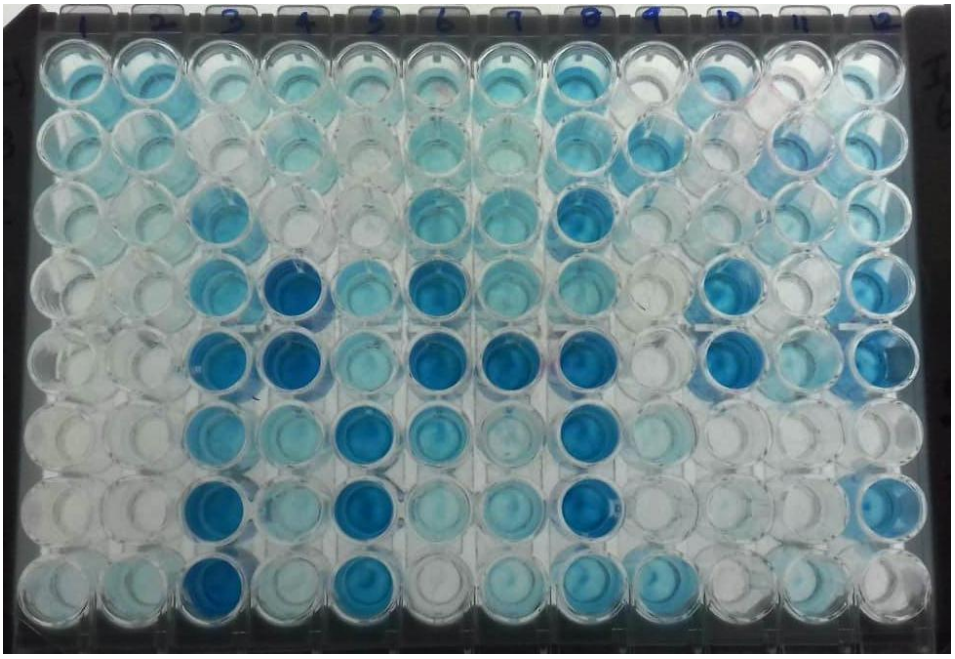
2. A CASE OF DENGUE WITH BLEEDING GUMS



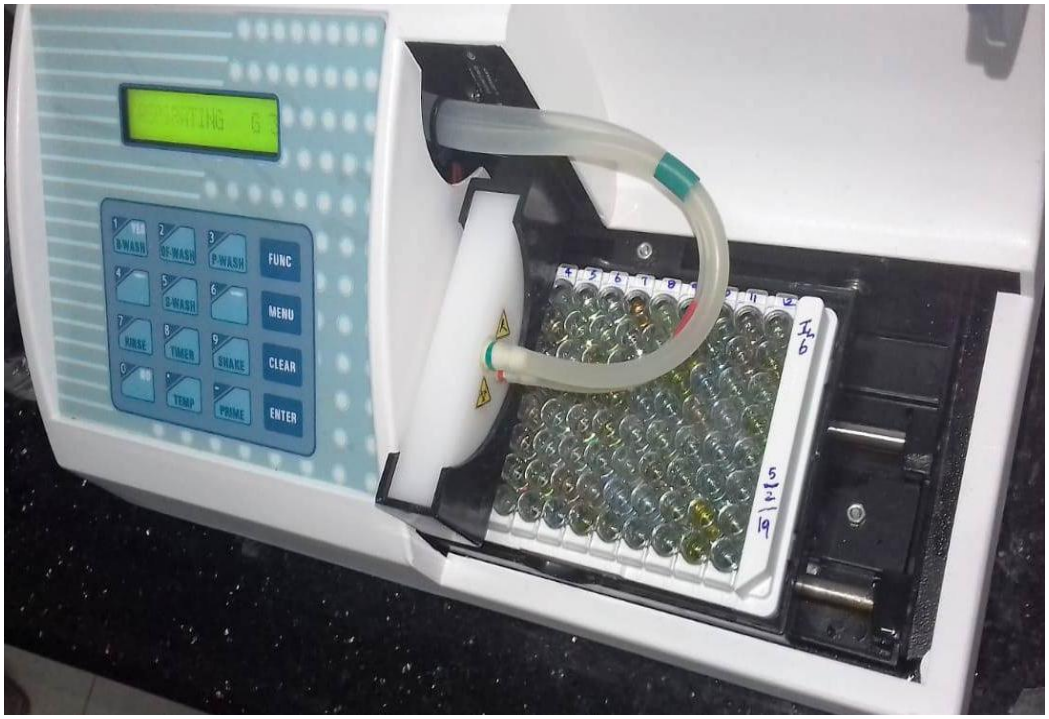
3. DIACLONE HUMAN INTERLEUKIN-6 ELISA KIT

4. INTERLEUKIN-6 ASSAY IN MICROTITRE PLATE





5. ELISA WASHER



6.PROTOCOL SHEET AND OD VALUES OF INTERLEUKIN-6 ASSAY

5/3/19

Report

IL-6

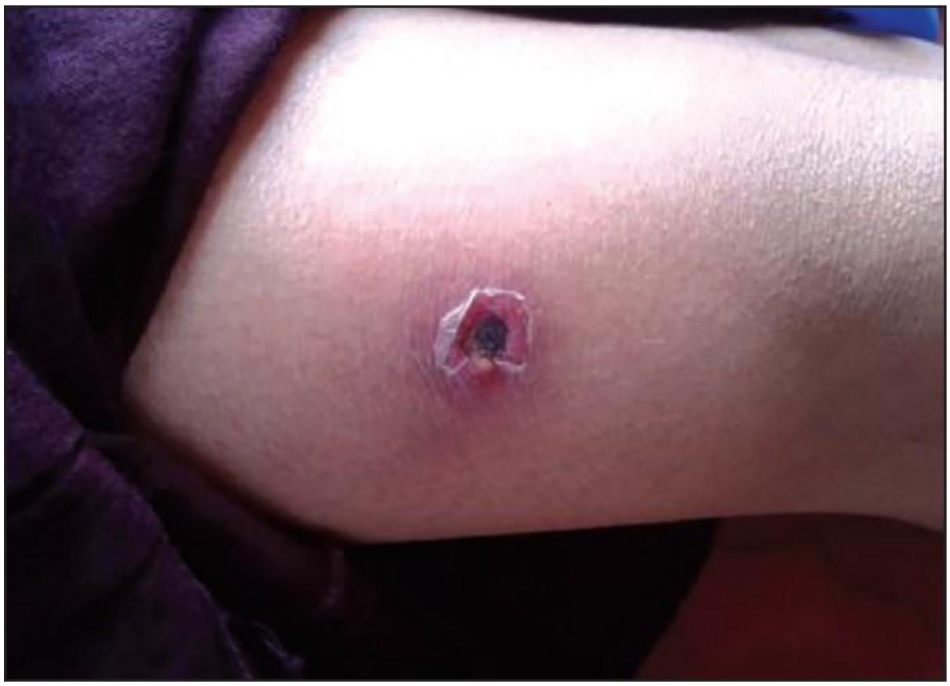
Item name: ~~Ds DNA~~ Complete name: Double std DNA

Reference: [0.000 ~ 50.000] Calculation method: Curve

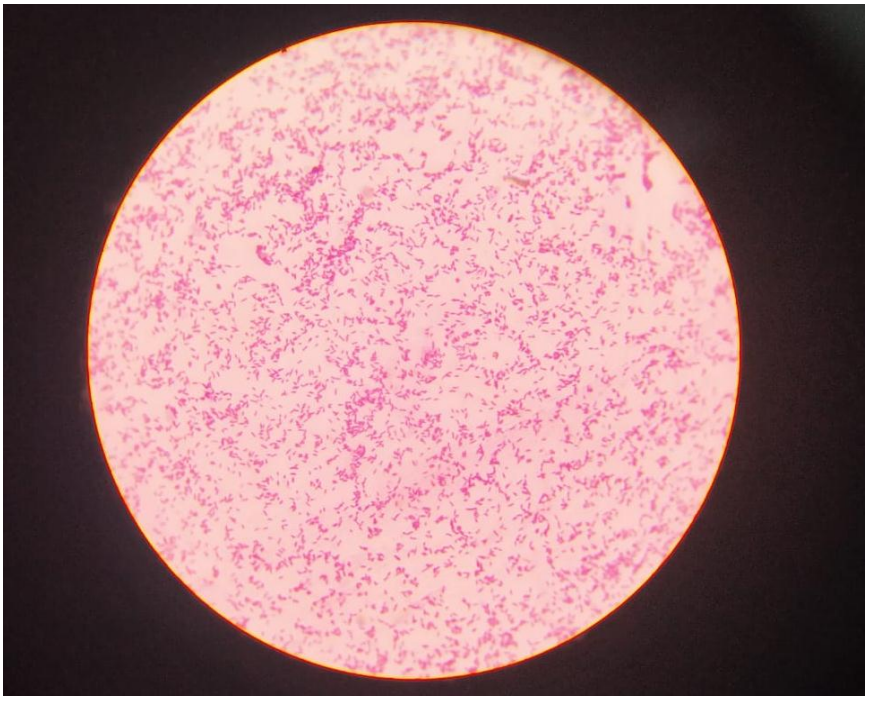
Reagent name: Batch: Manufacturer:

	1	2	3	4	5	6	7	8	9	10	11	12
A	0000001 2.796 429.313 Pos+	0000009 2.951 446.757 Pos+	0000017 1.127 15.625 Neg-	0000025 1.977 38.035 Neg-	0000033 1.728 23.999 Neg-	0000041 1.876 30.598 Neg-	0000049 2.983 450.381 Pos+	0000057 3.620 522.095 Pos+	0000065 0.222 3.031 Neg-	0000073 3.056 458.551 Pos+	0000081 0.141 1.901 Neg-	0000089 1.933 34.806 Neg-
B	0000002 1.710 23.742 Neg-	0000010 1.787 24.818 Neg-	0000018 0.445 6.135 Neg-	0000026 1.673 23.229 Neg-	0000034 0.626 8.654 Neg-	0000042 2.156 357.159 Pos+	0000050 1.351 18.745 Neg-	0000058 3.202 474.986 Pos+	0000066 3.151 469.225 Pos+	0000074 0.905 12.537 Neg-	0000082 2.959 447.617 Pos+	0000091 3.151 469.225 Pos+
C	0000003 1.039 14.405 Neg-	0000011 0.963 13.347 Neg-	0000019 2.664 414.418 Pos+	0000027 0.406 5.601 Neg-	0000035 0.522 7.206 Neg-	0000043 2.706 419.170 Pos+	0000051 2.753 424.434 Pos+	0000059 2.840 434.248 Pos+	0000067 0.962 13.331 Neg-	0000075 1.556 21.608 Neg-	0000083 2.664 414.418 Pos+	0000090 2.817 431.604 Pos+
D	0000004 0.522 7.204 Neg-	0000012 0.567 7.839 Neg-	0000020 2.401 384.797 Pos+	0000028 2.568 403.597 Pos+	0000036 2.341 378.007 Pos+	0000044 2.561 402.839 Pos+	0000052 2.568 403.597 Pos+	0000060 2.589 405.945 Pos+	0000068 0.156 2.121 Neg-	0000076 2.582 405.150 Pos+	0000084 0.101 1.351 Neg-	0000092 2.806 430.397 Pos+
E	0000005 0.287 3.933 Neg-	0000013 0.325 4.467 Neg-	0000021 2.902 441.180 Pos+	0000029 2.874 438.023 Pos+	0000037 2.209 363.123 Pos+	0000045 2.932 444.554 Pos+	0000053 3.078 461.010 Pos+	0000061 2.847 435.058 Pos+	0000070 0.397 5.465 Neg-	0000077 2.916 442.838 Pos+	0000085 2.811 430.923 Pos+	0000093 3.078 461.010 Pos+
F	0000006 0.233 3.183 Neg-	0000014 0.272 3.737 Neg-	0000022 3.030 455.654 Pos+	0000030 2.328 376.552 Pos+	0000038 3.282 484.012 Pos+	0000046 3.086 461.906 Pos+	0000054 1.443 20.033 Neg-	0000062 3.106 464.181 Pos+	0000069 1.571 21.810 Neg-	0000078 0.237 3.239 Neg-	0000086 0.213 2.914 Neg-	0000094 0.403 5.560 Neg-
G	0000007 0.167 2.262 Neg-	0000015 0.181 2.470 Neg-	0000023 3.399 497.153 Pos+	0000031 1.590 22.075 Neg-	0000039 3.621 522.136 Pos+	0000047 1.595 22.141 Neg-	0000055 3.098 463.254 Pos+	0000063 3.320 488.236 Pos+	0000071 0.533 7.367 Neg-	0000079 0.988 13.701 Neg-	0000087 0.566 7.829 Neg-	0000095 3.797 541.966 Pos+
H	0000008 1.228 17.038 Neg-	0000016 1.353 18.780 Neg-	0000024 3.790 541.185 Pos+	0000032 1.222 16.960 Neg-	0000040 4.000 564.865 Pos+	0000048 0.469 6.477 Neg-	0000056 2.072 45.032 Neg-	0000064 3.614 521.355 Pos+	0000072 3.438 501.525 Pos+	0000080 0.169 2.292 Neg-	0000088 2.528 399.151 Pos+	0000096 0.666 9.220 Neg-

7. A CASE OF SCRUB TYPHUS WITH ESCHAR



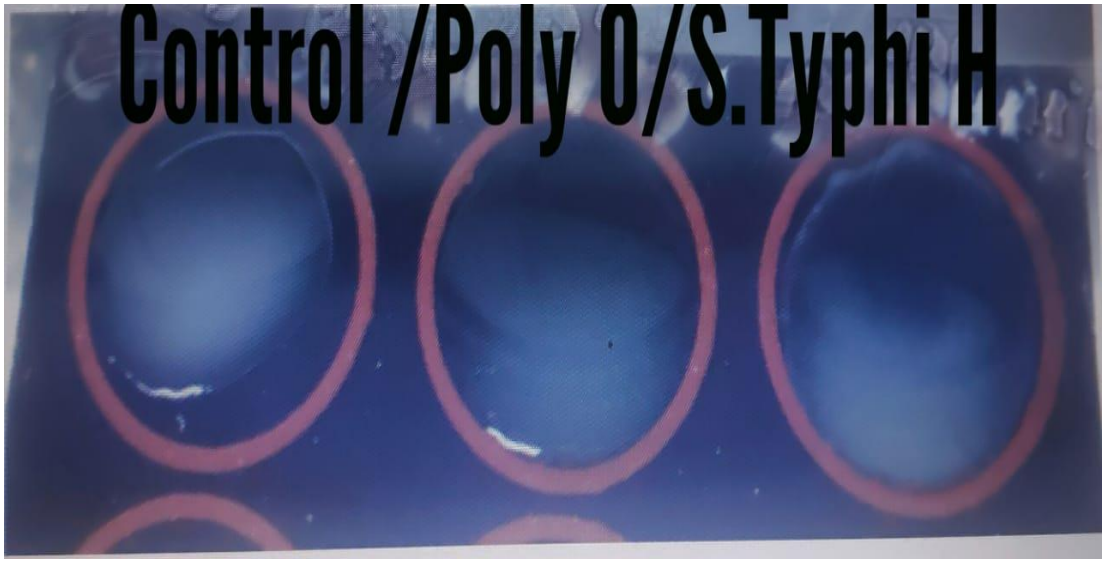
8. GRAM STAIN OF SALMONELLA TYPHI – GRAM NEGATIVE BACILLI IN SCATTERED ARRANGEMENT



9. COLONIES OF SALMONELLA TYPHI ON MAC CONKEY AGAR & BLOOD AGAR

10. BIOCHEMICAL REACTIONS , SUGAR FERMENTATION AND LYSINE DECARBOXYLATION TESTS OF SALMONELLA TYPHI

11. HIGH TITRE SERA FOR SALMONELLA TYPHI IDENTIFICATION



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ANNEXURE

LIST OF ABBREVIATIONS

CDC	–	Centre for Disease Control and Prevention
CFU	–	Colony Forming Unit
CO	–	Cut- Off calibrator
CRP	–	C Reactive Protein
DENV	–	Dengue Virus
DF	–	Dengue Fever
DHF	–	Dengue Hemorrhagic Fever
DIC	–	Disseminated Intravascular Coagulation
DSC	–	Drug Susceptible
DSS	–	Dengue Shock Syndrome
ELISA	–	Enzyme Linked Immuno Sorbent Assay
FUO	–	Fever Of Unknown Origin
HRP	–	Horse Radish Peroxidase
IL 1	–	Interleukin- 1
IL 6	–	Interleukin - 6
LPS	–	Lipopolysachharide
MAT	–	Microscopic Agglutination Test
MSAT	–	Macroscopic Slide Agglutination Test
NC	–	Negative Control
OMP	–	Outer Membrane Protein
PBS	–	Phosphate Buffered Saline

PC	–	Positive Control
PCR	–	Polymerase Chain Reaction
RANTES	–	Regulated upon Activation, Normal T-cell Expressed AndSecreted
RBC	–	Red Blood Cell
RT	–	Reverse Transcriptase
TMB	–	Tetra Methyl Benzidine
TNF	–	Tumour Necrosis Factor
UTI	–	Urinary Tract Infection
WBC	–	White Blood Cell

CERTIFICATE FOR APPROVAL

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.M.Sahana
I Year Post Graduate in MD Microbiology
Institute of Microbiology
MMC/Chennai

Dear Dr.M.Sahana,

The Institutional Ethics Committee has considered your request and approved your study titled **"A STUDY ON COMMON MICROBIAL AGENTS, THEIR CHARACTERISTICS AND IMMUNOLOGICAL RESPONSE IN PATIENTS PRESENTING WITH FEVER" - NO.37122017**

The following members of Ethics Committee were present in the meeting hold on **12.12.2017** conducted at Madras Medical College, Chennai 3

1. Prof.P.V.Jayashankar	:Chairperson
2. Prof.R.Narayana Babu,MD.,DCH., Dean,MMC,Ch-3	: Deputy Chairperson
3. Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	: Member Secretary
4. Prof.N.Gopalakrishnan,MD,Director,Inst.of Nephrology,MMC,Ch	: Member
5. Prof.S.Mayilvahanan,MD,Director,Inst. of Int.Med,MMC, Ch-3	: Member
6. Prof.A.Pandiya Raj,Director, Inst. of Gen.Surgery,MMC	: Member
7. Prof.Shanthy Gunasingh, Director, Inst.of Social Obstetrics,KGH	: Member
8. Prof.Rema Chandramohan,Prof.of Paediatrics,ICH,Chennai	: Member
9. Prof. Susila, Director, Inst. of Pharmacology,MMC,Ch-3	: Member
10.Prof.K.Ramadevi,MD., Director, Inst. of Bio-Chemistry,MMC,Ch-3	: Member
11.Prof.Bharathi Vidya Jayanthi,Director, Inst. of Pathology,MMC,Ch-3:	Member
12.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
13.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist
14.Thiru K.Ranjith, Ch- 91	: Lay Person

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary – Ethics Committee

PROFORMA

Name:

Age/sex:

Informant:

Occupation:

OP/IP No:

Ward No:
DOA:
DOD:

Chief complaints:

- Fever-Temperature,onset,duration,frequency,diurnalvariations,with or without chills /rigor.
- Associated symptoms-rash,bodyache,headache,nausea,vomiting,jointpain,petechiae,eschar

Past medical history:

Clinical Diagnosis:

Co-morbidities:

Investigations:

Microbiological Investigations:

Sample collected: Blood

CONSENT FORM

STUDY TITLE :"A STUDY ON COMMON MICROBIAL AGENTS , THEIR CHARACTERISTICS AND IMMUNOLOGICAL RESPONSE IN PATIENTS PRESENTING WITH FEVER"

I……, hereby give consent to participate in the study conducted byDr.M.SAHANA , First year Post graduate at Institute of Microbiology, Madras Medical College, Chennai-3 and to use my personal clinical data and the result of investigations for the purpose of analysis and to study the nature of the disease, I also give consent to give my clinical Specimen for further investigations.I also learn that there is no additional risk in this study. I also give my consent for my investigator to publish the data in any forum or journal.

Signature/ Thumb impression Place : Date:

Of the Patient/ relative/parents

Patient Name & Address:

Signature of the investigator:

Signature of the guide:

TAMIL CONSENT FORM

ஆய்வு தகவல் தாள்

ஆய்வு செய்யப்படும் தலைப்பு :
காய்ச்சலுக்கு காரணமான நுண்ணுயிரிகள் மற்றும் அதன் நோய் எதிர்ப்பு தன்மையை கண்டறிதல் பற்றிய ஆய்வு.

ஆய்வாளர் : மரு. மு. சஹானா
முதலாம் ஆண்டு முதுகலை பட்டபடிப்பு மாணவி,
நுண்ணுயிரியல் துறை,
சென்னை மருத்துவக் கல்லூரி,
சென்னை-600003.

இந்த ஆய்வினால் இரத்தம் பரிசோதனைக்கு உட்படுத்தப்படும் என்பதை தெரிவித்துக் கொள்கிறோம்.

இந்த ஆய்வின் வாயிலாக நோய்தொற்றை அறிவதன் மூலம் அதற்கான சிகிச்சை முறைகளையும், சிகிச்சை பலனையும் முன் கணிக்க முடியும். தங்களுடைய / தங்கள் குழந்தையின் பங்களிப்பும் ஒத்துழைப்பும் ஆராய்ச்சி நன்முறையில் வெற்றி பெற பெரிதும் உதவியாக அமையும்.

தாங்கள் / தங்கள் குழந்தை இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். இந்த ஆராய்ச்சியில் தாங்கள் / தங்களின் குழந்தைக்கு பரிசோதனைகள் செய்து அதன் தகவல்களை ஆராய்வோம். அதனால் தங்களின் / தங்கள் குழந்தையின் நோயின் ஆய்வறிக்கையோ அல்லது சிகிச்சையோ பாதிப்பு ஏற்படாது என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆய்வு முற்றிலும் தன்னார்வமிக்கது மற்றும் நோயாளிகள் இந்த ஆய்விலிருந்து எந்த நேரத்திலும் விலகிக்கொள்ளலாம். இந்த ஆய்வில் நோயாளிகளுக்கு எந்த செலவும் இல்லை. ஆய்வின் முடிவுகள் வெளியிடப்படும்.

