CLINICAL, BIOCHEMICAL AND IMAGING PROFILE IN DENGUE FEVER IN PSG IMSR, COIMBATORE - A PROSPECTIVE OBSERVATIONAL STUDY

Dissertation submitted to

The Tamil Nadu Dr. M.G.R Medical University, Chennai

In fulfilment of the requirements for the award of the degree of

Doctor of Medicine in General Medicine

Under the guidance of

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PSG INSTITUTE OF MEDICAL SCIENCES & RESEARCH, COIMBATORE

THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY, CHENNAI, TAMILNADU

MAY 2020

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled, **"Clinical, biochemical and imaging profile in Dengue fever in PSG IMSR, Coimbatore – A Prospective observational study"** is the bonafide original work of **Dr.V.KANCHANADEVI**, done under my direct guidance and supervision in the Department of General Medicine, PSG Institute of Medical Sciences and Research, Coimbatore in fulfilment of the regulations by The Tamil Nadu Dr.MGR Medical University, Chennai for the degree of Doctor of Medicine in General Medicine.

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CERTIFICATE BY THE HOD AND DEAN OF THE INSTITUTION

This is to certify that the dissertation entitled, **"Clinical, biochemical and imaging profile in Dengue fever in PSG IMSR, Coimbatore - A Prospective observational study"** is the bonafide original research work of **Dr.V.KANCHANADEVI** under the guidance of **Dr.K.JAYACHANDRAN MD.,** Professor of Medicine, PSG IMS&R, Coimbatore in partial fulfilment of the requirements for the degree of Doctor of Medicine in General Medicine.

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I hereby declare that this dissertation entitled **"Clinical, biochemical and imaging profile in Dengue fever in PSG IMSR, Coimbatore - A Prospective observational study"** is a bonafide and genuine research work carried out by me under the guidance of **Dr.K.JAYACHANDRAN MD.,** Professor of Medicine, PSG IMS&R, Coimbatore. This dissertation is submitted to The Tamil Nadu Dr.M.G.R Medical University in fulfilment of the university regulations for the award of MD degree in General Medicine. This dissertation has not been submitted for award of any other degree or diploma.

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Dr. V.KANCHANADEVI

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Guide & Supervisor sign with Seal.

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CONTENTS

INTRODUCTION

Dengue infection is one of the major public health issue in our country. Incidence of infection with dengue virus has been increased for the last two decades. In initial days, dengue presents as epidemics at longer intervals. But nowadays, dengue presents in sporadic and one of the important vector borne disease. Dengue infection found in tropical and sub - tropical countries worldwide, mostly in urban and semi-urban areas (1).

Dengue infection is transmitted by female mosquitoes mainly of the species AedesAegypti and, to lesser extent AedesAlbopictus infected with virus. There are 4 type of viruses that cause dengue are DEN-1, DEN-2, DEN-3 and DEN-4 (5). Infection with one dengue serotype confers lifelong homotypic immunity to the other serotypes, but a person can eventually be infected by all 4 serotypes (6,7).

Global burden of dengue:

In recent decades, global incidence of dengue has been grown dramatically. About half of the world's population is now at risk of developing infection with dengue (1).A majority of cases are asymptomatic, so the actual numbers of dengue cases are underreported. And many cases are misclassified.

One study by Bhatt S et al, estimated that 390 million people infected with dengue virus per year with credible interval of 95% (284–528 million), of which 96 million (67–136 million) people manifest clinically (2).

Another study, by Brady OJ et al, prevalence of dengue infection, estimated that 3.9 billion people, in 128 countries, are at risk of infection (3). The number of cases reported in 2010 was 2.2 million which was increased to 3.34 million in 2016 (1).

Distribution trends (1)

Throughout the tropics, Dengue infection is distributed widespread. Risk factors which influences dengue infection includes local spatial variations and depends on rainfall, temperature, humidity. Urbanization and vector control quality services in urban areas.

Before 1970, severe dengue epidemics, occurred only in nine countries. Butin recent years, more than 100 countries experiences dengue as an endemic in WHO's regions of African, Americas, Eastern Mediterranean, South-East Asia and Western Pacific; the Americas, South-East Asia and Western Pacific regions are most seriously affected(9).

In 2015,Americas alone reported 2.35 million cases, of which severe dengue was diagnosed in10,200 cases and causing 1181 deaths. There is a possible outbreak of dengue fever exists in Europe as local transmission and for the first time reported in France and Croatia in 2010. 3 other European countries experiences imported cases. Among the travellers those who are returning from low- and middle-income countries, dengue is the second most cause of fever after malaria.

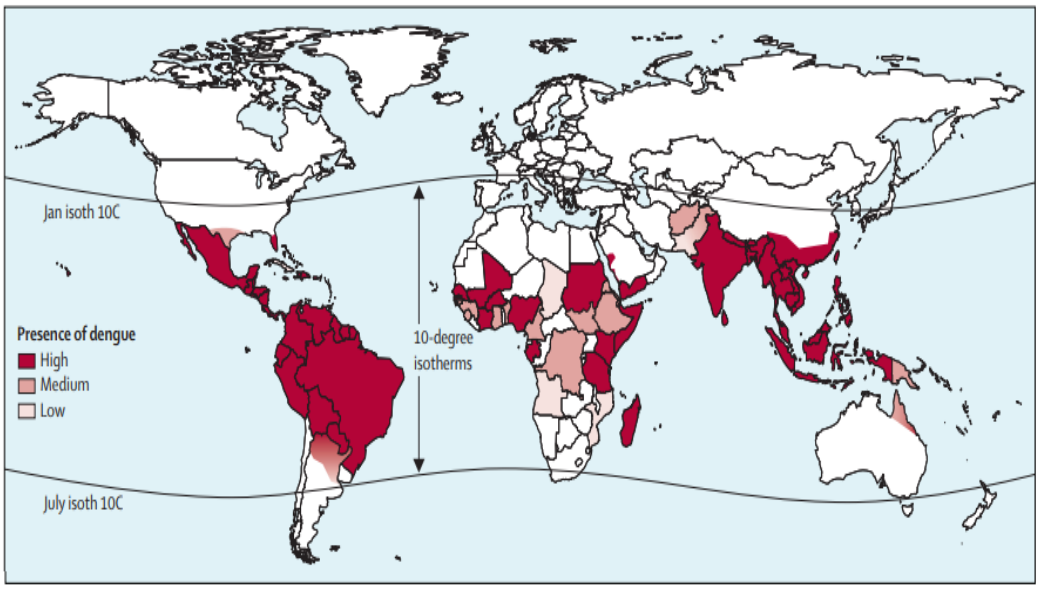


Figure 1: Global dengue burden, 2014
Data from Bhatt and colleagues,[1] Healthmap,[2] and WHO[3] were integrated to indicate the relative amount of dengue globally according to best estimates.

Figure.1. Global burden of dengue

Worldwide, large dengue outbreaks were occurred in the year 2016. Number of dengue cases were approximately 3 times higher than in 2014.

In 2017, there is a significant reduction in the number of dengue cases in the Americas. WHO's Western Pacific Region have been reported dengue outbreaks in several countries in the Pacific region. There is a sharp increase in number of cases in 2019, after a significant drop in the number of cases in 2017-18.

However, case fatality rate have been reduced to less than 1% in many countries, 28% reduction in case fatality rate globally have been recorded between 2010 and 2016. There is a significant improvement in case management at country level.

Member States in the three WHO regions regularly report the annual number of dengue cases to the Secretariat.

Figure.2. Shows the number of dengue cases (suspected or confirmed) notified to WHO since 1990.

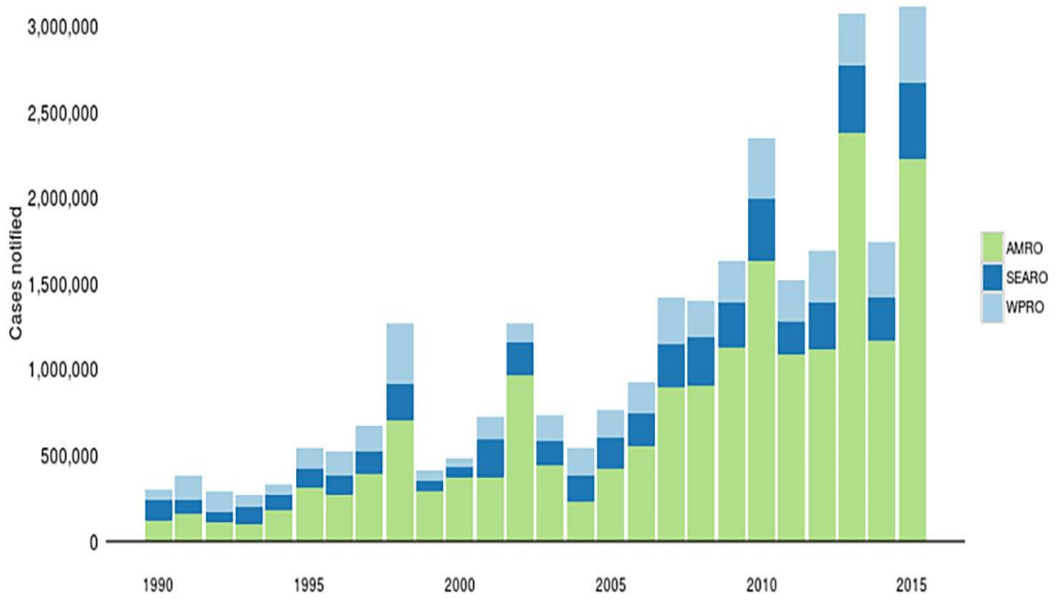


Figure 2: Number of suspected or laboratory - confirmed dengue cases notified to WHO, 1990-2015(8)

DENGUE IN INDIA:

Clinically dengue like illness was reported in Madras (Chennai) in 1780, but it was not proven virologically. In 1963- 64, first virologically proven epidemic dengue fever was occurred in Calcutta and eastern coast (109- 111). The first dengue hemorrhagic outbreak occurred in Calcutta in 1963 [27,28].

From where it spreads and reached Delhi in 1967(114) and in 1968 it reached Kanpur (115, 116), simultaneously it spreads to all over the country (117, 118).

Initially dengue epidemic was caused by DENV-4(115) in 1968, in 1969 DENV-2 & DENV-4 both serotypes caused dengue epidemic (119). In 1966 during dengue epidemic at Vellore, Myers et al (117)had reported the presence of DENV-3. And in 1968 all four serotypes were isolated (120). Till 1997, predominant serotype was DENV-2 circulating in northern India (112, 113,121). In 1997 during epidemic in Delhi, DENV-1 was isolated(122). From southern India, DENV-2 alongwith DENV-3 was reported (123).

Till 2003, DENV-2 was the predominant serotype in Delhi. In 2003, all four serotypes were found and changed to hyper endemic state(124) & in 2005 DENV 3 was the predominant serotype (125).

Several fatal cases of dengue were reported in Kolkata, Delhi, and Chennai (126- 129). In Tamil Nadu, all four serotypes was documented (130).

Figure: 3 Dengue incidence rates (per million population) in India from 1998 to 2014.

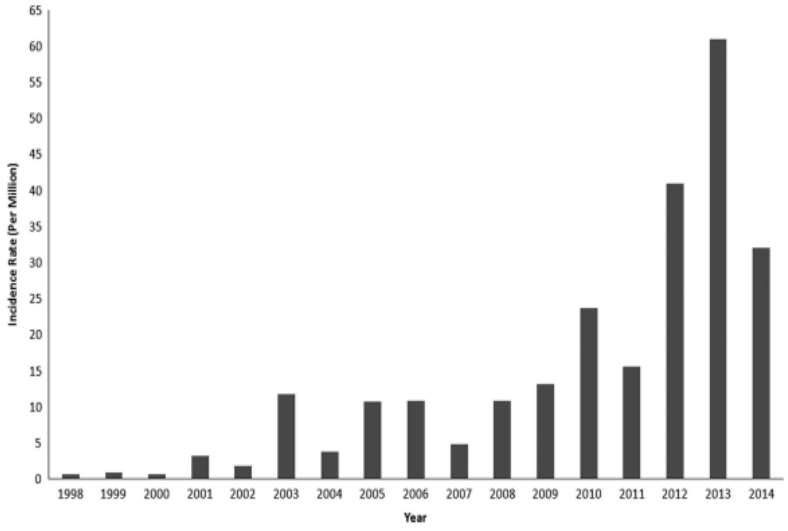


Figure:3 (Data source: NVBDCP, Govt. of India).

Figure.4. Average dengue incidence rates (per million population) by state in India from 1998 to 2014

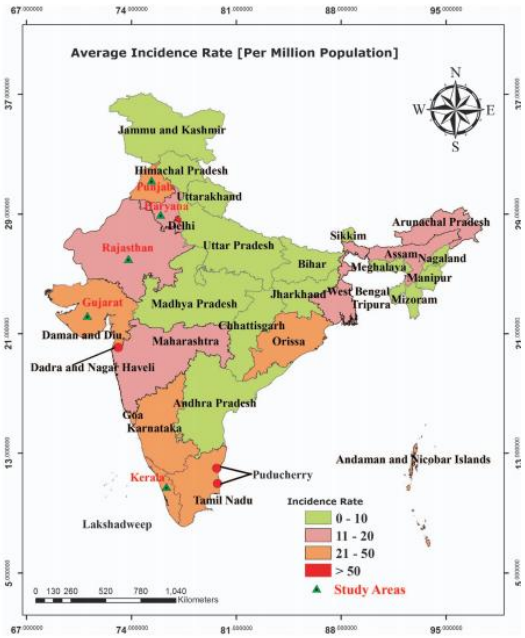


Figure :4 Average dengue incidence rates

In India, in almost all states dengue is an endemic disease. It is one of the leading cause of hospitalization (22,23). Initially, there was an urban distribution, but now also reported from peri-urban and rural areas as well (24,25). A good laboratory-based disease surveillance is essential for early detection of outbreaks and also for estimating the disease burden due to dengue.