இந்த ஆய்வையொட்டி எந்த விதமான சந்தேகங்களுக்கும் விளக்கம் பெற பங்கேற்பாளர்களுக்கு உரிமை உள்ளது. இந்த ஆய்வின் முடிவுகள் இறுதியில் வெளியிடப்படும். இந்த ஆய்வை பற்றிய சந்தேகங்களுக்கு தொடர்பு கொள்ள வேண்டியவர் : மரு. மு. சஹானா, செல் : 9941351162

ஆய்வாளர் கையொப்பம்

தேதி :

பங்கேற்பாளர் கையொப்பம்

பெற்றோர் / உறவினர் கையொப்பம் /
இடதுகை பெருவிரல் ரேகை

தேதி :

INFORMATION SHEET

STUDY TITLE :

"A STUDY ON COMMON MICROBIAL AGENTS , THEIR CHARACTERISTICS AND IMMUNOLOGICAL RESPONSE IN PATIENTS PRESENTING WITH FEVER"

INVESTIGATOR : **Dr.M. SAHANA**
First year Post Graduate,
Institute of Microbiology,
Madras Medical College,
Chennai – 600003.

GUIDE : **Dr.J.EUPHRASIA LATHA, M.D.D.G.O,**
Director and Professor ,
Institute of Microbiology,
Madras Medical College,
Chennai – 600003.

I am going identify and characterize the microbial agents causing fever and correlate the causative agent,clinical disease and fever patterns in febrile patients . I am going to collect blood samples for this study and process them accordingly.250 patients are included in this study after getting informed consent only. This study is entirely voluntary and patient can withdraw any time from this study. Extracost will not be incurred to the patients in this study. Any doubt regarding this study will be willingly clarified. Results of the study will be published. In case of any doubt please contact ,

Dr.M. SAHANA Cell:9941351162.

MASTER CHART

Sample No	NAME	AGE	SEX	Presenting complaints	Hb (g/Dl)	WBC (10/µl)	RBC (10/µl)	Hematocrit %	Platelet count (lakhs/cu.mm)	MCV	MCH	MCHC	Other investigations	Dengue IgM	Widal test	Scrub typhus IgM	MSAT-Lepto	Blood culture	IL-6	DIAGNOSIS
1	Senthamil selvan	13	Mc	Fever*1odays,cough*4days,altered sensorium*2days	9.3	17.1	4.8	42.3	2.1	77.2	26.2	27.6	USG- NORMAL	Negative	Negative	Positive	Negative	NG	23	Scrub typhus/Acute kidney injury
2	Vishal	7	Mc	Fever*2 days abdominal pain	8.2	6.8	4.55	34.1	2.2	82.4	28.3	27.9	NIL	Negative	Negative	Negative	Negative	NG	74	Acute gastroenteritis
3	Harish	13	Mc	Fever x 3days , Recurrent vomiting	8.5	6.2	4.98	38.2	0.83 (2 units transfused)	75.6	29.5	29.6	ALT-28, AST- 30, USG- normal	Positive	Negative	Negative	Negative	NG	67	Dengue hemmorrhagic fever
4	Mani	57	M	Fever*4days,Abdominal pain,dark colored stool,facial puffines	11.1	4.8	5.61	38.5	2.6	76	30.2	34.3	USG-NORMAL	Negative	Negative	Positive	Negative	NG	89	Scrub typhus/Acute renal failure
5	Indira	47	F	Fever*3days, abdominal pain, vomiting	8.3	11.1	3.83	29.1	1.3	78.2	30.8	34.1	MAT- 1: 80 dilution, icterus,USG-hydronephrosis	Negative	Negative	Negative	Positive	NG	98	Obstructive jaundice/ Leptospirosis
6	Asitha	11	Fc	Fever x 2days, chills	8.5	4.6	4.87	38.7	1.5	77.9	28.9	31.6	O-1:100, H-1:200	Negative	Positive	Negative	Negative	NG	3	Typhoid, Fever
7	Hariharan	17	M	High grade fever x 3 days, vomiting	9.1	10.1	4.91	39.2	0.24 (4 units transfused)	85.2	28.3	34.5	USG-GB thickening, ascites	Positive	Negative	Negative	Negative	NG	115	Dengue shock syndrome
8	James	23	M	Fever*6 days vomiting	9	5.9	5.98	40.3	0.69 (2 units transfused)	76.5	35.8	31.9	NIL	Negative	Negative	Negative	Negative	Escherichia coli	208	Bacteremia/ Sepsis
9	Devendiran	46	M	Fever*7days,cough, abdominal pain	12.6	12.2	4.34	39.6	1.4	85.7	32.3	32.3	USG-normal	Negative	Negative	Negative	Positive	NG	31	Leptospirosis
10	Lakshana	13	Fc	Fever*9 days	10.4	8.2	4.87	41.7	0.81(2 unit transfused)	78.1	33.4	35.9	NIL	Negative	Negative	Negative	Negative	NG	20	Acute pharyngitis
11	Kamatchi	54	F	Fever*11 days,abnominal pain	11.5	10.2	5.81	37.4	1.81	81.8	30.6	29.1	Urine C/S- Proteus vulgaris	Negative	Negative	Negative	Negative	NG	86	Urinary tract infection
12	Boopalan	28	M	Fever*10days,abdominal pain,clay colored stool	10.9	9.9	5.61	42.1	1.9	79.1	27.8	35.2	Eschar- Right infrascapular region, USG-thickened gallbladder edema/mild splenomegaly CT chest-septal thickness/bilateral pleural effusion/ARDS	Negative	Negative	positive	Negative	Pseudomonas aeruginosa- S* PT,Caz R*Cipr,Imp,Ak	226	Scrub typhus/Bilateral pleural effusion/ARDS
13	Jagan	21	M	Fever*5days, abdominal pain	10.6	13.5	3.96	34	1.7	75.2	27.9	36.1	CSF culture- Acinetbacter species, Patient - EXPIRED	Negative	Negative	Negative	Positive	NG	86	Acute meningoencephalitis/ Leptospirosis
14	Ganapathy	37	M	Fever*8 days,myalgia	7.5	9.3	4.97	36.8	1.76	80.2	29.1	27.9	Pus c/s- Staphylococcus aureus	Negative	Negative	Negative	Negative	NG	4	Type 2 DM/ Cellulitis
15	Govindhammal	63	F	High grade fever*4days, altered sensorium	10.7	12.6	5.18	33.1	63 (2units transferred)	70.1	23.4	33.4	Eschar- Right inframammary region, Neck stiffness	Negative	Negative	positive	Negative	NG	69	Scrub typhus
16	Bharath	13	Mc	Fever x 5days, bleeding gums,melena	9.5	3.9	5.13	44.2	0.27 (4 units transfused)	81.2	29.3	32.6	ALT-55, AST- 57, USG- GB thickening	Positive	Negative	Negative	Negative	NG	5	Dengue shock syndrome
17	Kumari	34	F	Fever*5 days	8.4	7.1	4.96	42.6	1.3	76.9	29.1	32.7	nil	Negative	Negative	Negative	Negative	NG	7	Perianal abscess
18	Kamalakannan	9	Mc	Fever*14 days breathlessness	9.4	11.6	5.75	36.7	2.23	77.7	32.8	30.2	Sputum C/S- NG	Negative	Negative	Negative	Negative	NG	91	Community acquired
19	Parameswari	34	F	Fever x 4days, abdominal pain	11.2	5.8	5.28	42.3	2.7	78.6	35.1	33	USG- Hepatomegaly	Positive	Negative	Negative	Negative	NG	75	Dengue hemmorrhagic fever
20	Selvaraj	19	M	Fever*6 days vomiting	10.3	5.2	4.56	39.4	2.4	82.1	31.7	27.9	nil	Negative	Negative	Negative	Negative	NG	11	Acute gastroenteritis
21	Mathialagan	27	F	Fever*8days,recurrent vomiting	9.6	9.6	5.64	36.4	2.7	79.1	27.3	30.5	nil	Negative	Negative	Negative	Negative	NG	60	Acute appendicitis
22	Vasanth	16	M	Fever x 2days, abdominal pain	9.3	8.8	5.76	35.7	2.5	78.3	30.5	33.4	O-1:100, H-1:200, Peritoneal Fluid-NG	Negative	Positive	Negative	Negative	NG	56	Typhoid, Fever/ Peritonitis
23	Rajaprasad	47	M	Fever x 6days, vomiting	10.4	6.2	5.69	43.5	1.9	79.2	32.5	27.9	USG-Pleural effusion	Positive	Negative	Negative	Negative	NG	83	Dengue hemmorrhagic fever
24	Sundaram	45	M	Fever*5 days	9.2	7.3	4.56	41.8	1.61	75.1	28	28.1	CSF C/S- NG	Negative	Negative	Negative	Negative	NG	112	Acute meningoencephalitis
25	Eshwar	28	M	Fever*12 days myalgia	9.5	10.3	5.76	38.1	1.56	80	32.9	35.3	NIL	Negative	Negative	Negative	Negative	NG	10	Chikungunya
26	Vajravel	35	M	Fever*3 days, diarrhoea	13.1	16	5.32	36.3	0.26(2units transfused)	77.6	27.1	29	USG-normal	Negative	Negative	Negative	Positive	NG	236	Leptospirosis
27	Sneha	8	Fc	Fever*7days,vomiting	9.1	3.4	4.3	44.5	0.57(2 units transferred)	78.4	28.9	30.1	USG- Hepatomegaly	Positive	Negative	Negative	Negative	NG	111	Dengue shock syndrome
28	Divya	18	F	High grade fever x 2 days, joint pain	10.5	6.8	5.26	37.3	1.4	85.6	35.7	28.6	USG- normal	Positive	Negative	Negative	Negative	NG	11	Dengue hemmorrhagic fever
29	Diwakar	14	Mc	Fever*6day	9	11	4.87	36.7	1.7	76.8	33.1	32.9	nil	Negative	Negative	Negative	Negative	NG	6	Acute pharyngitis
30	Chandran	54	M	Fever*4 days, headache	9.6	17	5.26	36.1	1.8	77.1	26.3	28.1	USG-normal, serum total bilirubin-elevated	Negative	Negative	Negative	Positive	NG	111	Leptospirosis/ Bilateral pyelonephritis/ Chronic kidney disease/Acute viral
31	Dhanalakshmi	59	F	Fever*11days,breathlessness	10.5	9.1	5.43	42.5	0.46 (2 units transfused)	79.1	32.1	29.1	NIL	Negative	Negative	Negative	Negative	Klebsiella pneumoniae	272	Type 2 DM/Bacteremia/ Sepsis
32	Suganya	12	Fc	Fever*8days,giddiness	10.4	7.7	5.67	35.3	1.63	80.2	34.6	27.9	CSF C/S- NG	Negative	Negative	Negative	Negative	NG	105	Acute meningitis
33	Suresh	23	M	Fever*6days,abnominal pain	10.9	5.9	4.32	34.5	1.85	83.8	29.8	34.6	NIL	Negative	Negative	Negative	Negative	NG	5	Acute diarrheal disease
34	Suriya	22	F	Fever x 3days, abdominal pain	9.6	7.1	5.68	39.2	0.46 (4 units transfused)	83.9	29.5	30.5	USG-Pleural effusion	Positive	Negative	Negative	Negative	NG	96	Dengue shock syndrome