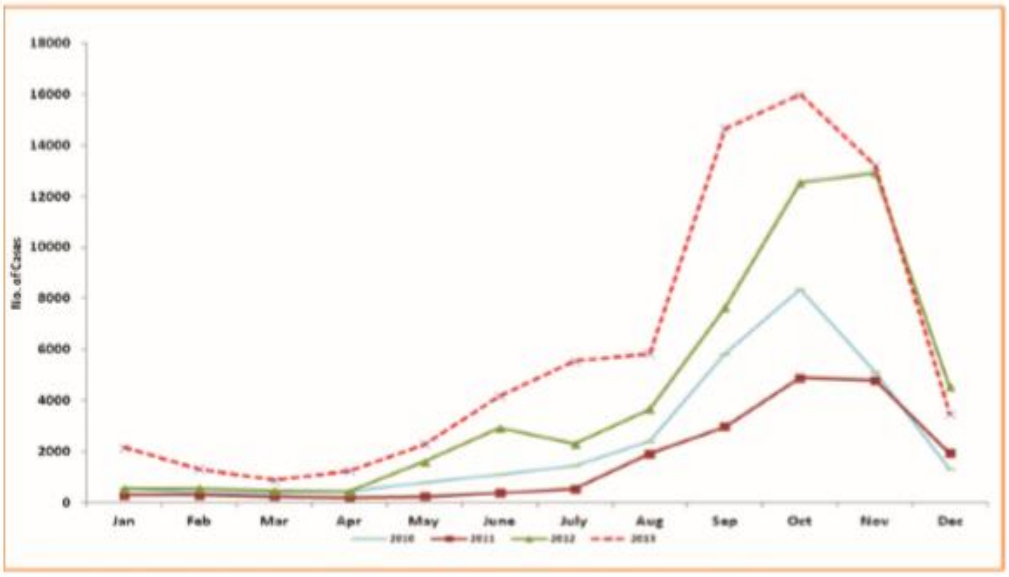


Figure: 5. Seasonal trend of dengue cases in India 2010–2013

There is an upsurge of dengue cases during the month of July to November. The disease expresses seasonal pattern, peak cases occur after the monsoons. But there is no uniform distribution throughout the year.

Initially breeding of Aedes mosquitoes was more prevalent in urban areas, but now a days, trend is changing as a result of urbanisation of rural areas, manmade ecological changes all leads to invasion of Aedes mosquitoes.

OBJECTIVES OF THE STUDY

OBJECTIVES

Primary Objective:

To evaluate the clinical, biochemical and imaging profile of 100 patients with dengue NS 1 Positive / Dengue Ig M /Ig G positive cases.

Secondary Objective:

1. To evaluate the complications secondary to dengue infection.

2. To evaluate the need for platelet transfusion in dengue infection.

MATERIALS AND NETHODS

STUDY DESIGN

Hospital based longitudinal observational study

STUDY POPULATION:

Patients aged > 16 years of age and those who are admitted in male and female medical wards, IMCU and MICU with positive dengue serology (Dengue NS 1 Ag / Dengue IgM /IgG Antibody) of 100 patients for a period of one year from January 2018 to December 2018.

INCLUSION CRITERIA:

- Age > 16 years
- Patients admitted with Dengue NS 1 and Dengue Ig M /Ig G serology positive.

EXCLUSION CRITERIA:

- Patients with mixed infections like malaria, typhoid, leptospirosis
- Those who are not willing to participate in the study.

METHODOLOGY:

Patients basic demographic data (such as age, sex) and detailed Clinical history was collected.

All patients included in this study undergone general physical examination and systemic examination. The preliminary laboratory investigations which included in this study were Complete blood count, liver function test, renal function test and ultrasound abdomen imaging was done in all patients.

Depending on the duration of fever Dengue NS1 Ag by ELISA method or IgM / Ig G ELISA was done. Patients were monitored daily by general physical, systemic examination and daily platelet count and hematocrit and also monitored for any bleeding and any associated complications.

Statistical analysis

Data will be collected in an excel spreadsheet and will be analysed using a SPSS statistical software. Data will be reported as mean + / - standard deviation depending on their distribution.Any association will be analysed using chi-square test. Correlation will be analysed by Pearson correlation.

A p value of <0.05 using two tailed test was taken as being significant for all statistical tests.

FLOWCHART


Proposal to ethics committee and approval from ethics committee
Dengue positive patients selected according to inclusion and exclusion criteria
History taking and clinical examination
Follow up of laboratory parameters, complications and platelet transfusion
Analysis of the collected data using a statistical software to achieve the objectives
Final report and submission

REVIEW OF LITERATURE

DENGUE VIRUS

The dengue virus (DENV) (12) is a RNA virus. It contains single stranded RNA. It categorised under flaviviridae family and genus of flavivirus.[13] There are four serotypes of dengue virus, DENV-1, DENV-2, DENV-3, DENV-4. Serotypes were classified based on biological and immunological criteria. All four serotypes can co-circulate in endemic areas. Each serotype has multiple genotypes. (4) The genotypes of the same serotype exhibit subtle antigenic differences (18,19) but these may not be clinically relevant.

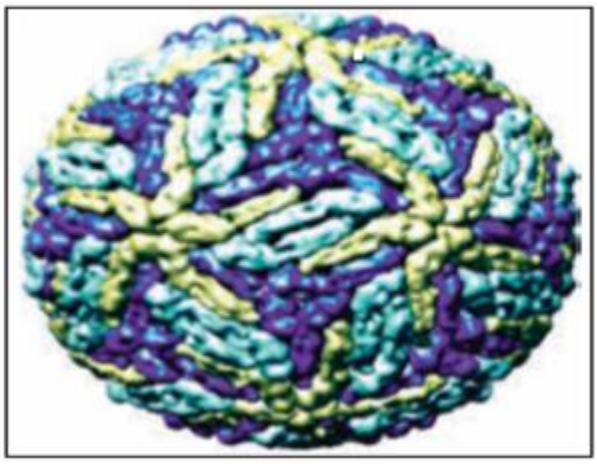


Figure: 6. Electron microscopic view of dengue virus

In 2013, in Malaysia, a fifth serotype of dengue virus was detected (21). Infection with one serotype gives lifelong immunity, which was serotype specific and in between serotypes, gives short lived cross immunity.(20)

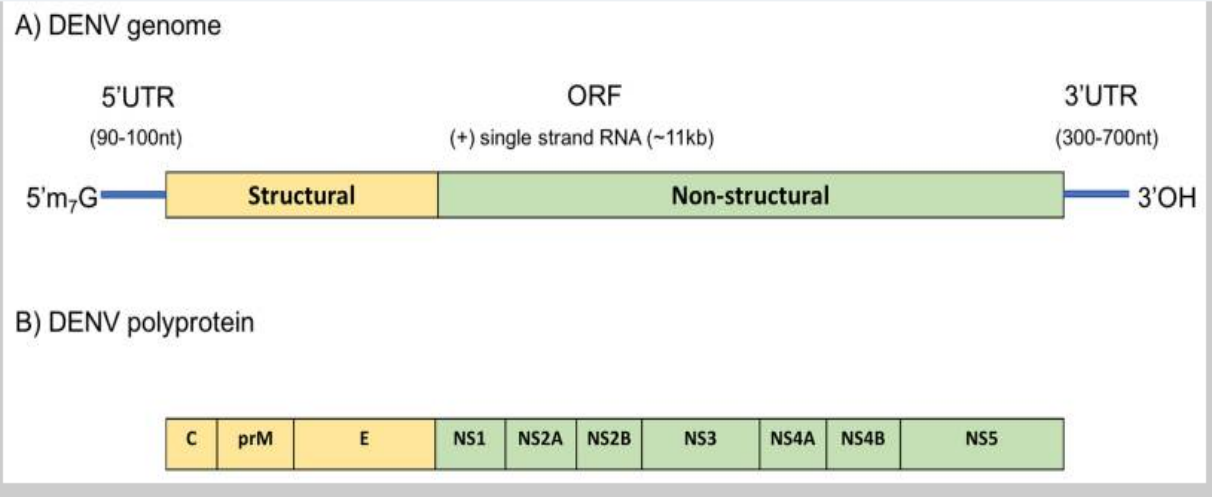


Figure: 7. Structure of the DENV genome.

Figure:7. A) The 5′ end is capped with N^7methylated guanosine cap while the 3′ end forms a hairpin loop. The genome translates into

B) a single polyprotein which will then be processed by the viral and host mechanism

The mature virion composed of three structuralprotein genes encoding the nucleocapsid protein(C),membrane associated protein (M), and an envelope protein (E) (10).

Structural Proteins (32):

C Protein:

Nucleocapsid(C) protein is the first polypeptide synthesized during viral translation. It introduces the viral genome into the host cells.

M protein:

Membrane associated protein (M) is derived from prM (precursor protein)during virus maturation. The role of these protein in the mature virion is not known.

E glycoprotein:

It is an envelope glycoprotein. It acts as target and modulator of host immune response. E gene carries most of the molecular markers for pathogenicity.

Non structural proteins:

There are seven non-structural (NS) proteins, which are NS1, NS2A & 2B, NS3, NS4A & 4B, and NS5 proteins (11).

Dengue NS1 is a glycoprotein. Its molecular weight is ranging from 46 to 55 k Da (33).NS1 protein is secreted as a hexamer into the blood circulation(34).

In early stages of infection, it plays an important role in replication of viral genome, along with NS4A and NS4B transmembrane proteins. (35, 36).In early stages NS1 detected in high levels in patients sera, which helps in early diagnosis of dengue fever (37). Titres are high in patients with dengue haemorrhagic fever than dengue fever (15). Within 72hours of onset of illness, elevated NS1 helps in identifying thepatients who are at risk of developing DHF(16). Hexameric form of NS1 protein transports lipids from tissues to the liver in dengue patients (38).

Via Toll-like receptor 4 (TLR4) NS1 activates macrophages ,which disrupts endothelial cells and causes vascular leakage, which is a distinct characteristic of dengue fever with warning signs and severe dengue (39, 40).

In patients with secondary dengue infections, found to have very high levels of NS1 proteins, compared toprimary dengue infection(17).

VECTOR:

The vector that transmits dengue virus is Female Aedes species mosquito(14). Dengue virus spreads through, by bite of these infected female mosquitoes. Aedesaegypti, Aedesalbopictus and Aedespolynesiensis comes under these species. Aedesaegypti is the main vector in transmitting dengue viruses [31].

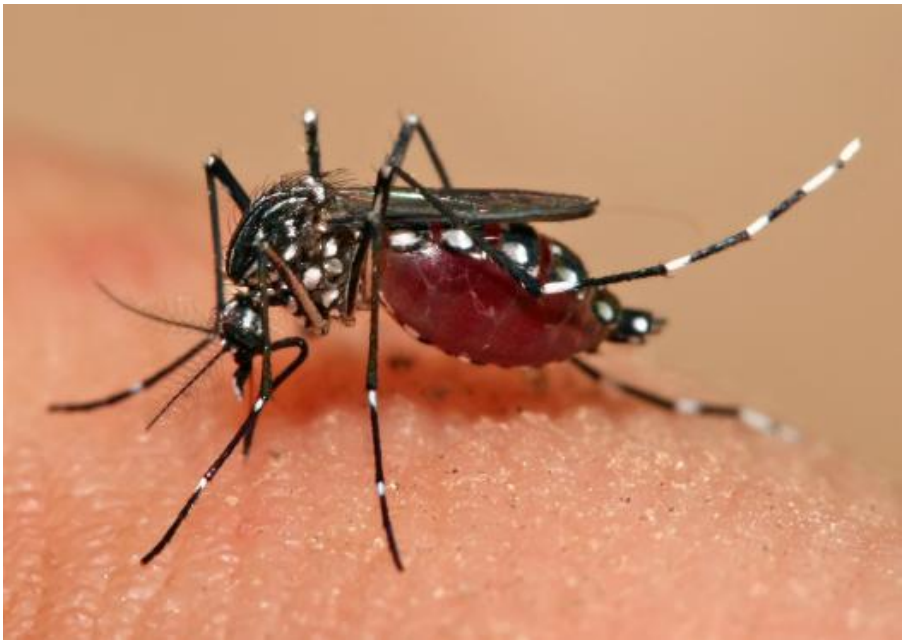


Figure: 8 picture of Aedesaegypti

Life cycle of Aedesaegypti:

The Aedes mosquitoes have 4 life stages:

(1) egg

(2) larva

(3) pupa and

(4) adult

The entire life cycle, from an egg to an adult, takes approximately 8-10 days[29].

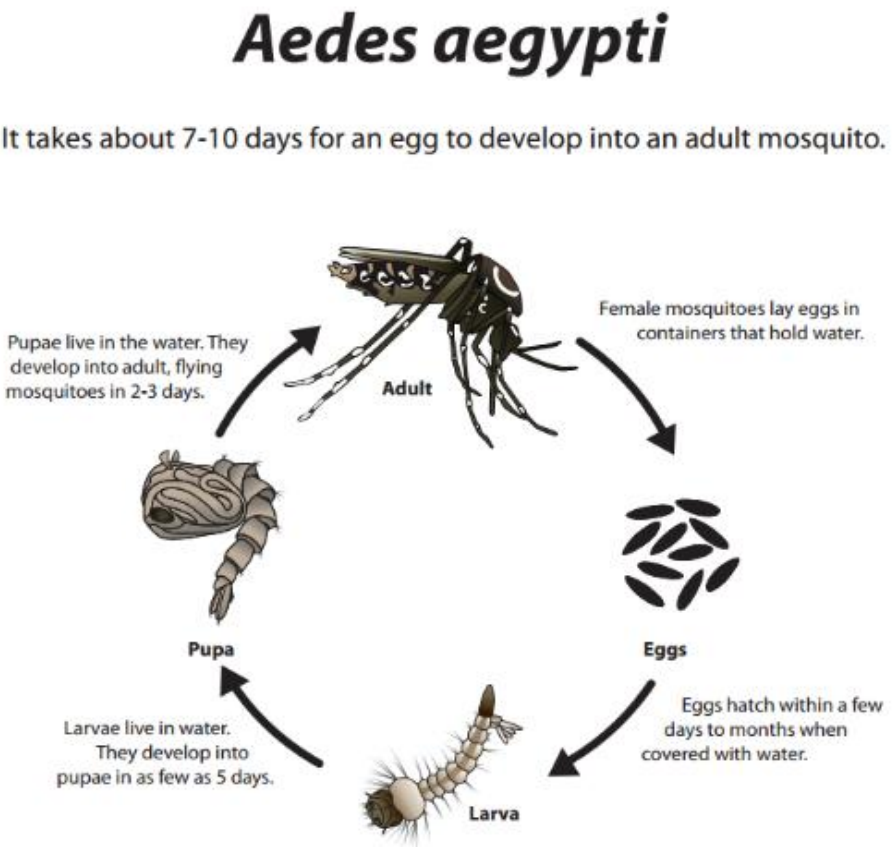


Figure: 9: Lifecycle of Aedesegypti

Adult, female mosquitoes lay eggs on the inner walls of containers with water, above the waterline. Eggs can survive drying out for up to 8 months. Larvae emerges from eggs once water level raises to cover the eggs. Larva develops into pupa in 4 – 5 days. Adult flying mosquito develop from pupae and emerges from the pupal skin and leaves the water. Male mosquitoes feed on nectar from flowers and female mosquitoes feed on humans and animals for blood to produce eggs (29).

Most female Aedesaegypti may spend their lifetime in or around the houses where they emerge as adults and they usually fly an average of 400 metres[9].

Environmental factors:

The population of mosquitoes fluctuates with rainfall and storage of water. Temperature and humidity of the environment influences lifespan of these mosquitoes. It best survives in the temperature between 16 C and 30 C and with a humidity of 60–80%. Altitude also plays a important role in distribution. Its distribution is restricted 1000 ft above sea level. Aedes mosquitoes are highly anthropophilic and usually rests in cool and shady places.

Due to environmental and life style changes in rural areas there is a serious threat of transmission in rural areas also.

Host factors:

People of all age groups are at risk of infection and both genders are equally affected.

Secondary infection with dengue plays a important risk factor for severe dengue. Infants, who acquired antibodies passively are also at risk of severe dengue. Recent travel to

dengue endemic areas is also most important risk factor. During viremia, migration to a nonendemic area may also introduce dengueinfection in nonendemic area.

Transmission cycle:

Aedes female mosquitoes gets infected with dengue virus when feeding a blood in a person who was in acute febrile / viremia phase of dengue.

After 8 to 10 days, of an extrinsic incubation period which occurs in mosquito after entry of dengue virus. Viral replication occurs in midgut and reaches haemocoel and haemolymph and it reaches different tissues. Once the virus reaches the salivary gland, infected mosquito able to transmit the dengue virus to another person during feeding.

After an extrinsic incubation period, when infected female mosquito bites a person and injects saliva into the bitten wound this process continues. Ultrastructural studies shows, viral particles seen within the mosquitoes of the nervous system, salivary glands, foregut, midgut, fat body, epidermal cells, ovary and internal body wall lining cells.

After an intrinsic incubation period which occurs in humans, range of 3–14 days dengue fever begins abruptly. Also there is a vertical transmission (transovarian transmission) of the virus from infected female mosquitoes to the next generation.

Rarely, dengue virus transmission occurs through blood transfusion and organ transplantation. When pregnant women gets infected with dengue during late pregnancy, congenital dengue infections in neonates are reported.

Pathogenesis of dengue fever:

Dengue fever caused by any of the serotypes of dengue virus. Infection with one serotype gives lifelong immunity against that particular serotype and gives short term immunity to other serotypes. If the person infected for second time with different serotype, more severe infection may occur due to antibody dependent enhancement.

Antibodies which are formed during infection with one serotype enhances antibody production when a person gets infected with second serotype. However, only 2%–4% of individuals develop severe disease during secondary infection, so antibody dependent enhancement alone itself cannot explain this process [71].

When infected mosquito bites, dengue virus enters into the body and replicates in the cells of mononuclear lineage (macrophages, monocytes, and B cells).Dengue virus also infects mast cells, dendritic cells, and endothelial cells[72–74]. The incubation period for dengue infections is 7–10 days. During febrile phase patient became infective and febrile. The severity of dengue infections can be correlated with peak plasma viraemia [75].

Antibody responses to the dengue virus:

In secondary dengue infections, anti-dengue virus antibodies which are already present in sub neutralising concentrations form complexes with dengue virus [77]. And augments infection of IgGFcR (Fc gamma R)-positive cells by dengue virus, by uptake of these dengue virus-antibody complexes by Fc gamma R [76]. These phenomenon is known as antibody dependent enhancement.

During primary dengue infection, antibodies formed against both structural and non-structural viral proteins. Although, role of these different antibodies are not known precisely, antibodies against NS1 protein induce endothelial cell apoptosis in a caspase dependent manner[79]. Different Ig G antibody subclasses, binds with antigen and activates the classical complement pathway.

Patients with severe dengue have higher levels of dengue virus specific IgG1 and IgG4 and lower levels of IgG2 compared those with dengue fever [80 81]. Complement activation contributes to increased vascular permeability and coagulation abnormalities [82].

Role of IgE antibodies:

Total IgE and dengue specific IgE antibody levels are higher in patients with severe dengue compared to patients with dengue fever(82).And total IgE levels are significantly higher in secondary dengue infections(83).Th1 responses are suppressed and predominant Th2 responses are also reported(84).

Mechanisms responsible for Thrombocytopenia are: (85)

1. Presence of IgM type of antiplatelet antibodies

2. Presence of specific antibodies to dengue virus

3. Hypocellularity of Bone marrow leads to defective megakaryocytes

4. Destruction of platelets in the liver and spleen.

In the presence of complement, antiplatelet antibodies cause platelet lysis and higher concentrations of antibodies found in severe dengue. That leads to severe thrombocytopenia in severe dengue (86). The number of atypical lymphocytes will be increased. There is an increase in B-cells and a decrease in T-cells due to presence of anti-T-cell antibodies (88). Anti-B cell antibodies are also found and modulates immune response (89).

Cytokine responses in dengue infections:

According to Chaturvedi et al,during initial days of fever Th1 responses are seen, Th2 responses occur later(84). In the first 3 days of fever, TNF-a, IL-2, IL-6, and IFN-c are highest and IL-10, IL-5, and IL-4 appears later(84).

IL-13 and IL-18 also increased in severe dengue infections. Highest levels of IL-12 seen in dengue fever, but it is undetectable in patients with severe dengue.

There is an inverse relationship between IL12 levels and transformimg growth factor-b and it correlates with disease severity (90).Th2 responses are more pronounced in severe dengue. In severe dengue, TNF-a, IL-6, IL-13, IL18, and cytotoxic factor levels are very high that leads to increased vascular permeability and profound shock (90–92). Autoantibodies against cytotoxic factor protects from severe disease and highest levels are detected in mild disease (93).

IL-6 levels are higher in patients with severe dengue (94) which also increases vascular permeability.

Activated neutrophils release elastase, which facilitates neutrophil mediated endothelial injury and activates complement and fibrinolytic systems (95, 96).

Lymphocytes which are infected by dengue virus produce IFN-a and IFN-c (97). Infection of monocytes by dengue virus gets inhibited by IFN-a(98). IL-10 also contribute to platelet defects (99).

Cellular immune responses in dengue infections:

CD4+ and CD8+ T-cells gets infected by dengue virus(100). Serotype specific memory T-cells are formed following primary infection. During secondary exposure to virus, these memory T-cells augment infection by producing various cytokines (101). Liver injury due to T-cell immune responses that causes destruction of hepatocytes. Bone marrow suppression leads to absolute lymphopenia (102). Suppression of T-cell responses are suppressed during infection with dengue virus and this suppression persists for two weeks after fever(103).

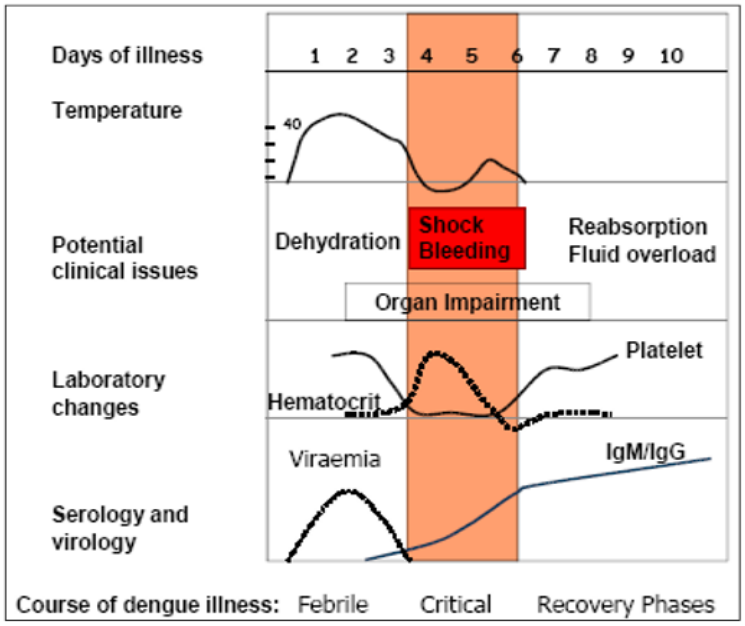
Course of dengue illness:

Infection with dengue virus manifests as symptomatic dengue infection or asymptomatic seroconversion. In symptomatic dengue infection, there are three phases-

(1) febrile phase,

(2) critical phase and

(3) recovery phase.



IgM = immunoglobulin M; IgG = immunoglobulin G. Temperature is given in degrees Celsius (°C)
Source: adapted from Yip, 1980 (2) by authors.

Fig.10. The course of dengue illness

Febrile phase:

Patients typically presents with sudden onset of high grade fever and usually lasts 2−7 days. Acute febrile phase often accompanied by arthralgia, generalised body pain, myalgia, retro-orbital pain, facial flushing, skin erythema(41). Also have anorexia, nausea and vomiting. In this phase, clinically difficult to distinguish dengue from non-dengue febrile diseases. In acute febrile phase, a positive tourniquet test indicates an increased probability of dengue (43,44).

Mild haemorrhagic manifestations such as bleeding from mucosal membranes, petechiae, bleeding from veni puncture site may be seen (43, 45). The liver may became enlarged and tender (43). There is a progressive decrease in total white cell count, in early phase suggests a high probability of dengue (43).

Critical phase:

During this transition phase, most of them does not have increase in capillary permeability and improve without going through the critical phase. Some patients develop increased capillary permeability and may manifest with warning signs of dengue. Clinically significant plasma leakage lasts for 24 – 48 hours.

Virological and serological markers in relation to time of dengue infection:

Plasma leakage usually preceded by progressive leukopenia (43) and rapid decrease in platelet count and rising haematocrit above the baseline is one of the earliest signs (47, 48).

Severity of plasma leakage is determined by degree of haemoconcentration above the baseline haematocrit values. Early intravenous fluid therapy reduces hemoconcentration. So frequent monitoring of haematocrit is essential and possible adjustments to intravenous fluid therapy was done according to haematocrit.

If there is a significant plasma leakage, patient develop pleural effusion, ascites and gall bladder wall oedema. In addition to that, patients develop bleeding manifestations such as easy bruising and bleeding from venepuncture sites occur frequently.

If critical volume of plasma is lost, shock occurs and usually preceded by warning signs. With profound and/or prolonged shock, leads to hypoperfusion of multiple organs and results in severe metabolic acidosis, severe organ impairment, disseminated intravascular

coagulation. This leads to severe haemorrhage and haematocrit gets decreased in severe shock.

There is an increase in total white cell count as a stress response to severe bleeding. Severe organ impairment leads to severe hepatitis, encephalitis, myocarditis, and/or severe bleeding, without obvious plasma leakage or shock (49).

Patients of dengue with warning signs usually recovers with intravenous rehydration. Some patients may deteriorate into severe dengue.

Warning signs of dengue:

Warning signs usually arises towards the end of the febrile phase and usually occurs 3- 7 days of illness. They had Persistent vomiting and severe abdominal pain, increasingly lethargic. Spontaneous mucosal bleeding or bleeding from venepuncture sites are important haemorrhagic manifestations. If plasma loss is significant patients develop clinical fluid accumulation.

Rapid fall in platelet count to less than 100 000 cells/mm3 and rise in haematocrit above the baseline may be the earliest sign of plasma leakage and usually preceded by leukopenia(44).

Recovery phase:

Once the patient survives the critical phase, there is gradual reabsorption of extravascular fluid in the following next 48−72 hours. General wellbeing improves, haemodynamic status stabilizes during this phase.

Haematocrit values get stabilized or it may became lower as a result of fluid reabsorption. The white blood cell count usually starts to rise and recovery of the platelet count occurs later.

During critical or recovery phase, if patients treated with excessive intravenous fluids, patient may develop respiratory distress secondary to massive pleural effusion and ascites, pulmonary oedema or congestive heart failure.