Sample No	NAME	AGE	SEX	Presenting complaints	Hb (g/Dl)	WBC (10/µl)	RBC (10/µl)	Hematocrit %	Platelet count (lakhs/cu.mm)	MCV	MCH	MCHC	Other investigations	Dengue IgM	Widal test	Scrub typhus IgM	MSAT-Lepto	Blood culture	IL-6	DIAGNOSIS
35	Niranjan	8	Mc	Fever*9 days	10.2	9.2	5.43	36.8`	1.67	78.6	31.5	34.5	NIL	Negative	Negative	Negative	Negative	NG	45	Acute tonsillitis
36	Murugesan	29	M	Fever*4 days,myalgia	9.3	6.6	5.83	40.5	1.32	79.5	29.1	33.9	NIL	Negative	Negative	Negative	Negative	NG	78	Chikungunya
37	Vishwanath	17	M	Fever x 2days , chills	10.3	5.4	5.12	42.6	1.6	82.6	28.3	31.5	PS- Positive for Plasmodium vivax	Negative	Negative	Negative	Negative	NG	7	Malaria
38	Gowri	32	F	Fever*12 days myalgia	9	8.5	4.21	36.4	1.89	83.9	30.1	27.5	NIL	Negative	Negative	Negative	Negative	NG	85	Acute febrile illness
39	Karthiga	12	Fc	Fever*10 days,giddiness	10.3	9.1	5.35	41.3	1.3	76.2	27.8	29.4	CSF C/S- NG	Negative	Negative	Negative	Negative	NG	8	Acute meningoencephalitis
40	Mani	62	M	Fever*9 days,vomiting	10.4	8.4	5.46	37.8	2.2	78.2	32.8	28.9	nil	Negative	Negative	Negative	Negative	NG	96	Acute gastroenteritis
41	Kiran	8	Mc	Fever*8days, giddiness	9.4	26	5.01	37.8	1.6	76.1	28.1	35.2	USG-Normal	Negative	Negative	Negative	Positive	Entercoccus species	10	Leptospirosis
42	Sownderiya	43	F	Fever x 3days, vomiting	10.6	10.1	4.95	43.3	1.4	81.6	31.5	33.6	USG- hepatomegaly	Positive	Negative	Negative	Negative	NG	64	Dengue hemmorrhagic fever
43	Veerammal	32	F	Fever*13 days	9.3	9.1	4.63	36.5	2.12	76.1	34.1	31.9	Sputum C/S- NG	Negative	Negative	Negative	Negative	NG	35	Community acquired
44	Varun	64	M	Fever*6days, vomiting, diarrhoea	9.7	10.8	4.1	34.8	1.6	80.6	28.1	34.8	Eschar- Right mammary gland	Negative	Negative	positive	Negative	NG	261	Scrub typhus/Type-II DM / CAD
45	Beeman	54	M	Low grade fever*5days, abdominal pain	8.8	11.6	4.6	29.1	68 (2units transferred)	81.7	27.3	33.5	Eschar- lower end of sternum	Negative	Negative	Positive	Negative	NG	56	Scrub typhus
46	Rajasekar	24	M	Fever*10days,myalgia	9.6	11.7	4.97	35.7	1.96	82.9	32.5	32.3	Chikungunya IgM- Positive	Negative	Negative	Negative	Negative	NG	3	Chikungunya
47	Vivek	25	M	Fever x 3days, abdominal pain	11.6	5.6	5.65	44.1	0.69 (2 units transfused)	79.2	33.5	35	USG-GB thickening	Positive	Negative	Negative	Negative	NG	107	Dengue hemmorrhagic fever
48	Kelvin	7	Mc	Fever*3 days	8.2	8.5	4.97	36.1	1.54	77.1	28.1	28.1	Pus c/s- Staphylococcus aureus	Negative	Negative	Negative	Negative	NG	65	Septic arthritis
49	Veerapan	43	M	Fever x 2days, chills	9.2	9.8	5.67	39.8	2.6	83.7	31.7	31.8	O-1:200, H-1:400	Negative	Positive	Negative	Negative	NG	89	Typhoid, Fever
50	Palani	29	M	Fever*8days,cough	10.5	5.6	5.78	36.7	1.67	82.8	27.9	27.7	H1N1 PCR- Positive	Negative	Negative	Negative	Negative	NG	5	Swine flu
51	Ashok	18	M	Fever*9 days,vomiting	9.5	7.2	4.67	42.7	0.84 (2 units transfused)	76	29.6	29.6	NIL	Negative	Negative	Negative	Negative	NG	9	Acute febrile illness
52	Sakthivel	30	M	Fever*6days,breathlessness	9.3	9.4	5.56	40.9	1.36	82.7	28.6	30.9	nil	Negative	Negative	Negative	Negative	NG	96	COPD- Acute exacerbation
53	Velu	38	M	Fever x 3days, diarrhoea	8.4	8.9	5.32	40.6	0.26 (4 units transfused)	77	31.5	33.9	USG-Hepatomegaly	Positive	Negative	Negative	Negative	NG	77	Dengue shock syndrome
54	Banu	10	Fc	Fever*3 days,cough	9.9	6.2	4.57	36.4	1.7	81.7	33.2	27.8	NIL	Negative	Negative	Negative	Negative	NG	45	Acute pharyngitis
55	Santha Lakshmi	32	F	High grade fever*5 days, vomiting,abdominal pain	8.1	7.9	3.56	33.4	18 (4 units transferred)	76	29.4	34.3	Eschar- Right infraclavicular region, Patient- EXPIRED	Positive	Negative	positive	Negative	NG	234	ARDS/ Pulmonary edema/ Dengue hemorrhagic fever with scrub typhus
56	Mathivanan	56	M	Fever*8 days,abnominal pain	10.4	10.4	4.32	35.2	1.81	83.9	35.7	29.6	NIL	Negative	Negative	Negative	Negative	NG	8	Acute gastroenteritis
57	Lalitha	19	F	Fever*14 days breathlessness	10.4	9.6	4.91	42.7	1.2	76.9	29.5	28.8	nil	Negative	Negative	Negative	Negative	NG	85	Acute exacerbation of
58	Kuppammal	37	F	Fever*8 days	9.5	6.8	5.77	33.6	1.6	75.1	28.1	35.7	pus c/s- NG	Negative	Negative	Negative	Negative	NG	4	Cellulitis
59	Sivakumar	19	M	High grade fever*7days, breathlessness	8.6	23.1	4.91	39.3	1.91	72.2	27.1	33.6	USG-Normal, CSF culture- Escherichia coli	Negative	Negative	Negative	Positive	NG	119	Septic meningitis/ Leptospirosis
60	Nithish	11	Mc	Fever*4days,cough	9.4	10.3	5.55	37.9	1.91	83.5	30.1	32.9	NIL	Negative	Negative	Negative	Negative	NG	112	Acute exacerbation of
61	Jaya	45	F	Fever*8days,abdominal pain	9.3	9.6	4.81	36.1	1.67	76.9	34.1	30.6	Urine C/S- Escherichia coli	Negative	Negative	Negative	Negative	NG	253	Urinary tract infection
62	Munna	22	M	Fever*5 days,abnominal pain	10.5	6.8	4.94	35.7	1.4	78.2	29.4	28.4	nil	Negative	Negative	Negative	Negative	NG	5	Acute gastroenteritis
63	Ammu	34	F	Fever x 2days, abdominal pain	9.2	9.8	5.41	39.3	1.5	81.2	28.9	29.5	USG- Hepatomegaly	Positive	Negative	Negative	Negative	NG	88	Dengue hemmorrhagic fever
64	Balu	35	M	Fever*11 days,giddiness	9.8	9.3	5.56	34.8	1.58	75.9	28.5	27.9	CSF C/S- NG	Negative	Negative	Negative	Negative	NG	37	Acute meningitis
65	Sathya	56	F	Fever*4days,vomiting	9.5	7.9	4.78	37.6	1.6	82.9	30.7	29.3	Urine C/S- Klebsiella pneumoniae	Negative	Negative	Negative	Negative	NG	103	Urinary tract infection
66	Vignesh	37	M	Fever*5days,rashes, epistaxis	10.3	17	4.09	38.1	2.2	76.9	29.7	27.9	USG- normal	Positive	Negative	Negative	Positive	NG	98	Dengue hemmorrhagic
67	Anu	8	Fc	Fever*5days,cough	10.1	8.3	5.72	40.5	1.2	79.2	34.1	28.3	nil	Negative	Negative	Negative	Negative	NG	7	Acute exacerbation of
68	Srikanth	37	M	Fever x 2days, rigor	9.1	5.9	4.87	36.3	2.9	81.3	33.9	32.6	O-1:200, H-1:200, CSF C/S-NG, CSF-glucose-61mg/dL, protein-106.4mg/dL	Negative	Positive	Negative	Negative	NG	36	Typhoid, Fever/Acute Meningoencephalitis/ Septic Shock
69	Kalyani	34	F	Fever*9days	8.7	11	4.78	32.7	2.4	80.2	32.9	31.8	nil	Negative	Negative	Negative	Negative	NG	119	Type 2 DM/ Sepsis
70	Vetrivel	27	M	Fever*5 days,breathlessness	11.1	9.3	4.98	41.7	0.98	75.9	27	29.5	nil	Negative	Negative	Negative	Negative	NG	9	COPD- Acute exacerbation
71	Nagalakshmi	33	F	Fever*8days, breathlessness	8.9	16.5	4.32	40.1	1.86	75.1	27.3	28.5	HbsAg & HCV- Negative	Negative	Negative	Negative	Positive	NG	28	Leptospirsis/ Bilateral pneumonia
72	Mohammed Kasim	65	M	Fever*4days,breathlessness,abdominal pain	8.2	8.6	5.09	38.5	44 (2 units transferred)	79.2	27.5	29.7	Electrolytes- Na(142.4 mmol/L),K (3.2 mmol/L), Cl (106.8 mmol/L), Urea-43mg/dL, Creatinine - 3.1 , PATIENT EXPIRED	Positive	Negative	positive	Negative	Entercoccus species	8	Acute pulmonary edema/ Bronchpneumonia/ SHTN/ Type II-DM, Dengue hemorrhagic fever with scrub typhus
73	Sanjay	15	Mc	Fever*7days	9.4	7.2	5.67	37.8	1.3	82.6	34.6	34.9	NIL	Negative	Negative	Negative	Negative	NG	5	Perianal abscess
74	Mohammed basha	60	F	Fever*8 days ,abnominal pain	10.4	6.7	5.36	39.6	1.7	82	28.6	35.7	Urine C/S- Escherichia coli	Negative	Negative	Negative	Negative	NG	49	Urinary tract infection