Severe dengue:

Severe dengue is defined if patients has one or more of the following

(1)Severe plasma leakage that leads to shock and/or

(2)Fluid accumulation leads to respiratory distress;

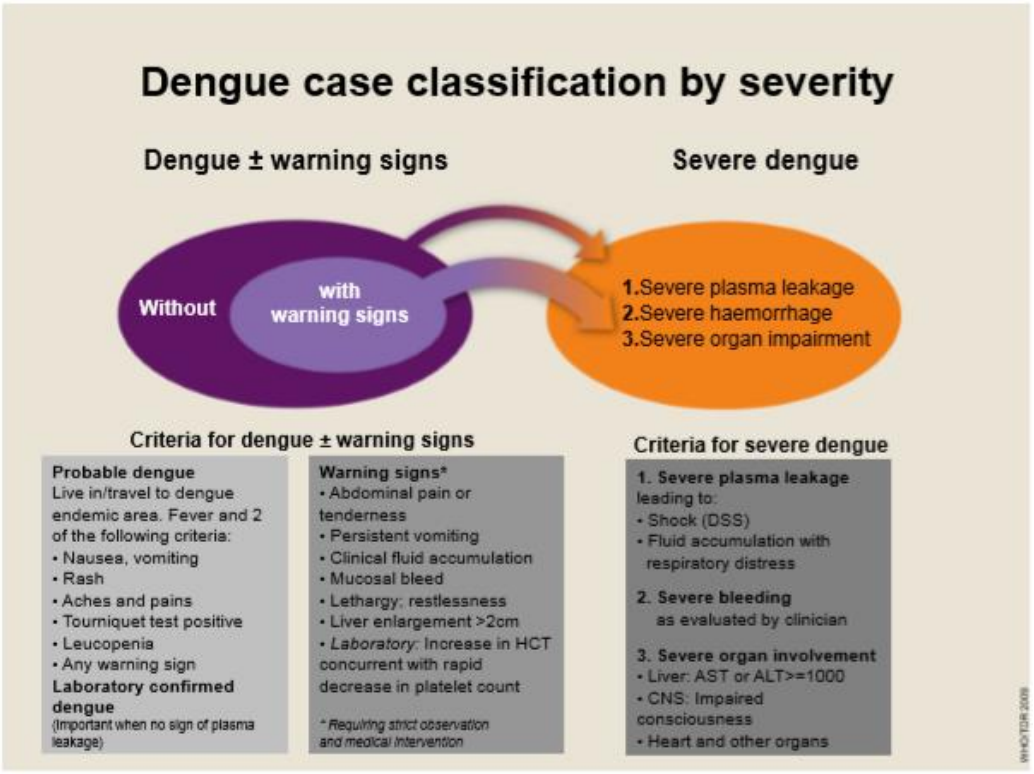
(3)Severe bleeding

(4)Severe organ impairment.

Severe plasma leakage and dengue shock:

During defervescence period (on days 4−5 of illness), there will be an increased vascular permeability leads to capillary leakage and results in hypovolemic shock. Shock usually preceded by warning signs.The course of the shock progresses from asymptomatic capillary leakage phase, followed by compensated shock and progressed to hypotensive shock to cardiac arrest.

One of the important sign during initial stage of shock phase is tachycardia. Other compensatory mechanisms are peripheral vasoconstriction and poor perfusion of peripheries &tachypnea (51).Poor perfusion of extremeties are clinically monitored by cold peripheris, capillary refill time > 2 seconds and low volume pulses. As peripheral vasoconstriction increases, the diastolic pressure rises and the pulse pressure narrows.Pulse pressure of less than 20 mmHg indicates severe shock.



ALT = alanine aminotransferase; AST = aspartate aminotransferase; CNS = central nervous system; DSS = dengue shock syndrome; HCT = haematocrit

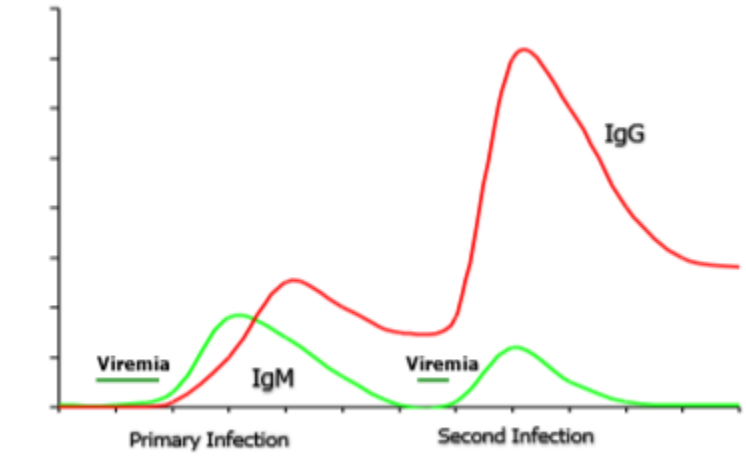
Fig. 11. Dengue case classification by severity

During incubation period of 4–10 days dengue virus replicates and an antibody response to dengue virus develops. After incubation period patient develops symptoms at that time viraemia is detectable serum and it is no longer detectable once patient enters into

defervescence phase. There is a coincidence between disappearance of viraemia and development of IgM antibody (56).

In a primary infection, viraemia develops 1–2 days before the onset of fever and lasts for 4–5 days after onset of fever. Anti IgM dengue specific antibodies detected from serum after 3−6 days of fever onset & low levels of IgM antibodies persists upto 3 months of fever. In primary infection, also there is a slowly raising dengue-specific IgG antibodies, detectable after 9−10 days of fever onset at low levels. Persistence of low IgG levels, indicates past dengue infection(52–55, 57, 58).

In secondary infection, there is a rapid increase of anti-dengue specific IgG antibodies & will be in higher levels, persists for 30- 40 days. There is a slower rise in IgM antibodies and in lower levels.



IgG = immunoglobulin G; IgM = immunoglobulin M

Fig.12 .Virological and serological markers of dengue infection according to time of illness

The diagnostic method to confirm an acute infection depends on the time of clinical illness:

Virus and its components detected during febrile phase, antibodies detected during critical and convalescent phases

During febrile phase (day 1 to day 5 of fever):

Virus genome detection done using reverse transcriptase polymerase chain reaction (RT-PCR) and real-time RT-PCR. It is a confirmatory test for an acute dengue infection. Both tests have high sensitivity and allows for identification of serotypes and for quantification of genome copies (52-55, 59-61). NS1 Ag is used for diagnosis of acute infection (63). NS1 Ag detection done by enzyme-linked immunosorbent assay (ELISA) method. Rapid commercial tests are also available (62).

Table .1 . Dengue diagnostics and sample characteristics

	Clinical sample	Diagnostic method	Methodology	Time to results
Virus detection and its components	Acute serum (1–5 days of fever) and necropsy tissues	Viral isolation	Mosquito or mosquito cell culture inoculation	One week or more
		Nucleic acid detection	RT-PCR and real time RT-PCR	1 or 2 days
		Antigen detection	NS1 Ag rapid tests	Minutes
			NS1 Ag ELISA	1 day
			Immuno-histochemistry	2–5 days
Serological response	Paired sera (acute serum from1–5 days and second serum 15–21 days after)	IgM or IgG seroconversion	ELISA HIA	1–2 days
			Neutralization Test	Minimum 7 days
	Serum after day 5 of fever	IgM detection (recent infection)	ELISA	1 or 2 days
			Rapid tests	Minutes
		IgG detection	IgG ELISA HIA	1 or 2 days

ELISA = enzyme-linked immunosorbent assay; HIA = haemagglutination inhibition assay; IgG = immunoglobulin G; IgM = immunoglobulin M; NS1 Ag = non-structural protein 1 antigen; RT-PCR = reverse transcriptase polymerase chain reaction

During Critical and recovery phases (from day 5 of illness):

Specific IgM dengue antibodies is used for recent dengue infection. IgM detection done by MAC-ELISA method and rapid tests. Rapid tests has a low sensitivity (64, 65). Anti IgG specific antibodies detected in high levels by ELISA suggests recent dengue infection (54,55).

A single serum sample is collected after day 5 of fever onset for IgM determination. If both antibodies are positive, IgM/IgG optical density ratio is used for classify into primary or secondary infection. Ratio of more than 1.2 (patient's sera at 1 in 100 serum dilution) or 1.4 (serum dilution of 1 in 20) suggests primary infection (52). In addition to that, higher titres of IgG more than 1/1280 by HIA or ELISA, suggests secondary infection (52-55,57,58).

IgM antibodies persist in serum for three months after fever onset, so if IgM is detected in sample it indicates recent infection and classified as probable dengue. Confirmation of dengue infection done by study of paired sera which is collected 15–21 days after the first sample. Rising titres of dengue antibodies confirms dengue infection (52-55, 57, 66).

Table 2 Confirmed and probable dengue diagnosis, interpretation of results and sample characteristics

	Method	Interpretation	Sample characteristics
Confirmed dengue infection	Viral isolation	Virus isolated	Serum (collected at 1–5 days of fever) Necropsy tissues
	Genome detection	Positive RT-PCR or positive real-time RT-PCR	
	Antigen detection	Positive NS1 Ag	
		Positive immunohistochemical	Necropsy tissues
	IgM seroconversion	From negative IgM to positive IgM in paired sera	Acute serum (days 1–5) and convalescent serum (15–21 days after first serum)
	IgG seroconversion	From negative IgG to positive IgG in paired sera or 4-fold increase IgG levels among paired sera	
Probable dengue infection	Positive IgM	Positive IgM	Single serum collected after day 5
	High IgG levels	High IgG levels by ELISA or HI (≥ 1280)	

ELISA = enzyme-linked immunosorbent assay; IgG = immunoglobulin G; IgM = immunoglobulin M; NS1 Ag = non-structural protein 1 antigen; RT-PCR = reverse transcriptase polymerase chain reaction

Laboratory findings

Platelets and serum biochemistries may be normal in some dengue patients. Leucopenia, thrombocytopenia, elevated liver enzymes seen in most of the dengue patients. Initial Leucopenia of 5 $X10^9$/l predicts severity of dengue (42) and relative lymphocytosisalong with more than 15% of atypical lymphocytes at the end of febrile phase. Coagulation abnormalities such as elevated prothrombin time, prolonged aPTT, elevated degraded products of fibrinogen seen in patients with severe dengue (30).If patient had prolonged shock, they also develop metabolic acidosis, low sodium, pre renal acute renal failure.

Management of dengue:

Step I:

Overall assessment includes history, physical examination and lab diagnosis

The history should include:

- Date of onset of fever/illness;
- Quantity of oral fluid intake;
- Diarrhoea; urine output;
- Assessment of warning signs;
- Change in mental state/seizure/dizziness;

and other relevant histories, such as family history of dengue or dengue fever in neighbourhood, travel to dengue-endemic areas, co-existing conditions (e.g. infancy, pregnancy, obesity, diabetes mellitus, hypertension);

The physical examination should include:

- Assessment of mental state;
- Assessment of hydration status;
- Assessment of haemodynamic status;
- Look for tachypnea /pleural effusion;
- Look for abdominal tenderness /hepatomegaly/ ascites;
- Look for rashes and any bleeding;
- Tourniquet test.

Investigation:

- Full blood count should be done at the first visit; and repeated count should be done daily till critical phase is over.
- The haematocrit should be monitored daily (haematocrit measured in early febrile phase used as the patient's own baseline).
- Leukopenia usually precedes the onset of the critical phase and has been associated with severe disease.
- A rapid fall in platelet count along with a rising haematocrit from the baseline, indicates progression of disease to plasma leakage/critical phase of the disease. Usually leukopenia (≤ 5000 cells/mm3) precedes platelet fall.
- Liver function test, serum electrolytes, blood urea, serum creatinine, cardiac enzymes, ECG (If needed)

Step II

Diagnosis, assessment of disease phase and severity:

Based on history, physical examination and/or full blood count and haematocrit, whether the disease is dengue & which phase it is in (febrile /critical /or recovery) should be determined.

Step III

Management:

Group A (67):

In this group patients able to tolerate oral liquids & does not have any warning signs.

Advised for bed rest and plenty of oral fluids. These patients can be sent to home and instructed about warning signs. If patient develops any warning signs, advised to brought to the nearest hospital immediately. • For high fever give paracetamol. (Recommended dose is 10 mg/kg/dose and not more than 3 g/day in adults). If patient still has high fever give sponge with tepid water. Avoid intramuscular injections. Admission is advised in these patients, who are not able to take adequate oral liquids at home and those with co-existing conditions.

Group B (67):

Patients with warning signs comes under this group. Rapid fluid replacement prevents progression to shock and modifies the disease course and severity of the disease.

For intravenous fluids isotonic solutions (0.9% saline, Ringer's lactate) are used. Obtain baseline haematocrit values before starting intravenous fluids. Initially for first 1-2 hours fluids started at a rate of 5-7 mg/kg/hour followed by 3-5ml/kg/hour for next 2-4 hours, and continue with 2-3ml/kg/hour or less based on clinical response.

- Repeat haematocrit remains the same or minimally raised and vital signs are stable, continue intravenous fluids at same rate of 2−3 ml/kg/hour.

If repeat haematocrit rises rapidly or any worsening of vital signs increase the rate of intravenous fluids to 5−10 ml/kg/hour for 1−2 hours.

Minimum intravenous fluid should be required to maintain adequate perfusion and urine output of about 0.5 ml/kg/hour.

Intravenous fluids are needed only for 24−48 hours and gradually reduced when plasma leakage decreases.

Group C (67):

Severe dengue:

These patients are in critical phase of the disease and have severe plasma leakage and shock and/or fluid accumulation and respiratory distress, severe haemorrhagic manifestations and severe organ impairment (liver damage, renal damage, cardiomyopathy, encephalopathy / encephalitis).

Plasma leakages should be replaced rapidly with isotonic solution. Intravenous fluids should be continued to maintain effective circulation for 24−48 hours and to improve central and peripheral circulation. Blood transfusion should be reserved for those who have severe bleeding or suspected severe bleeding along with unexplained hypotension.

Treatment of shock: (104-108)

If patient had shock start intravenous fluid resuscitation at a rate of 5−10 ml/kg/hour over one hour in adults. Reassess the patient's vital signs, capillary refill time, haematocrit and

urine output. If condition improves, intravenous fluids should be gradually reduced and to continue the intravenous fluids as followed in group B patients.

If patient had unstable vitals & shock persists, check the haematocrit after the first bolus of intravenous fluids. If the haematocrit is still high or it rise from baseline, repeat a second bolus of crystalloid solution at a rate of 10−20 ml/kg/hour for one hour. After one hour based on clinical assessment reduce fluids as mentioned above.

If the haematocrit decreases but patient still have unstable vital signs, indicates bleeding. If patient had severe bleeding transfuse fresh whole blood or fresh packed red cells.

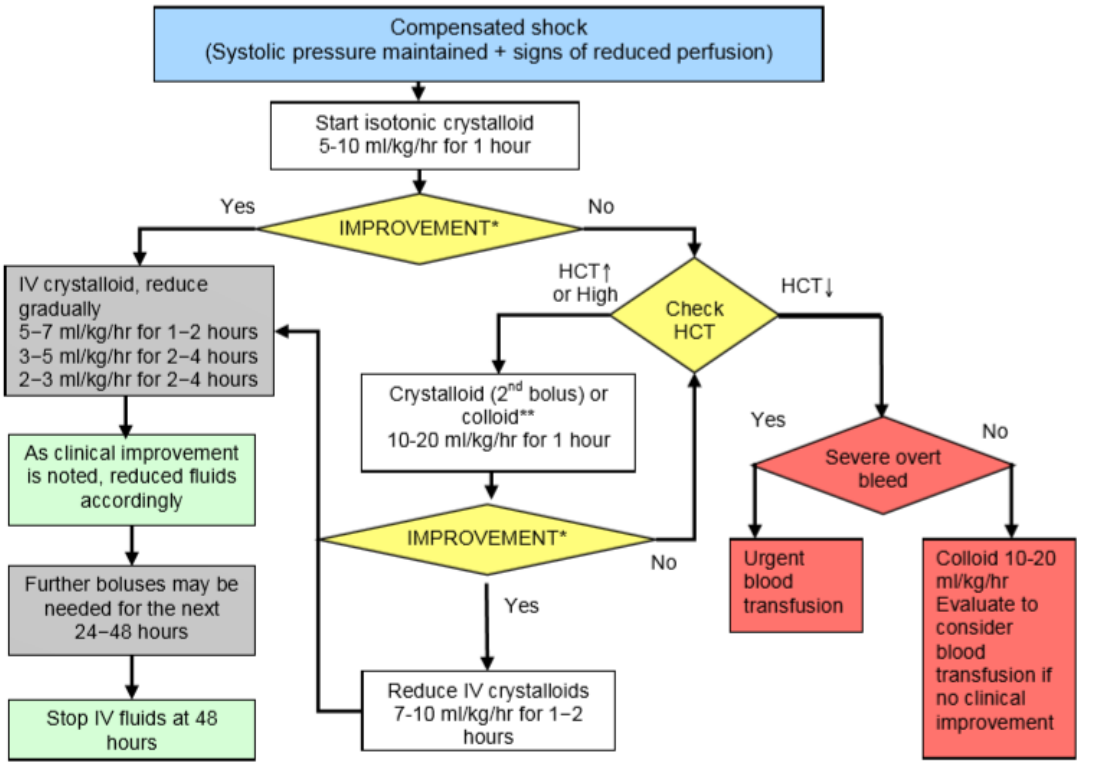


Fig. 13. Algorithm for fluid management of compensated shock: in adults

Treatment of haemorrhagic complications:

Blood transfusion (fresh packed red cells or fresh whole blood) should be given if severe bleeding is suspected or recognized.

- There is no evidence of transfusing platelet concentrates or fresh-frozen plasma for severe bleeding in dengue (68)

Platelet transfusion considered in anticipation of severe bleeding.

Complications:

Severe dengue infections leads to complications like liver failure, coagulopathy, encephalopathy, myocarditis, acute renal failure, and haemolytic uraemic syndrome (8).Generally, these complications are rare, but these complications are reported in increased frequency (69).

Liver failure:

Replication of dengue virus takes place in hepatocytes and Kupffer cells, so liver gets involved in all forms of dengue infection (50). Severity of liver involvement depends on severity of dengue infection. There is significant elevation of aspartate transaminase and alanine transaminase, significantly lower levels of globulins are seen in severe dengue infection (69, 70).

Severity of liver involvement also varies with serotypes of dengue virus. liver involvement is greater in infection with DEN-3 or DEN-4 serotypes when compared with

other two serotypes (78). Due to hepatitis or focal necrosis of hepatocytes leads to fulminant hepatic failure and progress to hepatic encephalopathy and even death (79).Acute liver failure presents with jaundice, altered sleep cycle, altered sensorium or convulsions

Encephalopathy:

In severe dengue 0.5% of patients reported as encephalopathy & mortality rate was 22% (87). Number of factors leads to development of encephalopathy, which includes ; liver failure with hepatic encephalopathy, metabolic encephalopathy secondary to electrolyte imbalances, fluid extravasation secondary to vascular changes leads tocerebral oedema, hypo-perfusion due to shock, and dengue encephalitis (131).

Myocarditis:

Acute myocarditis which is reversible has been reported in dengue infections. There is a significant ST segment and T wave changes found in electrocardiogram. Low ejection fractions and global hypokinesia have been found on Echocardiogram. None of the patients shown any myocardial necrosis (132).Left ventricular failure may contribute to dengue shock syndrome and worsen the clinical condition (132, 133).

RESULTS

In our study, we collected data regarding clinical presentation, biochemical parameters, ultrasonographic findings of 100 dengue patients positive for NS1 antigen or IgM /IgG positive serology.

According to revised WHO classification these patients were classified into dengue fever without warning signs, dengue fever with warning signs and severe dengue based on severity of infection.

Severity of dengue classification:

Table .3.Classification based on severity

Diagnosis	**No of patients**	**Percent**
Dengue fever	45	45.0
DF with warning signs	53	53.0
Severe Dengue	2	2.0
Total	100	100.0

In our study, 45 patients had dengue fever (45%), 53 patients had dengue fever with warning signs (53%), and 2 patients had severe dengue (2%).

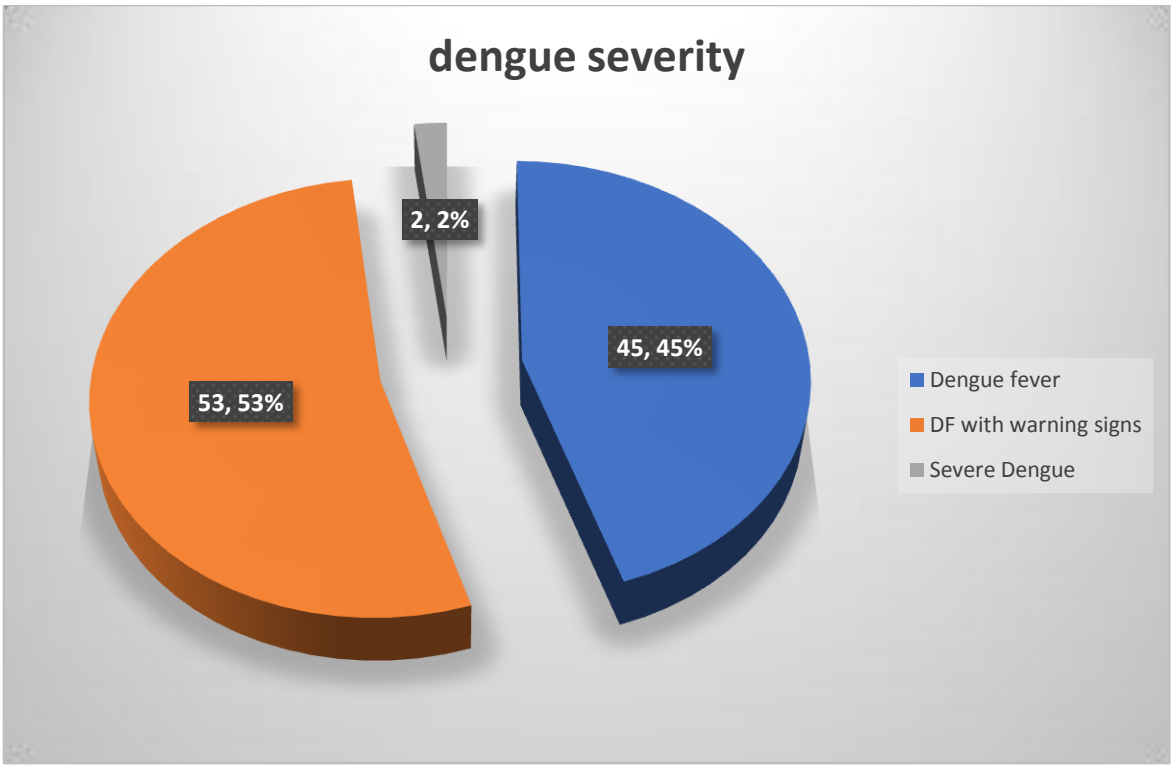


Figure.14.Graphic representation of dengue severity classification

Table:.4. Age distribution among study population:

Age in years	No of patients	Percent
Less than 20	18	18.0
21 - 30	39	39.0
31 - 40	22	22.0
41 - 50	9	9.0
51 - 60	7	7.0
Above 60	5	5.0
Total	100	100.0

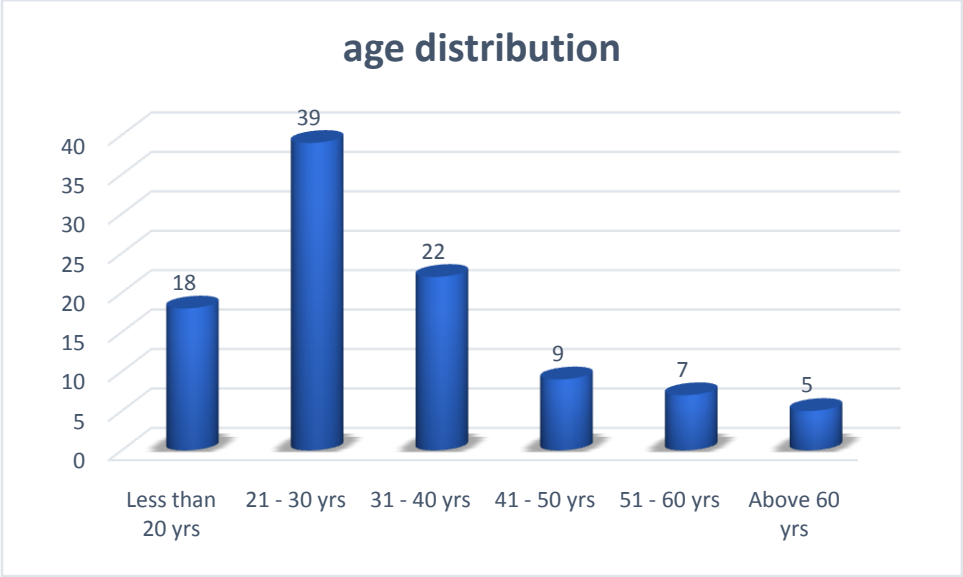


Figure:15 graphic representation of age distribution

Patients of 21- 30 years of age (39%) was most commonly affected followed by 31 – 40 years of age (22%), less than 20 years of age (18%), 41-50 years of age (9%), 51 – 60 years of age (7%), 5% seen in above 60 years of age.

Age and dengue severity:

Table:5. Age distribution and severity of dengue fever among study population:

	Dengue fever	DF with warning signs	Severe dengue
< 20 years	8	10	0
21- 30 years	21	17	1
31- 40 years	4	17	1
41-50 years	2	7	0
51-60 years	6	1	0
>60 years	4	1	0

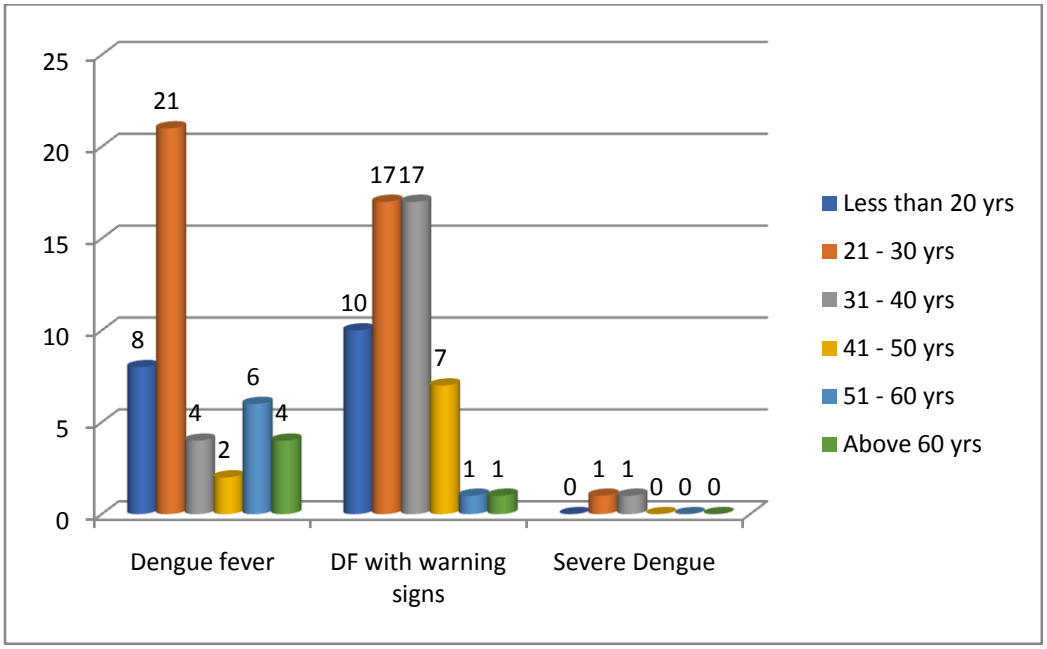


Figure :16. Graphic representation of age distribution and dengue severityamong study population

There is no statically significant differences between different age groups and severity of dengue (p value = 0.057)

Sex distribution:

Table .6. Sex distribution among study population:

Gender	No of patients	Percent
Male	59	59.0
Female	41	41.0
Total	100	100.0

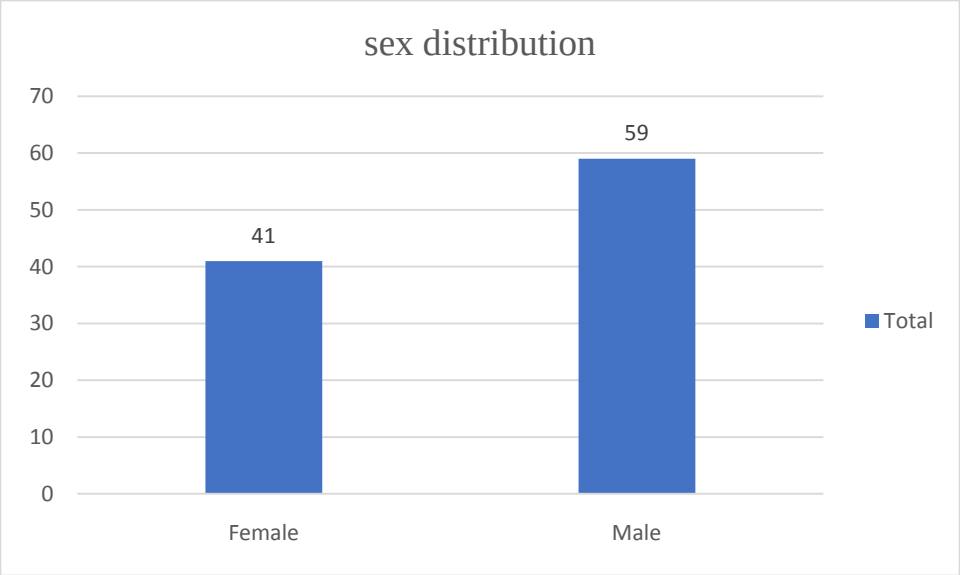


Figure :17.graphic representation of sex distribution among study population

Of 100 patients , 59 patients were male (59%), 41 patients were female (41%). Males were more commonly affected than females.