Sample No	NAME	AGE	SEX	Presenting complaints	Hb (g/Dl)	WBC (10/µl)	RBC (10/µl)	Hematocrit %	Platelet count (lakhs/cu.mm)	MCV	MCH	MCHC	Other investigations	Dengue IgM	Widal test	Scrub typhus IgM	MSAT-Lepto	Blood culture	IL-6	DIAGNOSIS
75	Raghul raj	21	M	Fever*7days,cough	10.9	5.9	4.76	40.2	1.12	76.1	32.6	31.7	PUS c/s- Proteus mirabilis	Negative	Negative	Negative	Negative	NG	79	Septic arthritis
76	Rajendran	56	M	Fever*4 days,giddiness	9.4	4.8	5.26	38.6	1.56	82.7	31.5	29.3	nil	Negative	Negative	Negative	Negative	NG	4	Acute meningoencephalitis/
77	Rose	67	F	Fever x 4days, vomiting	8.2	6.5	5.42	38.7	1.3	85.1	27.8	27.3	USG- normal	Positive	Negative	Negative	Negative	NG	69	Dengue hemmorrhagic fever
78	Vanitha	37	F	Fever*6days,vomiting	9.6	5.1	5.62	41.2	0.54 (2 units transfused)	76.9	30.6	28.5	Urine C/S- Escherichia coli	Negative	Negative	Negative	Negative	NG	6	Urinary tract infection
79	Maran	32	M	Fever*5days,myalgia	9.5	9.4	4.79	34.6	1.6	83.4	35.2	32.7	Chikungunya IgM- Positive	Negative	Negative	Negative	Negative	NG	98	Chikungunya
80	Ananya sree	23	F	Fever*10 days,giddiness	10	10.3	4.98	33.2	2.4	78.3	29.4	31.9	NIL	Negative	Negative	Negative	Negative	NG	56	Acute febrile illness
81	Sathish	31	M	Fever*8days,vomiting	10.4	9.4	5.21	39.4	1.8	81	32.1	28.4	Urine C/S- Proteus vulgaris	Negative	Negative	Negative	Negative	NG	7	Urinary tract infection
82	Kalimuthu	29	M	High grade fever x 3 days, chills	9.3	6.8	5.45	40.4	1.63	78.4	28.4	31.7	USG- pleural effusion with ascites	Positive	Negative	Negative	Negative	NG	60	Dengue hemmorrhagic fever
83	Harichander	12	Mc	Fever*7 days	10.7	5.1	5.18	31.6	2.3	78	32.9	27.4	Urine C/S- Escherichia coli	Negative	Negative	Negative	Negative	NG	5	Urinary tract infection
84	Saravanan	35	M	Fever*8days,abdominal pain	9.9	13.6	5.79	37.7	1.9	80.4	30.3	32.7	USG-normal	Positive	Negative	Negative	Positive	NG	70	Dengue hemmorrhagic
85	Priyanka	29	F	Fever*8days	9.7	8.4	4.78	33.8	1.5	80.2	30.1	29.7	BAL C/S- Klebsiella pneumoniae	Negative	Negative	Negative	Negative	NG	96	Community acquired pneumonia
86	Jayanth	16	M	Fever*7days,malgia	9.9	6.7	5.27	32.6	1.8	83.4	34.7	28.9	nil	Negative	Negative	Negative	Negative	NG	9	Acute febrile illness
87	Aruna Chalam	42	M	Low grade fever*3days, vomiting, convulsions	9.2	12.1	3.8	26.4	89	91.1	33.1	35.5	Known alcoholic/ bilateral pedal edema	Negative	Negative	positive	Negative	NG	272	Alcoholic liver disease/ Obstructive jaundice / Scrub typhus
88	Saranya	63	F	Fever*5 days,abnominal pain	10.1	11.5	5.23	39.5	1.45	77.2	29.4	30.4	nil	Negative	Negative	Negative	Negative	NG	25	Ureteric calculi
89	Sandeep	9	Mc	Fever*9days	9.6	4.6	5.15	33.2	1.9	79.6	27.4	35	nil	Negative	Negative	Negative	Negative	NG	3	Acute follicular tonsillitis
90	Perumal	35	M	Fever*7days,cough	9.1	8.1	4.98	34.7	1.63	82.9	29.4	32.6	nil	Negative	Negative	Negative	Negative	NG	4	COPD- Acute exacerbation
91	Ramasami	40	M	Fever x 2days, chills	10.4	9.3	5.76	31.6	3.3	75.8	35.8	31.9	O-1:100, H-1:200, Sputum- C/S- NG	Negative	Positive	Negative	Negative	NG	73	Typhoid, Fever
92	Yamuna	25	F	Fever*5days,giddiness	10.3	8.9	4.45	32.3	1.8	83	32.8	31.6	nil	Negative	Negative	Negative	Negative	NG	9	Acute meningitis
93	Deepika	8	Fc	Fever*6days	9.4	4.7	4.98	36.7	2.2	77.2	30.3	29.4	nil	Negative	Negative	Negative	Negative	NG	103	Acute follicular tonsillitis
94	Balamohan	60	M	Fever*6 days,cough	11	6.8	5.78	35.6	1.9	76.1	34.5	27.9	nil	Negative	Negative	Negative	Negative	NG	10	Acute exacerbation of
95	Venu Gopal	40	M	Fever*6 days, difficulty in breathing	9.8	14.7	4.48	36.1	76	83.9	30.4	36.2	Bleeding gums, Eschar- Left axilla, USG- pleural effusion with ascites	Positive	Negative	Positive	Negative	NG	18	Dengue hemorrhagic fever with Scrub typhus/ Alcoholic liver disease
96	Manoj	32	M	Fever*4days, bodyache	11.1	15.6	4.23	36.9	1.4	79.2	32.2	26.1	USG-GB thickening	Positive	Negative	Negative	Positive	NG	83	Dengue hemmorrhagic
97	Jeeva sree	40	F	Fever*11days,breathlessness	8.3	9.2	5.24	41.7	0.86	80.3	31.9	28.1	NIL	Negative	Negative	Negative	Negative	Escherichia coli	253	SEPSIS/Type 2 DM
98	Ajith	20	M	Fever*3days,myalgia	9.6	10.7	5.11	33.2	1.32	83.1	29.8	34.9	H1N1 PCR- Positive	Negative	Negative	Negative	Negative	NG	36	Swine flu
99	Sangeetha	25	F	Fever*7days, breathlessness	9.1	7.9	3.09	32.3	1.1	78.7	29.4	34.3	Eschar- left infraclavicular region	Negative	Negative	positive	Negative	NG	112	Scrub typhus
100	Poongodi	52	F	Fever*8days,vomiting	9.3	5.9	4.55	37.8	2.4	79.4	33	30.4	nil	Negative	Negative	Negative	Negative	NG	89	Acute gastroenteritis
101	Muniyammal	48	F	Fever*5days, bleeding gums	8.1	10.3	2.86	41.9	13(4 units transferred)	88.5	28.1	31.6	Melena, Signs of shock -present, CT chest- Pneumthorax , PATIENT EXPIRED	Positive	Negative	positive	Negative	Klebsiella pneumoniae	5	Dengue shock syndrome with Scrub typhus/CAD/ CKD/SHTN
102	Deepan	28	M	Fever*11days	9.9	7.6	4.78	32.5	2.3	72	32.8	32	Pus C/S- ng	Negative	Negative	Negative	Negative	NG	5	Cellulitis
103	Damodharan	29	M	Fever*7 days	10.5	8.5	4.99	33.4	2.14	82.4	29.7	34.8	nil	Negative	Negative	Negative	Negative	NG	11	Acute exacerbation of
104	Tamil Arasu	38	M	Fever x 1day, abdominal pain	10.5	5.5	5.55	36.1	3.6	79.4	31.7	32.9	O-1:200, H-1:200	Negative	Positive	Negative	Negative	Salmonella Typhi	212	Typhoid, Fever
105	Ifran Ahamed	11	Mc	Fever*6days,cough	9.5	4.9	4.76	35.7	1.9	79.3	27.7	31.8	ET Aspirate- Acinetbacter species	Negative	Negative	Negative	Negative	NG	263	Community acquired pneumonia
106	Kumar	58	M	Fever*8days,abdominal pain	7.2	17.1	5.63	39.1	0.51(2units transfused)	76.9	27.9	27	USG- Hepatomegaly, pleural effusion	Positive	Negative	Negative	Positive	NG	90	Dengue shock syndrome/Leptospirosis
107	Anjali	26	F	Fever*4days,altered sensorium	9.3	14.9	4.21	37.8	0.95	81.5	28.1	29	USG-normal	Positive	Negative	Negative	Positive	NG	29	Dengue hemmorrhagic fever/ Leptospirosis
108	Arun Kumar	34	M	Fever*3days, bleeding gums	8.7	19.2	5.32	38.8	1.1	79.3	30.6	30	USG-GB Thickening	Positive	Negative	Negative	Positive	NG	115	Dengue hemmorrhagic
109	Venda	39	F	Fever*5 days,abdominal pain	9.3	7.9	5.86	33.1	2.3	80.4	29.1	32.4	Urine C/S- Escherichia coli	Negative	Negative	Negative	Negative	NG	65	Urinary tract infection
110	Kaviraj	28	M	Fever*6dayss,giddiness	9.1	9.6	5.86	32.6	2.54	78	32.8	29.4	nil	Negative	Negative	Negative	Negative	NG	7	Acute febrile illness
111	Ramesh	44	M	High grade fever x 4 days, abdominal pain	10.3	9.2	5.65	43.7	1.51	81.7	32.5	32.8	USG-normal	Positive	Negative	Negative	Negative	NG	23	Dengue hemmorrhagic fever
112	Amritha	9	Fc	Fever*10 days	10.9	5	4.56	34.7	2.8	82.9	34.8	30.1	nil	Negative	Negative	Negative	Negative	NG	9	Acute febrile illness
113	Venkatachalam	54	M	Fever*5 days,abdominal pain	10.4	4.9	4.68	40.3	1.23	78.9	35.1	32.8	NG	Negative	Negative	Negative	Negative	NG	256	Urinary tract infection
114	Rangasamy	49	M	Fever*10 days myalgia	10.5	7.7	4.97	36.9	2.7	75.2	29.4	35.9	nil	Negative	Negative	Negative	Negative	NG	76	Viral hepatitis
115	Kamala	56	F	Fever*14 days, rigor	9.7	9.1	4.79	42.8	0.48 (2 units transfused)	80.2	26.1	27	PS- Positive for Plasmodium vivax	Negative	Negative	Negative	Negative	NG	46	Malaria
116	Gopalakrishnan	36	M	Fever*9days	9.9	11.3	4.76	31.5	2.8	79.4	28.9	29.4	nil	Negative	Negative	Negative	Negative	NG	5	Acute febrile illness
117	Revathy	36	F	Fever*11 days,vomiting	10.2	10.5	5.78	.32.4	2.3	76.9	31.4	28.6	Pus C/S- NG	Negative	Negative	Negative	Negative	NG	58	Septic arthritis
118	Elumalai	34	M	Fever*7 days,myalgia	9.7	8.6	4.95	33.5	2.1	80.4	30.1	30.2	nil	Negative	Negative	Negative	Negative	NG	3	Acute febrile illness

Sample No	NAME	AGE	SEX	Presenting complaints	Hb (g/Dl)	WBC (10/µl)	RBC (10/µl)	Hematocrit %	Platelet count (lakhs/cu.mm)	MCV	MCH	MCHC	Other investigations	Dengue IgM	Widal test	Scrub typhus IgM	MSAT-Lepto	Blood culture	IL-6	DIAGNOSIS
119	Parameshwaran	64	M	Fever x 1day, abdominal pain	9.8	13.5	5.03	34.2	1.3	77.1	28.5	34.8	USG-normal	Negative	Negative	Negative	Positive	NG	76	Leptospirosis
120	Durairaj	50	M	Fever x 4days, abdominal pain	11.5	5.6	4.98	43.0	0.40 (4 units transfused)	79.5	32.6	29.8	USG-Pleural effusion	Positive	Negative	Negative	Negative	NG	74	Dengue shock syndrome
121	Datschnamoorthy	10	Mc	Fever*5days,cough	9.1	5.9	4.68	31.4	1.9	80.2	28.9	27.4	nil	Negative	Negative	Negative	Negative	NG	36	Acute exacerbation of
122	Dinashree	29	F	Fever*7days,breathlessness	9.5	8.6	5.12	43.6	0.67 (2 units transfused)	76.5	27	28.6	nil	Negative	Negative	Negative	Negative	NG	88	Acute exacerbation of Bronchial asthma
123	Varsha	14	Fc	Fever*5 days	9	4.2	4.03	34.5	1.8	79.3	31.5	34.8	Urine C/S- Escherichia coli	Negative	Negative	Negative	Negative	NG	228	Urinary tract infection
124	Bavani	62	F	Fever*5days,abdominal pain	10.5	8.4	5.98	35.7	2.3	83	34.8	30.1	nil	Negative	Negative	Negative	Negative	NG	8	Acute gastroenteritis
125	Kavitha	29	F	Fever*5 days, oliguria	11.3	14.5	5.19	36.8	1.5	77.9	32.4	28,4	USG-normal	Positive	Negative	Negative	Positive	NG	58	Dengue hemmorrhagic
126	Anand kumar	43	M	Fever*8days,cough	10.3	9.5	4.56	36.1	1.6	79.3	29.8	32	nil	Negative	Negative	Negative	Negative	NG	9	COPD- Acute exacerbation
127	Kaveri	27	F	Fever*6 days,vomiting	9.2	10.5	4.32	35.6	2.4	75.1	34.8	34.9	nil	Negative	Negative	Negative	Negative	NG	6	Acute appendicitis
128	Valarmathi	36	F	Fever*9days	9.3	8.5	5.78	32.5	2.6	81.7	35.9	35.1	Urine C/S- Proteus vulgaris	Negative	Negative	Negative	Negative	NG	96	Urinary tract infection
129	Arun vijay	26	M	Fever*4days,myalgia	10.8	9.3	4.51	31.6	2.2	82.5	31.9	29.5	nil	Negative	Negative	Negative	Negative	NG	56	Acute febrile illness
130	Vadivelu	34	M	Fever*13 days	10.6	8.5	5.18	34.8	1.8	76.2	30.1	27.4	Pus c/s- Staphylococcus aureus	Negative	Negative	Negative	Negative	NG	7	Osteomyelitis
131	Sudharsan	27	M	Fever*7days, melena-2 episodes	9.1	16.2	4.23	36.2	1.6	79.4	30.1	32	USG- Hepatomegaly	Positive	Negative	Negative	Positive	NG	82	Dengue hemmorrhagic fever/Leptospirosis
132	Anbarasi	46	F	Fever x 3days, vomiting	9.2	15	5.01	34.7	1.8	76.2	34.7	33.7	Elevated bilirubin	Negative	Negative	Negative	Positive	NG	201	
133	Amala	48	F	Fever*7days,abdominal pain	9.7	11.7	5.16	38.9	2.1	77.8	28.5	28.2	Urine C/S- Escherichia coli	Negative	Negative	Negative	Negative	NG	112	Urinary tract infection
134	Velmurugan	64	M	Fever*5days	10.7	9.5	4.17	34.1	2.45	76.1	29.1	29.3	Pus C/S- NG	Negative	Negative	Negative	Negative	NG	9	Osteomyelitis
135	Shanthi	38	F	Fever*9 days,vomiting	9.8	6	4.65	37.6	2.32	83.4	34.7	35.2	Pus C/S- NG	Negative	Negative	Negative	Negative	NG	74	Septic arthritis
136	Harshiv	11	Mc	Fever*3 days,cough	10.5	4.9	4.32	40.8	1.2	80.1	32.8	33.2	nil	Negative	Negative	Negative	Negative	NG	5	Acute exacerbation of
137	Chandrika	38	F	Fever*8days,abdominal pain	9.5	8.2	5.21	41.5	1.14	76.2	30.3	34.1	Urine C/S- Escherichia coli	Negative	Negative	Negative	Negative	NG	25	Urinary tract infection
138	Venkat prabhu	26	M	Fever*8days,myalgia	10.4	9.9	4.85	36.4	2.4	80.4	34.8	28.6	nil	Negative	Negative	Negative	Negative	NG	98	Acute febrile illness
139	Vivekanandhan	42	M	Fever*4 days,giddiness	9.8	10.5	4.65	37.5	1.8	76.3	35.1	27.5	CSF C/S- NG	Negative	Negative	Negative	Negative	NG	229	Acute meningoencephalitis
140	Ponni	28	F	Fever x 3days, vomiting	9.2	4.9	4.01	36.7	3.6	83.5	35.9	29.1	O-1:200, H-1:400	Negative	Positive	Negative	Negative	NG	49	Typhoid, Fever
141	Dilfar	45	F	Fever*10days, breatthlessness	9.5	7.9	5.03	42.6	0.89	83.7	29.8	29.5	Sputum C/S- NG	Negative	Negative	Negative	Negative	NG	6	Community acquired pneumonia
142	Raja	24	M	Fever x 3days, vomiting	10.2	18.7	5.15	31.7	1.9	80.5	32.8	35.3	USG-normal	Negative	Negative	Negative	Positive	NG	78	Leptospirosis
143	Monika	8	Fc	Fever*8 days	10.6	11.5	5.61	34.6	1.32	79.3	30.4	34.9	NIL	Negative	Negative	Negative	Negative	NG	4	Pharyngitis
144	Muthusamy	36	M	Fever*5 days,vomiting	10.9	8.7	5.45	37.1	2.4	78.2	27	32.8	nil	Negative	Negative	Negative	Negative	NG	101	Acute gastroenteritis
145	Rajamani	59	M	Fever*12 days myalgia	9.5	7.4	4.65	35.4	2.1	76.1	28.4	31.4	nil	Negative	Negative	Negative	Negative	NG	8	Acute febrile illness
146	Subramani	55	M	Fever x 4days, vomiting	9.0	5.7	4.96	41.1	0.74 (2 units transfused)	81.5	31.1	27.3	USG-GB thickening	Positive	Negative	Negative	Negative	NG	103	Dengue shock syndrome
147	Praabhu	36	M	Fever x 3days, vomiting	10.2	9.1	4.75	37.1	2.9	82.6	30.5	33.2	Eschar- Right mammary gland	Negative	Negative	Positive	Negative	NG	45	Scrub typhus
148	Janaki	30	F	Fever*6days,abnominal pain	9.6	8.6	4.61	39.7	2.8	82.3	29.4	29.5	Urine C/S- Klebsiella pneumoniae	Negative	Negative	Negative	Negative	NG	9	Urinary tract infection
149	Sidharthan	33	M	Fever*11days,breathlessness	9.2	4.7	5.46	41.3	1.4	80.2	32.7	27.9	nil	Negative	Negative	Negative	Negative	NG	36	COPD- Acute exacerbation
150	Krishnaveni	58	F	Fever*10days	10.6	6.9	4.13	32.4	2.3	78.1	33.3	28.4	NIL	Negative	Negative	Negative	Negative	NG	99	Type 2 DM/ Osteomyelitis
151	Dhanush	9	Mc	Fever x 3days, vomiting	9.5	5.2	5.21	31.6	3.6	80.4	28.9	36.2	O-1:200, H-1:200 , Urine C/S- Escherichia Coli ESBL	Negative	Positive	Negative	Negative	Salmonella Typhi	241	Typhoid, Fever/ Ureteric calculi
152	Sandhya	23	F	Fever x 3days, vomiting	8.9	16.9	4.75	34.5	0.43 (2units transfused)	76.9	27.9	34.3	USG-normal	Negative	Negative	Negative	Positive	NG	48	Leptospirosis
153	Deva rajan	32	M	Fever*14 days breathlessness	10.5	8.9	4.25	41.3	1.45	76.1	35	34.6	nil	Negative	Negative	Negative	Negative	NG	4	Acute exacerbation of
154	Pooja	23	F	Fever*5days,cough	10.4	7.1	5.36	35.7	2.5	79.2	29.1	32.3	nil	Negative	Negative	Negative	Negative	NG	10	Acute pharyngitis
155	Reshma	27	F	Fever*12 days myalgia	11	4.9	5.21	34.5	2.7	80.2	27.9	30.5	Pus C/S- NG	Negative	Negative	Negative	Negative	NG	89	Septic arthritis
156	Selvi	37	F	High grade fever*5days, intermittent, cough	11	5.4	4.75	37.5	1.8	77.6	29.6	27.1	USG-normal	Positive	Negative	Positive	Negative	NG	3	Dengue hemmorrhagic fever/scrub typhus
157	Anbarassu	50	M	Fever*8days,abdominal pain	9.7	10	4.13	37.8	2.1	83.2	31.7	33.8	Urine C/S- Escherichia coli	Negative	Negative	Negative	Negative	NG	231	Urinary tract infection
158	Amsaveni	52	F	Fever*8days,giddiness	9.5	9.3	4.36	36.7	1.95	76.2	28.8	31.6	CSF C/S- NG	Negative	Negative	Negative	Negative	NG	5	Meningitis/ Septic shock
159	Kannan	24	M	Fever*6days, abdominal pain	10	17.8	5.62	38.9	0.9	80.2	28.1	28.9	USG- Hepatomegaly	Positive	Negative	Negative	Positive	NG	257	Dengue hemmorrhagic
160	Gowtham	34	M	Fever*6 days,abdominal pain	9.2	7.5	5.25	41.2	0.87	80.4	27.1	29.5	Urine C/S- Proteus vulgaris	Negative	Negative	Negative	Negative	NG	25	Urinary tract infection
161	Selvam	63	M	Fever*9days	10.7	4.7	5.06	33.2	1.3	76.3	26.9	27.3	Pus c/s- Pseudomonas aeruginosa	Negative	Negative	Negative	Negative	NG	6	Type 2 DM/ Osteomyelitis
162	Sivani	7	Fc	Fever*4days	10.4	6.4	5.47	31.8	2.4	83.5	31.9	29.5	nil	Negative	Negative	Negative	Negative	NG	77	Acute pustular tonsillitis
163	Easwari	63	F	Fever*8days,abdominal pain	9.5	8.1	4.88	42.4	0.16 (4 units transfused)	78.5	30.6	32.1	USG-GB thickening	Positive	Negative	Negative	Negative	NG	84	Dengue shock syndrome
164	Kumudha	39	F	Fever*10 days myalgia	9.5	9.1	4.49	34.6	2.8	79.2	28.1	31.5	nil	Negative	Negative	Negative	Negative	NG	7	Acute febrile illness