Sex distribution and severity of dengue:

Table: 7. Sex distribution and severity of dengue among study population

Diagnosis	Male	Female	Total
Dengue fever	29	16	45
Dengue fever with warning signs	30	23	53
Severe dengue	0	2	2
Total	59	41	100

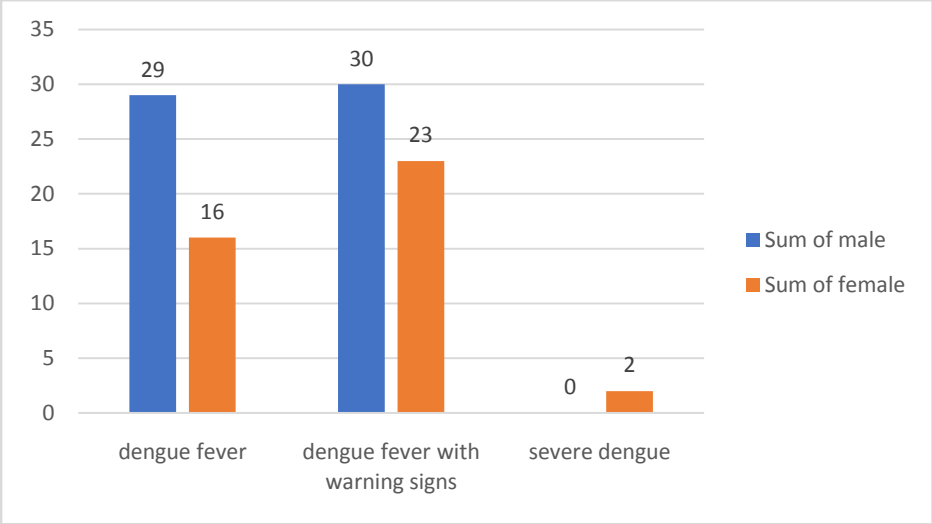


Figure: 18 - Graphic representation of Sex distribution and severity of dengue among study population

In 59 male patients, 29 (49.1%) patients had dengue fever and 30 (50.8%) patients had dengue fever with warning signs and no severe dengue in males.

In 41 female patients, 16 (39.02%) patients had dengue fever, 23 (56.09%) patients had dengue fever with warning signs, and 2 patients had severe dengue.

There is no statistical difference between sex and severity of dengue fever.(p value= 0.15)

Day of presentation:

Table: 8. No of patients and day of presentation to hospital

Day of illness	No of patients	Percent
1	3	3.0
2	5	5.0
3	25	25.0
4	23	23.0
5	24	24.0
6	16	16.0
7	4	4.0
Total	100	100.0

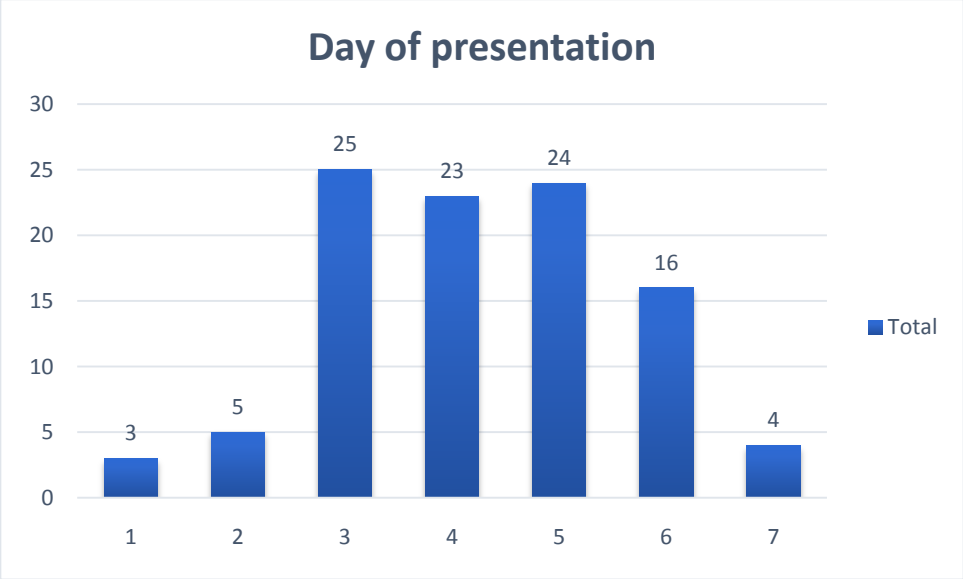


Figure :19. No of patients and day of presentation to hospital

In 100 patients , about 25 cases (25%) presented to hospital on day 3 of illness, 23 cases (23%) on day 4 illness, 24 cases on day 5 of illness, 16 cases(16%) on day 6 of illness, 4 cases (4%) on day 7 of illness, 5 cases and 3 cases on day 2 and 1 of illnesses respectively.

NS1:

Table:9. NS1 Serology among study population

	Positive	Negative
Ns1	**68**	**14**

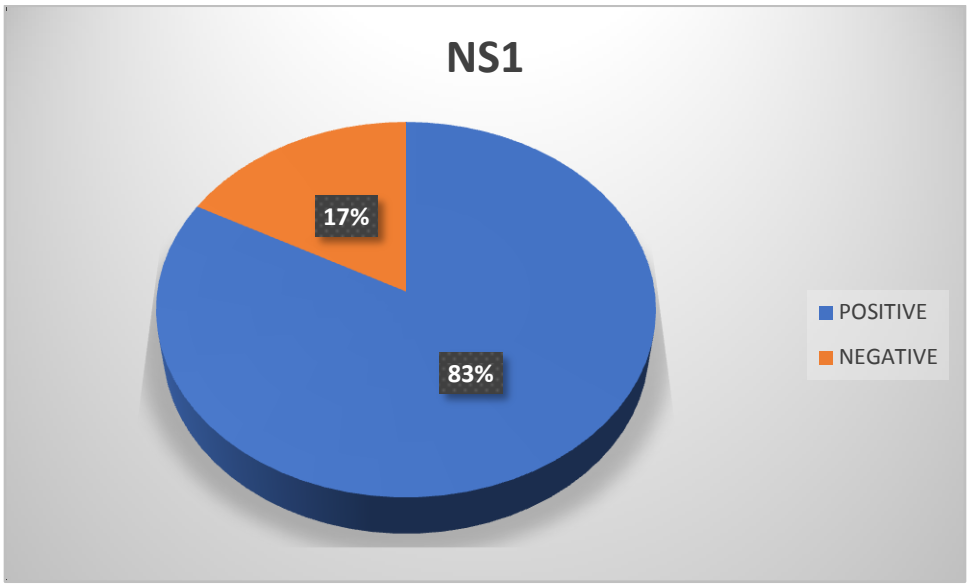


Figure 20: Graphic representation of NS1 status among study population:

Dengue NS1 antigen assay was done in 82 patients and it was positive in 68 (68%) patients, negative in 14 (14%) patients, not done in 18 (18%) patients.

NS1 antigen not done in 18 patients, in which 16 patients presented to hospital after day 5 of illness. For 2 patients done outside and found to be positive.

For these 18 patients dengue Ig M / Ig G serology was done in which Ig M was positive in 4 patients, Ig G was positive in 2 patients and 12 were positive for both Ig M &Ig G.

NS1 was negative in 14 patients.

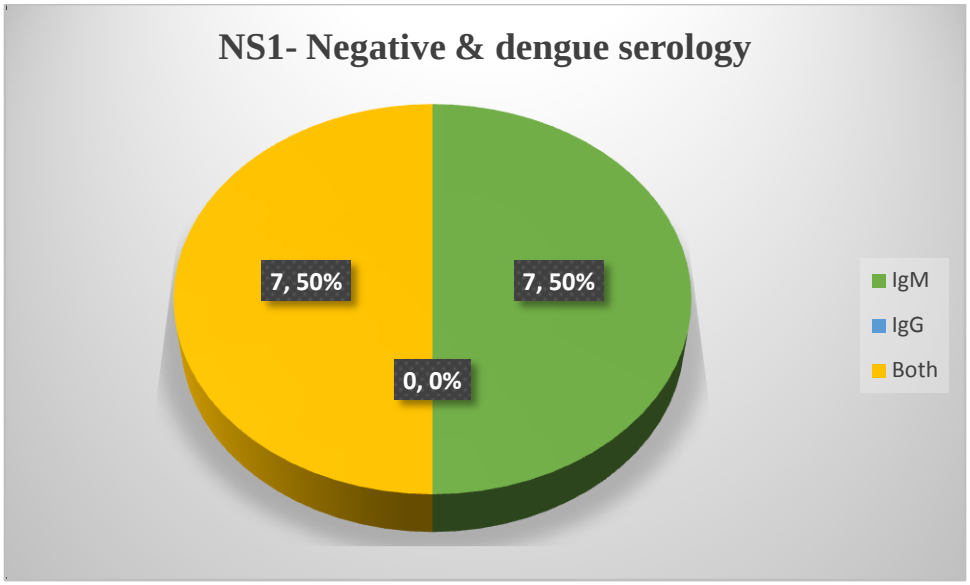


Figure: 21.NS1- Negative & dengue serology among study population

Dengue serology was done in NS1 negative (14) patients, in which 7 were positive for IgM, 7 were positive for both IgM&IgG.

Dengue serology:

Table:10. Dengue serology among study population

Antibodies	Positive
IgM	54
IgG	2
Both	44

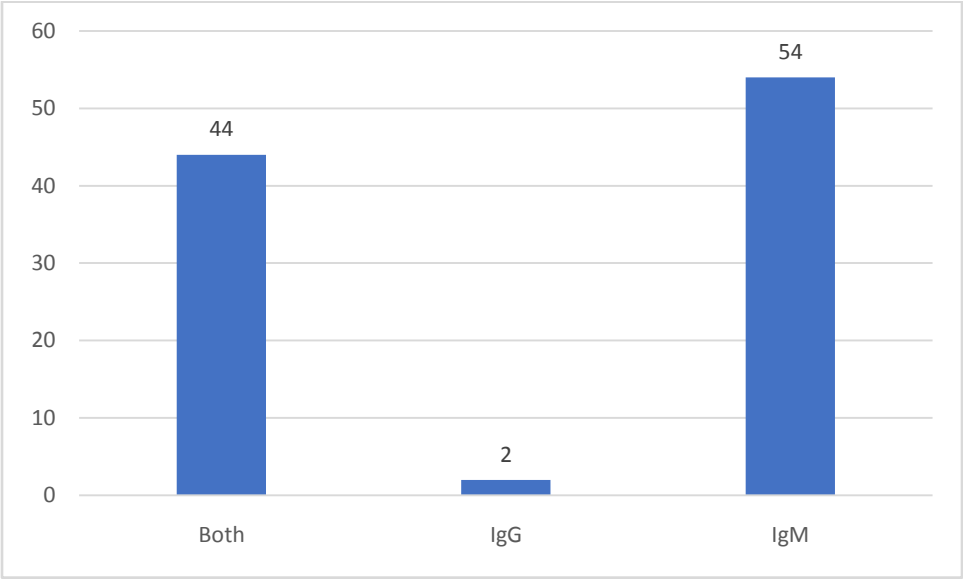


Figure:22. Dengue serology among study population

In 100 patients, 54 (54%) patients were positive for IgM, 2 patients were positive for IgG, 44 patients were positive for both IgM and IgG.

Table :11. Severity of dengue in primary and secondary dengue infection among study population

	Dengue fever	**Dengue with warning signs**	**Severe dengue**
Primary dengue	30 (55.55%)	23 (42.59%)	1(1.85%)
Secondary dengue	14 (31.81%)	29 (65.9%)	1(2.27%)

54 patients had primary dengue infection, in which 30 patients had dengue fever without warning signs, 23 patients had dengue with warning signs, 1 had severe dengue.

44 patients had secondary dengue infection, in which 14 patients had dengue fever without warning signs, 29 patients had dengue with warning signs, 1 had severe dengue.