Sample No	NAME	AGE	SEX	Presenting complaints	Hb (g/Dl)	WBC (10/µl)	RBC (10/µl)	Hematocrit %	Platelet count (lakhs/cu.mm)	MCV	MCH	MCHC	Other investigations	Dengue IgM	Widal test	Scrub typhus IgM	MSAT-Lepto	Blood culture	IL-6	DIAGNOSIS
165	Gunasekar	23	M	Fever x 3days, vomiting	8.1	8.3	5.21	32.8	2.6	78.4	29.5	33.3	Eschar- Right infraclavicular region	Negative	Negative	Positive	Negative	NG	101	Scrub typhus
166	Kumaravel	52	M	Fever*11 days,vomiting	9.5	10.5	4.35	39.6	1.32	76.3	29.6	35.8	nil	Negative	Negative	Negative	Negative	NG	41	Acute gastroenteritis
167	Baghyalakshmi	61	F	Fever*9days,abdominal pain	10.3	8.9	4.87	38.5	1.1	82.6	30.6	33.7	Urine C/S- Escherichia coli	Negative	Negative	Negative	Negative	NG	9	Urinary tract infection
168	Narmadha	35	F	Fever*10days,giddines	10.2	5.8	5.06	33.8	2.3	83.1	34.4	31.6	nil	Negative	Negative	Negative	Negative	NG	95	Acute meningoencephalitis
169	Vasanthi	38	F	High grade fever x 5 days, vomiting	9.8	6.5	5.12	43.7	2.3	79.2	29.5	34.6	USG- normal	Positive	Negative	Negative	Negative	NG	27	Dengue hemmorrhagic fever
170	Kuppan	54	M	Fever x 3days, vomiting	10.9	16.5	4.25	34.6	1.1	76.9	28.6	36.1	USG-normal	Negative	Negative	Negative	Positive	NG	5	Leptospirosis
171	Thulasi mani	30	M	Fever*8 days, vomiting	9.6	5.4	5.78	41.5	0.95	77.9	28	35.7	CSF C/S- NG	Negative	Negative	Negative	Negative	Escherichia coli	212	Septic meninigitis
172	Surjith	10	Mc	Fever*9days	9.3	8.6	5.63	34.1	2.2	78.2	29.5	31.4	nil	Negative	Negative	Negative	Negative	NG	8	Acute tonsillitis
173	Prakash	32	M	Fever*5days,cough	10.8	5.7	4.1	33.7	2.51	81.7	32.9	30.2	nil	Negative	Negative	Negative	Negative	NG	5	Acute exacerbation of
174	Bubal	28	M	Fever x 6days, abdominal pain	8.8	8.3	4.86	38.3	0.54 (2 units transfused)	82.1	33.5	29.7	USG- normal	Positive	Negative	Negative	Negative	NG	96	Dengue shock syndrome
175	Keerthi	10	Fc	Fever*4days,myalgia	9.4	21	5.89	32.9	1.5	82.5	30.5	29.7	USG-normal	Negative	Negative	Negative	Positive	NG	32	Leptospirosis
176	Arrumugam	37	M	Fever*13 days	9.1	5.7	5.36	34.7	2.7	76	35	28	Pus C/S- NG	Negative	Negative	Negative	Negative	NG	65	Cellulitis
177	Maheshwari	19	F	Fever*8days, altered sensorium	9.7	8.6	4.75	39.4	1.71	77.7	29.9	29	USG-Normal, CK > 2000, CKMB 125 , LDH 592, EF 24%, ECHO- Dilated Cardiomyapathy/ Severe LV Systolic Dysfunction, Patient- EXPIRED	Positive	Negative	Positive	Negative	NG	35	Dengue hemmorrhagic fever/scrub typhus/Myocarditis/ Cardiogenic shock
178	Roshan	14	Mc	Fever*10days,myalgia	10.3	11.8	4.78	36.4	2.4	76.8	34.8	31.6	nil	Negative	Negative	Negative	Negative	NG	6	Acute febrile illness
179	Amudhavalli	33	F	Fever*8 days	10.4	8.9	5.63	35.1	2.3	80.1	32.8	33.7	nil	Negative	Negative	Negative	Negative	NG	26	Osteomyelitis
180	Shankar	65	M	Fever*4days,myalgia	9.5	9.3	5.42	31.7	3	84.1	33.9	31.2	O-1:200, H-1:200, Peritoneal Fluid-NG, Acid Fast Staining-positive for tubercle bacilli	Negative	Positive	Negative	Negative	NG	116	Typhoid, Fever/ Tuberculous Peritonitis
181	Gunasekar	19	M	Fever x 7days, vomiting	9.6	6.4	5.75	39.0	1.53	81.9	35.8	31.8	USG-normal	Positive	Negative	Negative	Negative	NG	100	Dengue hemmorrhagic fever
182	Balaji	58	M	Fever*8days,abdominal pain	10.2	6.1	4.78	38.7	1.35	76.4	34.2	35.7	nil	Negative	Negative	Negative	Negative	NG	8	Right Renal calculi
183	Kanchana	31	F	Fever*4days,myalgia	9.5	16.5	4.65	34.2	1.6	80.2	34	35.4	Elevated bilirubin	Negative	Negative	Negative	Positive	NG	212	Leptospirosis/Obstructive
184	Savithri	42	F	Fever*8 days, vomiting	9.2	9.7	4.02	41.6	1.23	82.5	28.7	32.8	nil	Negative	Negative	Negative	Negative	NG	79	Viral hepatitis
185	Muhammed	23	M	Fever x 4days, vomiting,abdominal pain	10.3	7.2	5.13	37.3	0.38 (4 units transfused)	77.6	29.8	32.2	USG-normal	Positive	Negative	Negative	Negative	NG	10	Dengue shock syndrome
186	Lakshman babu	29	M	Fever*8 days,vomiting	9.5	7.4	5.46	40.3	1.14	75.9	30.4	29.5	PS- Positive for Plasmodium vivax	Negative	Negative	Negative	Negative	NG	224	Malaria
187	Ravikumar	40	M	Fever*5days,breathlessness	9.2	5.8	4.35	41.7	1.47	79.3	32.8	27.3	nil	Negative	Negative	Negative	Negative	NG	10	Acute exacerbation of
188	Syed ahamed	48	M	Fever*9days	9.6	9.7	4.81	32.5	2.6	82.9	29.5	28.4	nil	Negative	Negative	Negative	Negative	NG	4	Type 2 DM/ Septic arthritis
189	Priyadharshini	20	F	Fever*6days,myalgia	8.4	10.3	5.08	34.8	2.4	78.3	34.8	30.3	nil	Negative	Negative	Negative	Negative	NG	36	Acute febrile illness
190	Sridharan	29	M	Fever*10days,giddines	10.4	6.8	5.13	32.6	2.3	82.4	31.8	28.9	Pus C/S- NG	Negative	Negative	Negative	Negative	NG	96	Septic arthritis
191	Pavitharan	13	Mc	Fever x 6days, diarrhoea	10.7	8.3	5.36	41.7	0.69 (2 units transfused)	78.5	27.5	28.1	ALT-27 AST- 29, USG- normal	Positive	Negative	Negative	Negative	NG	95	Dengue hemmorrhagic fever
192	Sriram	27	M	Fever*12 days myalgia	9.5	4	4.54	31.7	2.1	83.2	30.2	29.2	nil	Negative	Negative	Negative	Negative	NG	8	Acute febrile illness
193	Shakthi	22	M	Fever*4days,myalgia	9.3	18.6	4.25	32.7	1.7	81.8	34.8	34	USG-normal	Negative	Negative	Negative	Positive	NG	89	Leptospirosis
194	Lekha	13	Fc	Fever*9 days,vomiting	9.7	4.9	5.36	33.4	2.8	78.4	29.2	27.6	Urine C/S- Escherichia coli	Negative	Negative	Negative	Negative	NG	7	Urinary tract infection
195	Karthikeyan	40	M	Fever*5,abdominal pain	9.9	6.5	4.32	36.8	2.4	73.9	28.1	28.3	nil	Negative	Negative	Negative	Negative	NG	59	Viral hepatitis
196	Iyyapan	28	M	Fever*4days,myalgia	9.1	10	4.85	31.5	2.9	78.2	25.9	34.5	Eschar- lower end of sternum	Negative	Negative	Positive	Negative	NG	65	Scrub typhus
197	Jaganadhan	41	M	Fever*11 days	10.4	9.8	4.76	32.9	1.8	76.3	32.9	34.5	Pus C/S- NG	Negative	Negative	Negative	Negative	NG	5	Cellulitis
198	Boopathi	28	M	Fever*9days	10.7	7.4	5.69	34.7	2.3	81.9	34.8	31.7	nil	Negative	Negative	Negative	Negative	NG	9	Septic arthritis
199	Thandapani	33	M	Fever x 5days, vomiting	11.1	9.4	5.46	42.4	2.3	79.8	35.2	30.8	USG-normal	Positive	Negative	Negative	Negative	NG	47	Dengue hemmorrhagic fever
200	Ramraj	61	M	Fever*10days,vomiting	9.6	4.1	5.42	35.8	1.9	76.3	32	32.6	nil	Negative	Negative	Negative	Negative	NG	11	Acute gastroenteritis
201	Varadhan	53	M	fever * 5 days, vomitting	9.3	11.4	5.18	41.9	0.58 (2units transfused)	80.3	26.8	32.8	Eschar- left infraclavicular region	Negative	Negative	Positive	Negative	NG	78	Scrub typhus
202	Siranjeevi	37	M	Fever*13 days	9.1	9.3	4.75	39.5	2.4	80.3	28.6	34.9	nil	Negative	Negative	Negative	Negative	NG	221	Hepatitis/ Obstructive
203	Chinnasamy	59	M	Fever*4days,abdominal pain	10.4	4.1	4.68	43.7	0.48 (2 units transfused)	77	29.5	31.5	Urine C/S- Proteus vulgaris	Negative	Negative	Negative	Negative	NG	35	Urinary tract infection
204	Anand	27	M	fever * 5 days, abdominal pain	10.9	8.5	5.74	40.5	1.1	79.2	27.1	33.1	Eschar- Right infrascapular region,	Negative	Negative	Positive	Negative	NG	49	Scrub typhus
205	Vasu	33	M	Fever*5days,myalgia	11.5	5.1	5.68	36.8	1.71	81.5	34.9	33.1	nil	Negative	Negative	Negative	Negative	NG	6	Acute febrile illness
206	Tamil selvi	49	F	Low grade fever x 6days	10.6	10.2	5.35	38.3	1.52	80.5	33.8	33.5	Eschar- Right mammary gland	Positive	Negative	Negative	Negative	NG	67	Dengue hemmorrhagic fever
207	Murugan	36	M	fever * 5 days, myalgia	9.3	15.9	5.21	37.2	2	76.9	28.9	32.6	Eschar- lower end of sternum	Negative	Negative	Negative	Positive	NG	8	Leptospirosis
208	David	29	M	Fever*12 days myalgia	9.4	8.9	4.35	36.7	2.4	75.4	32.9	32.1	nil	Negative	Negative	Negative	Negative	NG	9	Acute febrile illness