Symptoms:

Table:12. Symptoms of dengue fever among study population

Symptoms	No of patients
Fever	100
Joint pain	68
Myalgia	52
Headache	72
RO pain	36
Abdominal pain	14
Vomiting	43
Diarrhea	14
Erythematous skin Rashes	15
Petechiae	11
Bleeding gums	7
Epistaxis	2
Increased bleeding PV	6
Malena	11
Hematuria	2

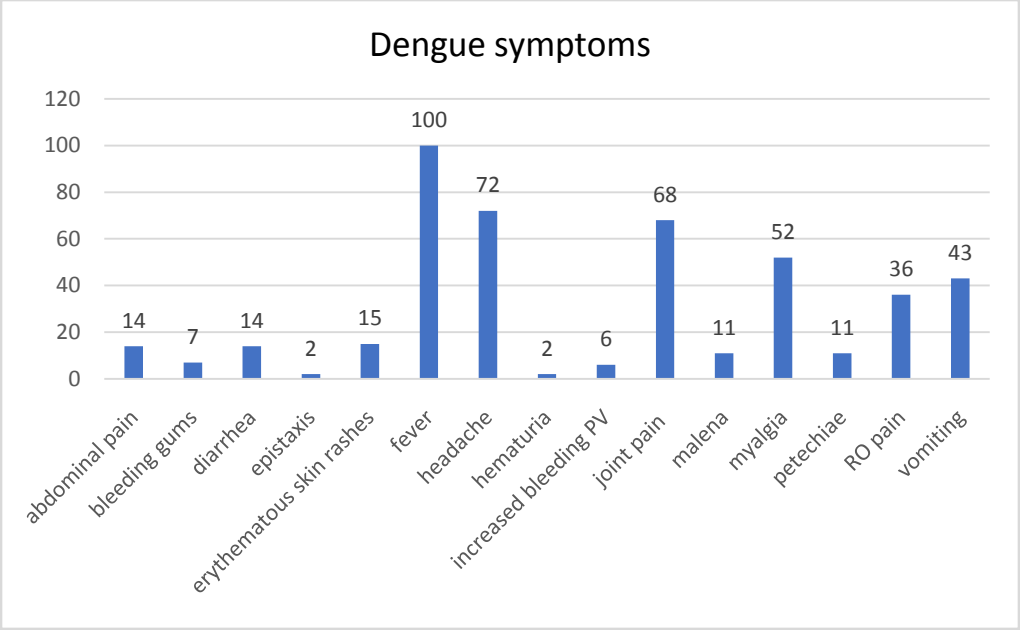


Figure.23. Symptoms of dengue among study population

In the present study, symptoms observed in decreased order of frequency were : fever (100 %), headache (72%), joint pain (68%), myalgia (52%), vomiting (43%) ,retro orbital pain (36%), erythematous skin rashes (15%), abdominal pain (14%), diarrhea (14%), malena (11%), petechiae (11%),bleeding gums (7%), excessive bleeding per vaginum (6%), hematuria (2%), epistaxis (2%).

Haematocrit:

Table: 13. Haematocrit among study population

	Frequency	Percent
Normal	58	58.0
Elevated	42	42.0
Total	100	100.0

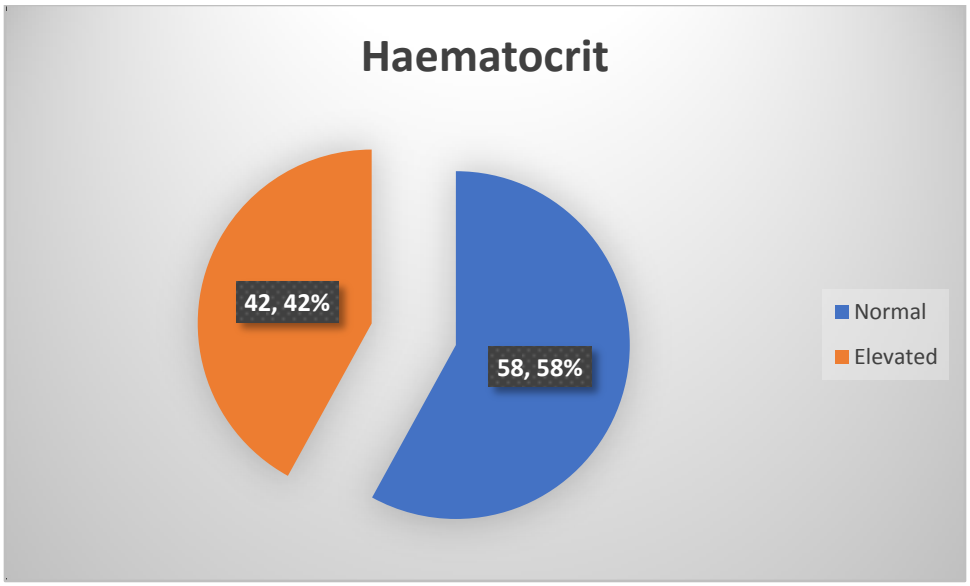


Figure:24. Haematocrit among study population:

Haematocrit elevated the above normal values were seen in 42 (42%) patients. Haematocrit elevation was statistically insignificant between three groups.

Leukopenia:

Table: 14. Leukopenia in dengue among study population

	< 4000	**4,000 – 10,000**	**>10,000**
Dengue fever	24	19	2
Dengue fever with warning signs	25	24	4
Severe dengue	1	1	0
	50	44	6

Table :15. leucopenia and dengue severity among study population

DIAGNOSIS		**LEUKOPENIA**		**Total**	**P value**
		Yes	**No**		
Dengue fever	No	24	21	45	0.831
	%	53.3%	46.7%	100.0%	
DF with warning signs	No	25	28	53	
	%	47.2%	52.8%	100.0%	
Severe Dengue	No	1	1	2	
	%	50.0%	50.0%	100.0%	
Total	No	50	50	100	
	%	50.0%	50.0%	100.0%	

In our study, leucopenia was seen 24 (53.3%) of patients in dengue fever without warning signs, 25 (47.2%) patients in dengue fever with warning signs, 1 (50%) in severe dengue, but there is no statistically significant leucopenia between these groups.

ACTIVATED LYMPHOCYTES

Table: 16. Activated lymphocytes among study population

	No of patients	Percent
Yes	53	53.0
No	47	47.0
Total	100	100.0

In 100 patients activated lymphocytes was seen in 53 (53%) patients, and there was no statistical significance between these groups.

MONOCYTOSIS

Table:17. Monocytosis in dengue among study population

	No of patients	Percent
Yes	8	8.0
No	92	92.0
Total	100	100.0

Monocytosis was seen in 8 (8%) of patients.

Thrombocytopenia:

All patients (100) patients had thrombocytopenia.

All patients were categorised into mild, moderate, severe thrombocytopenia.

Mild thrombocytopenia – 50,000 - 1,00,000

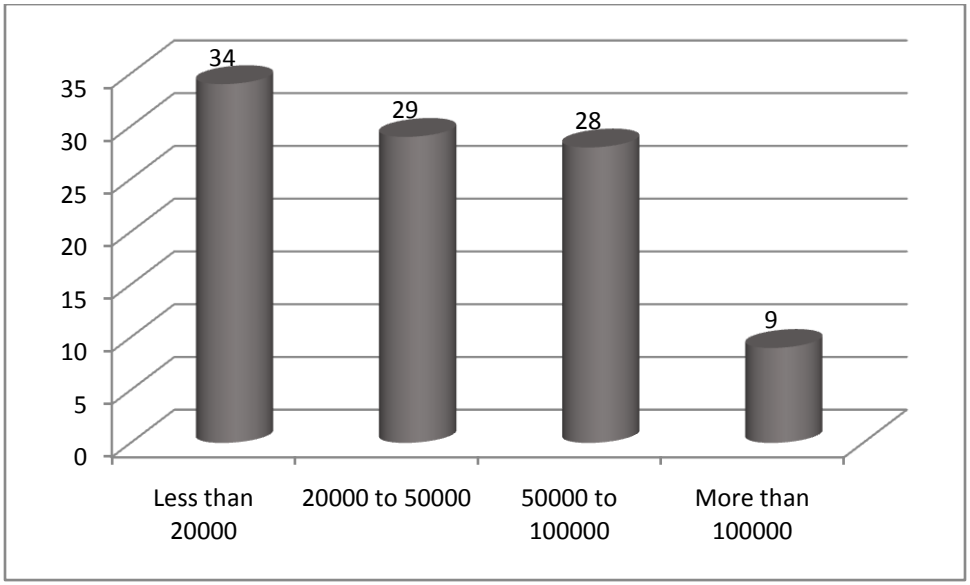
Moderate thrombocytopenia – 20,000 – 50,000

Severe thrombocytopenia - < 20,000

Table: 18. Frequency distribution of Thrombocytopenia among study population

	Frequency	**Percent**
Less than 20000	34	34.0
20000 to 50000	29	29.0
50000 to 100000	28	28.0
More than 100000	9	9.0
Total	100	100.0

Figure:25. Frequency distribution of Thrombocytopenia among study population

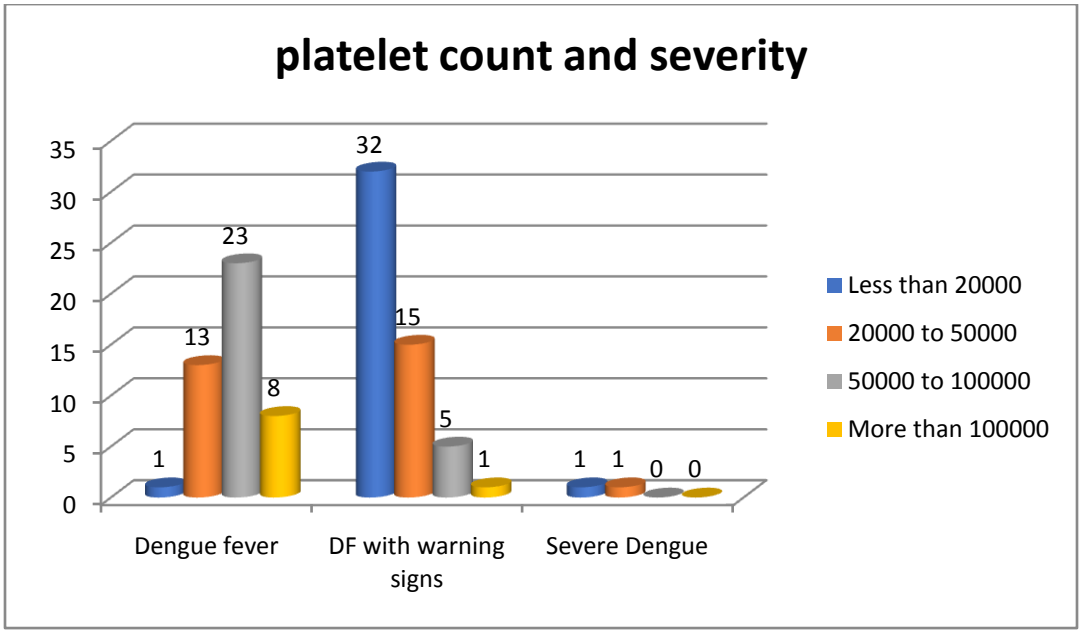


Thrombocytopenia was seen in all 100 patients. In which severe thrombocytopenia (<20,000 cu mm^3) seen in 34 (34%) patients, moderate thrombocytopenia (20,000 – 50,000 cu mm^3) seen in 29 (29%) patients, mild thrombocytopenia seen in 28 (28 %) patients.

Table:19. Platelet count and dengue severityamong study population

Diagnosis		Platelet					P value
		Less than 20000	20000 to 50000	50000 to 100000	More than 100000	Total	
Dengue fever	No	1	13	23	8	45	0.000
	%	2.2%	28.9%	51.1%	17.8%	100.0%	
DF with warning signs	No	32	15	5	1	53	
	%	60.4%	28.3%	9.4%	1.9%	100.0%	
Severe Dengue	No	1	1	0	0	2	
	%	50.0%	50.0%	.0%	.0%	100.0%	
Total	No	34	29	28	9	100	
	%	34.0%	29.0%	28.0%	9.0%	100.0%	

Figure.26. Platelet count and dengue severity among study population



Severe thrombocytopenia was seen in 34 (34%) patients, in which 32 (60.4%) patients had dengue fever with warning signs, 1 patient in each dengue fever (2.2%) and severe dengue (50%) group.

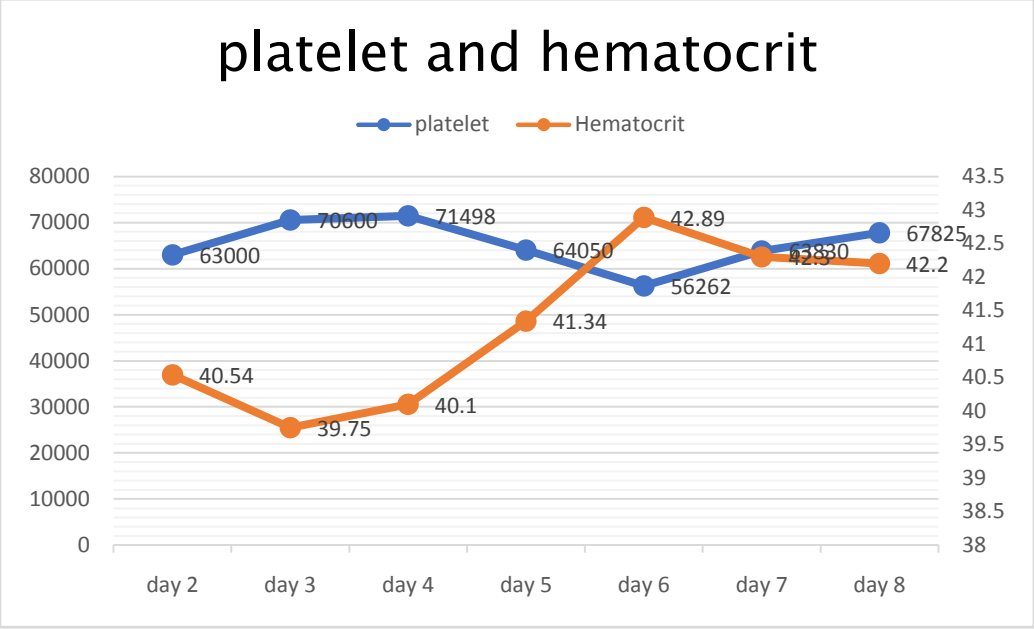
Moderate thrombocytopenia was seen in 29 (29%) patients, in which 13 (28.9%) patients had dengue fever, 15 (28.3%) patients had dengue fever with warning signs, 1 (50%) patient in severe dengue.

Mild thrombocytopenia was seen in 28 (28%) patients, 23 (51.1%) patients had dengue fever, 5 (9.4%) patients had dengue fever with warning signs. There was a stastically significant difference in mean platelet count between these groups (p value= 0.00).