Sample No	NAME	AGE	SEX	Presenting complaints	Hb (g/Dl)	WBC (10/µl)	RBC (10/µl)	Hematocrit %	Platelet count (lakhs/cu.mm)	MCV	MCH	MCHC	Other investigations	Dengue IgM	Widal test	Scrub typhus IgM	MSAT-Lepto	Blood culture	IL-6	DIAGNOSIS
209	Kalingaraj	34	M	Fever*8 days, vomiting	9	5.1	4.47	41.8	0.98	78.1	30.8	27.5	Pus C/S- NG	Negative	Negative	Negative	Negative	NG	111	Septic arthritis
210	Pradeep	9	Mc	Fever*13 days	10.3	4.2	4.65	39.2	1.08	82.8	33.9	29.5	nil	Negative	Negative	Negative	Negative	NG	48	Acute febrile illness
211	Asitha	17	F	Fever x 2days , Recurrent vomiting	9.6	3.8	5.16	40.0	0.81 (2 units transfused)	81.6	31.9	32.9	USG-normal	Positive	Negative	Negative	Negative	NG	278	Dengue shock syndrome
212	Iniya	11	Fc	Fever*8days,abdominal pain	10.7	9.3	5.28	38.5	1.32	78.2	30.5	27.6	Urine C/S- Escherichia coli	Negative	Negative	Negative	Negative	NG	7	Urinary tract infection
213	Ramlingam	62	M	Fever x 5days, abdominal pain	8.7	4.6	4.92	43.1	1.11	76.9	29.8	30.1	USG-GB thickening	Positive	Negative	Negative	Negative	NG	54	Dengue hemmorrhagic fever
214	Nisha	34	F	fever * 5 days, vomitting	9.5	5.5	5.03	36.4	2.9	77.7	29.4	34.8	Eschar- Right mammary gland	Negative	Negative	Positive	Negative	NG	97	Scrub typhus/Bilateral pleural effusion/ARDS
215	Anbalagan	60	M	fever * 5 days, abdominal pain	8.8	7.2	4.16	41.6	1.15	79.2	34.9	33.5	nil	Negative	Negative	Negative	Negative	NG	216	Viral hepatitis
216	Mithra	17	F	fever * 5 days, myalgia	9.7	8.5	4.98	33.8	2.6	79	28.9	31.8	nil	Negative	Negative	Negative	Negative	NG	5	Acute febrile illness
217	Manish	10	Mc	fever * 5 days, abdominal pain	9.2	18.6	5.89	37.4	1.3	83.5	30.4	31.5	Elevated bilirubin	Negative	Negative	Negative	Positive	NG	271	Leptospirosis/Obstructive jaundice/ septic shock
218	Ashwini	10	Fc	Fever*10days,diarrhoea	9.4	11.4	6.21	39.6	1.25	80.2	29.1	34.6	nil	Negative	Negative	Negative	Negative	NG	10	Acute gastroenteritis
219	Mohammed Ali	39	M	fever * 5 days, myalgia	9.8	9.4	5.36	40.2	3.6	86.9	31.9	32.6	Eschar- lower end of sternum	Negative	Negative	Positive	Negative	NG	77	Scrub typhus
220	Naga karthik ram	8	Mc	Fever*8 days, vomiting	10.7	4.1	5.67	40.7	1.6	82.1	35.3	31.8	nil	Negative	Negative	Negative	Negative	NG	29	Acute appendicitis
221	Lakshmi	44	F	Fever x 7days, abdominal pain	10.4	4.8	5.16	38.7	1.36	79.8	30.2	29.5	USG-Pleural effusion	Positive	Negative	Negative	Negative	NG	75	Dengue hemmorrhagic fever
222	Laavanya	38	F	fever * 5 days, vomitting	10.3	19	4.18	34.1	1.2	80.3	32.6	33.9	USG-normal	Negative	Negative	Negative	Positive	NG	68	Leptospirosis
223	Aadhavan	12	Mc	fever * 5 days, abdominal pain	10.6	8.5	4.13	37.9	2.6	76.3	33.8	29.1	Eschar- Right infraclavicular region	Negative	Negative	Positive	Negative	NG	98	Scrub typhus
224	Gokulraj	23	M	Fever x 4days, vomiting	10.4	9.5	5.17	37.7	1.86	81.5	33.8	30.2	USG-normal	Positive	Negative	Negative	Negative	NG	315	Dengue shock syndrome
225	Sathya mohan	38	M	Fever*9days,cough	9.6	6.6	4.09	42.8	0.97	76.2	32.9	27.4	nil	Negative	Negative	Negative	Negative	NG	5	Acute exacerbation of
226	Adhithya	13	Mc	Fever*5days	9.3	7.9	5.78	33.7	2.7	80.2	33.8	29.6	NG	Negative	Negative	Negative	Negative	NG	9	Urinary tract infection
227	Kamalesh	34	M	fever * 5 days, myalgia	10.3	18.3	5.12	36.7	1.8	79.4	34.8	30.3	USG-normal	Negative	Negative	Negative	Positive	NG	45	Leptospirosis
228	Ramya	11	Fc	Fever*13 days,myalgia	11.4	4.2	4.33	35.7	2.3	75.2	34.9	27.4	nil	Negative	Negative	Negative	Negative	NG	38	Membranous tonsillitis
229	Munish	31	M	fever * 5 days, vomitting	10.5	8.4	5.88	32.7	2.9	77.4	35.9	28.6	Eschar- Right inframammary region	Negative	Negative	Positive	Negative	NG	89	Scrub typhus
230	Arun devan	29	M	Fever*9days,abdominal pain	9.5	5.8	4.36	41.9	1.9	78.2	29.5	28.6	Urine C/S- Escherichia coli	Negative	Negative	Negative	Negative	NG	7	Urinary tract infection
231	Mowshik	10	Mc	Fever*7days	9.6	7.2	4.89	40.2	2.1	82.9	28.7	30.5	nil	Negative	Negative	Negative	Negative	NG	10	Acute follicular tonsillitis
232	Neelakandan	42	M	Fever*5days,diarrhoea	9.1	6.9	5.66	41.7	1.47	79.2	29.6	33.6	nil	Negative	Negative	Negative	Negative	NG	5	Acute gastroenteritis
233	Manikandan	14	Mc	Fever*12 days myalgia	10.3	8.9	5.78	38.4	2.6	80.2	32.8	31.8	nil	Negative	Negative	Negative	Negative	NG	11	Acute tonsillitis
234	Sekar	19	M	fever * 5 days, abdominal pain	9.4	4.6	5.21	36.4	3.5	76.2	28.9	31.2	Eschar- left infraclavicular region	Negative	Negative	Positive	Negative	NG	71	Scrub typhus
235	Vinodhini	9	Fc	Fever*11days,breathlessness	10.8	8.5	5.04	39.8	2.1	81.2	30.6	32.1	nil	Negative	Negative	Negative	Negative	NG	51	Acute exacerbation of
236	Sai kumar	14	Mc	Fever x 3days, vomiting	11.3	9.52	5.77	41.7	1.94	83.2	29.7	31.9	ALT-41, AST- 38, USG- B/l pleural effusion	Positive	Negative	Negative	Negative	NG	36	Dengue hemmorrhagic fever
237	Susila	21	F	fever * 5 days, myalgia	9.5	13.6	5.62	37.1	1.7	78.7	26.9	34.8	USG-normal	Negative	Negative	Negative	Positive	NG	75	Leptospirosis
238	Elango	40	M	Fever*8 days, vomiting	10.7	6.2	4.51	32.7	2.2	76.2	34.9	35.6	nil	Negative	Negative	Negative	Negative	NG	9	Obstructive jaundice
239	kiran raj	34	M	fever * 5 days, vomitting	9.6	4.9	4.06	33.8	2.6	83.7	26.5	27.8	Eschar- left infraclavicular region	Negative	Negative	Positive	Negative	NG	96	Scrub typhus
240	Akilan	12	Mc	Fever*10days	10.5	7.6	5.78	39.4	1.7	82.6	32	31.6	Pus c/s- Staphylococcus aureus	Negative	Negative	Negative	Negative	NG	203	Septic arthritis
241	Pandian	59	M	Fever*8days,abdominal pain	9.6	5.9	4.13	42.3	1.56	82.1	31.7	34.2	nil	Negative	Negative	Negative	Negative	NG	4	Acute appendicitis
242	Nandini	23	F	Fever*8days,abdominal pain	9.2	8.8	4.07	40.7	1.4	79.2	29.2	32.7	Urine C/S- Escherichia coli	Negative	Negative	Negative	Negative	NG	8	Urinary tract infection
243	Vijayakumar	36	M	Fever*10 days myalgia	9.8	5.2	5.24	39.5	2.3	82.9	28.9	31.8	nil	Negative	Negative	Negative	Negative	NG	9	Septic arthritis
244	Aravindhan	36	M	fever * 5 days, abdominal pain	9.9	11.9	5.31	36.7	0.63 (2units transfused)	80.6	28.1	31.9	Elevated bilirubin	Negative	Negative	Negative	Positive	NG	224	Leptospirosis/Obstructive jaundice
245	Anitha	31	F	Fever*10days,giddines	10.2	8.3	4.96	35.7	2.7	76.9	34.8	35	nil	Negative	Negative	Negative	Negative	NG	7	Acute febrile illness
246	Harshitha	15	Fc	Fever*8 days, vomiting	10.8	10.5	4.23	37.8	2.1	82.3	32.7	29.3	nil	Negative	Negative	Negative	Negative	NG	5	Viral hepatitis
247	Balu	38	M	Low grade fever x 5days	9.0	7.25	5.39	42.6	2.2	78.5	31.7	29.4	USG-normal	Positive	Negative	Negative	Negative	NG	90	Dengue hemmorrhagic fever
248	Jansi	12	Fc	fever * 5 days, myalgia	9.4	6.4	5.12	39.7	1.1	82.4	28.6	33.1	Eschar- lower end of sternum, Patient-EXPIRED	Negative	Negative	Positive	Negative	NG	119	Scrub typhus/Bilateral pleural effusion/Pulmonary Edema/Hypo tensive shock
249	Saraswathi	33	F	Fever x 8days, abdominal pain	9.1	7.56	5.59	39.9	2.3	79.7	29.6	32.6	USG-GB thickening	Positive	Negative	Negative	Negative	NG	79	Dengue hemmorrhagic fever
250	Santhosh	34	M	Fever*9 days,vomiting	10.6	9.7	5.26	41.9	1.84	78.1	29.5	28.7	nil	Negative	Negative	Negative	Negative	NG	6	Obstructive jaundice