Table.20. correlation between mean haematocrit and mean platelet count among study population

category	day 2	day 3	day 4	day 5	day 6	day 7	day 8
mean platelet count	63000	70600	71498	64050	56262	63830	67825
Hematocrit	40.54	39.75	40.1	41.34	42.89	42.3	42.2

Figure.27. correlation between mean haematocrit and mean platelet count among study population



This above graph shows correlation between mean platelet count and haematocrit. There was a negative correlation between mean platelet count and haematocrit (r = -0.72) and was insignificant.

Bleeding manifestations:

Petechiae were seen in 11 (11 %) patients at a mean platelet count of 14,272. 10 patients had dengue fever with warning signs. 1 patient had severe dengue.

Table.21. Petechiae and dengue severity among study population

DIAGNOSIS		Petechiae		Total	P value
		Yes	No		
Dengue fever	No	0	45	45	0.002
	%	.0%	100.0%	100.0%	
DF with warning signs	No	10	43	53	
	%	18.9%	81.1%	100.0%	
Severe Dengue	No	1	1	2	
	%	50.0%	50.0%	100.0%	
Total	No	11	89	100	
	%	11.0%	89.0%	100.0%	

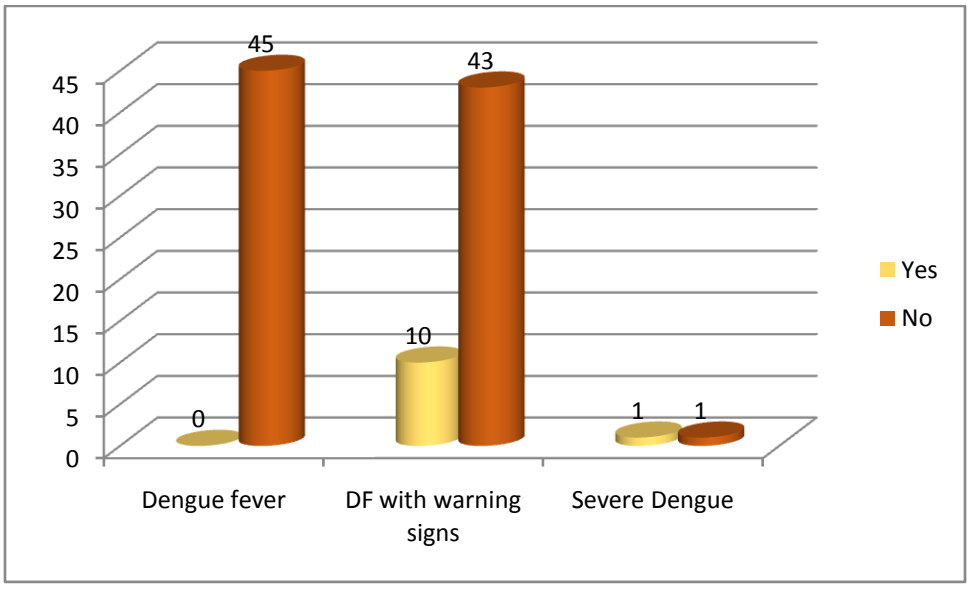


Figure.28. Petechiae and dengue severity among study population

Malena:

Malena seen in 11(11%) patients, 1 patient (2.2%) had dengue fever, 10 patients (18.9%) had dengue fever with warning signs. There is a statistical difference between both groups (p value 0.028).

Table.22. Malena and dengue severity among study population

DIAGNOSIS		Malena		Total	P value
		Yes	No		
Dengue fever	No	1	44	45	0.028
	% within Diagnosis	2.2%	97.8%	100.0%	
DF with warning signs	No	10	43	53	
	% within Diagnosis	18.9%	81.1%	100.0%	
Severe Dengue	No	0	2	2	
	% within Diagnosis	.0%	100.0%	100.0%	
Total	No	11	89	100	
	% within Diagnosis	11.0%	89.0%	100.0%	

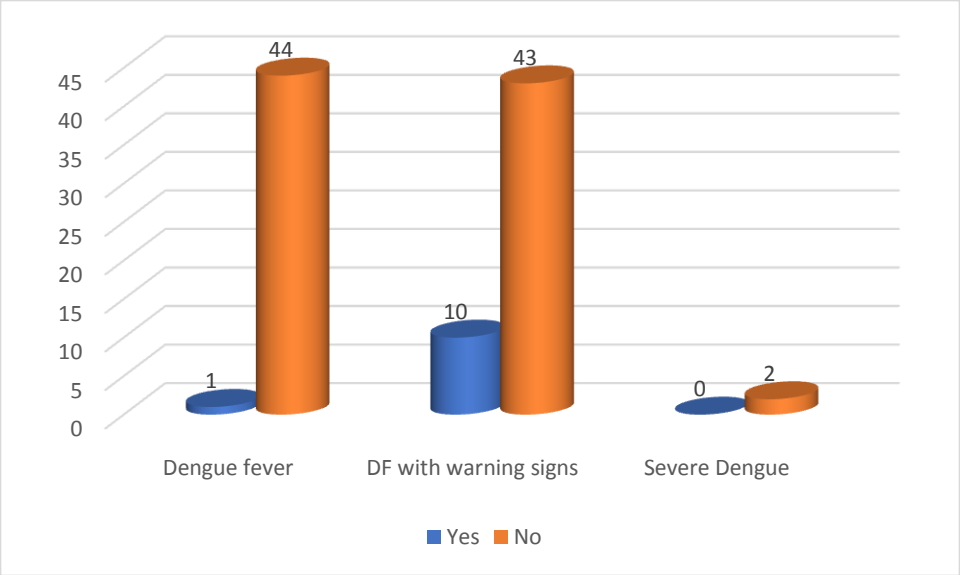


Figure.29. Malena and dengue severity among study population

Bleeding gums seen in 7 (7%) patients at a mean platelet count of 20,428. In 7 patients , 6 patients had dengue fever with warning signs and 1 patient had dengue fever, but there is no stasticial difference between groups (p value 0.19)

Table:23. Bleeding gums and dengue severity among study population

DIAGNOSIS		Bleeding gums		Total	P value
		Yes	No		
Dengue fever	No	1	44	45	0.197
	% within Diagnosis	2.2%	97.8%	100.0%	
DF with warning signs	No	6	47	53	
	% within Diagnosis	11.3%	88.7%	100.0%	
Severe Dengue	No	0	2	2	
	% within Diagnosis	.0%	100.0%	100.0%	
Total	No	7	93	100	
	% within Diagnosis	7.0%	93.0%	100.0%	

Bleeding per vaginum:

In 41 female patients, increased bleeding per vaginum seen in 6 patients, 1 patient (2.2%) had dengue fever, 4 patients (7.5%) had dengue fever with warning signs, 1 patient (50%) had severe dengue.

Epistaxis:

Table. 24. Epistaxis and dengue severity among study population

DIAGNOSIS		Epistaxis		Total	P value
		Yes	No		
Dengue fever	No	1	44	45	0.973
	% within Diagnosis	2.2%	97.8%	100.0%	
DF with warning signs	No	1	52	53	
	% within Diagnosis	1.9%	98.1%	100.0%	
Severe Dengue	No	0	2	2	
	% within Diagnosis	.0%	100.0%	100.0%	
Total	No	2	98	100	

2 patients had epistaxis, 1 patient (2.2%) had dengue fever, 1 patient (1.9%) had dengue fever with warning signs. There is no stastical differences between these groups.

Hematuria:

Table. 25. Hematuria and dengue severityamong study population

DIAGNOSIS		Dengue fever	DF with warning signs	Severe Dengue	Total	P value
Yes	No	1	1	0	2	0.973
	%	2.2%	1.9%	.0%	2.0%	
No	No	44	52	2	98	
	%	97.8%	98.1%	100.0%	98.0%	
Total	No	45	53	2	100	
	%	100.0%	100.0%	100.0%	100.0%	

2 patients had hematuria, 1 patient (2.2%) had hematuria, 1 patient (1.9%) had dengue fever with warning signs. There is no statistical difference between these groups.

In this study bleeding manifestations were seen in 39 (39%) patients.

Table :26.Platelet count and bleeding manifestations: among study population

Bleeding Manifestations	Platelet			Total
	<20000	20000-50000	50000-1 lakh	
Bleeding gums	5	2	0	7
Petechiae	9	2	0	11
Malena	6	5	0	11
Epistaxis	2	0	0	2
Increased Bleeding PV	4	2	0	6
Hematuria	1	0	1	2
Total	27	11	1	39

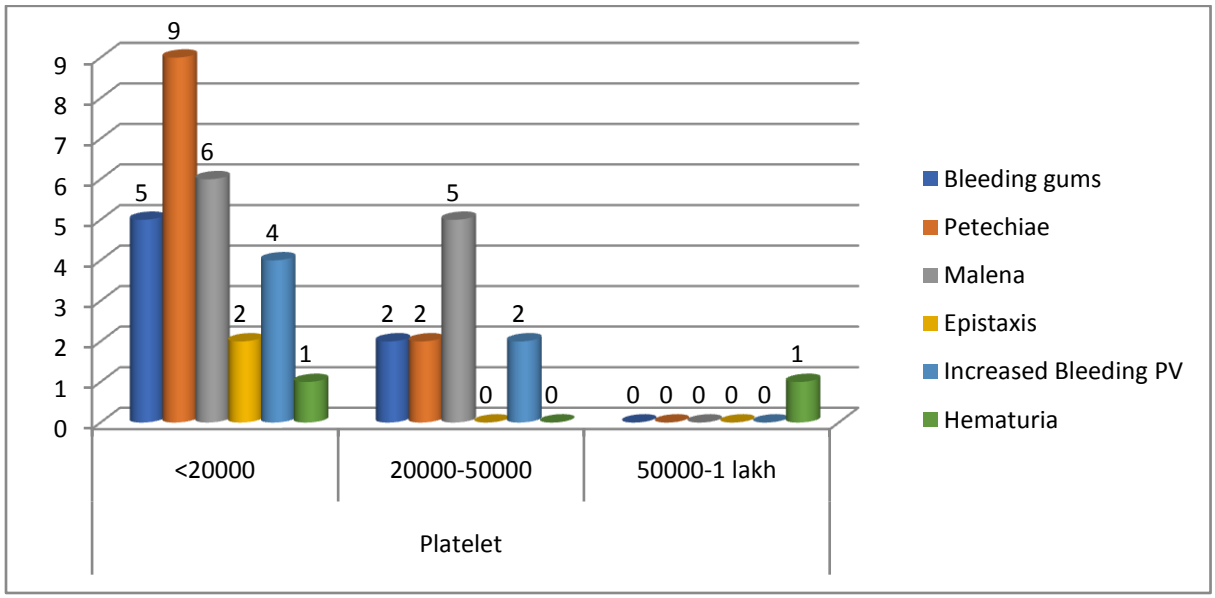


Figure.30: Bleeding manifestations and mean platelet count among study population

In 39 patients, 27 patients had bleeding manifestation occurred with severe thrombocytopenia, 11 patients had bleeding manifestation with moderate thrombocytopenia, 1 patient had bleeding manifestation with mild thrombocytopenia.

Biochemical profile:

Table:27. SGOT in dengue among study population

DIAGNOSIS		SGOT		Total	P value
		Normal	Elevated		
Dengue fever	No	13	32	45	0.001
	% within DIAGNOSIS	28.9%	71.1%	100.0%	
DF with warning signs	No	1	52	53	
	% within DIAGNOSIS	1.9%	98.1%	100.0%	
Severe Dengue	No	0	2	2	
	% within DIAGNOSIS	.0%	100.0%	100.0%	
Total	No	14	86	100	
	% within DIAGNOSIS	14.0%	86.0%	100.0%	

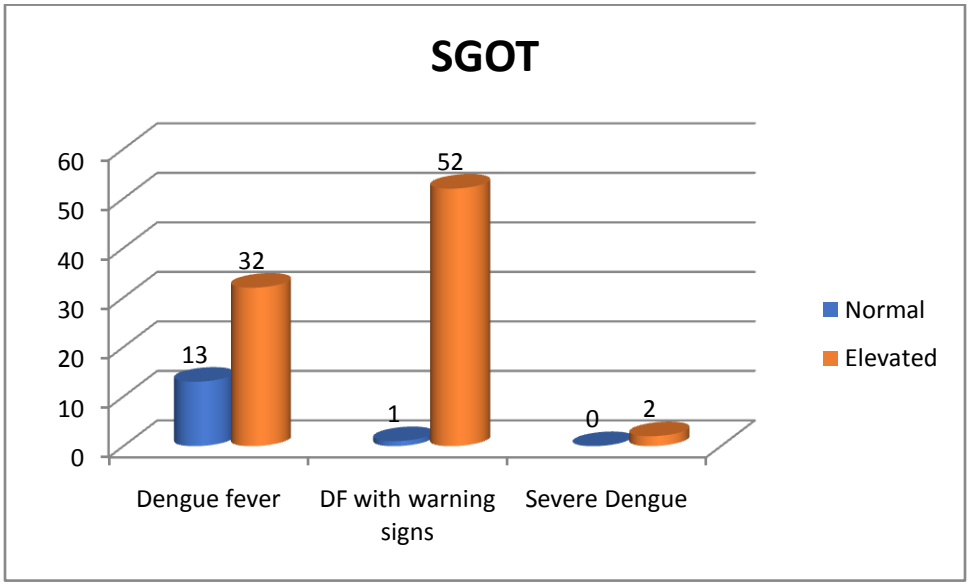


Figure .31. SGOT in dengue

In 100 patients, 86 (86%) patients had elevated AST. 32 (71.1%) patients had dengue fever, 52 (98.1%) in dengue with warning signs and 2 (100%) patients in severe dengue. There is a significant differences in these groups (p value = 0.001). There is a strong association between AST elevation and severity of dengue.

ALT:

Table:28. SGPT (ALT) in dengueamong study population

DIAGNOSIS		SGPT		Total	P value
		Normal	Elevated		
Dengue fever	No	25	20	45	0.000
	% within DIAGNOSIS	55.6%	44.4%	100.0%	
DF with warning signs	No	9	44	53	
	% within DIAGNOSIS	17.0%	83.0%	100.0%	
Severe Dengue	No	1	1	2	
	% within DIAGNOSIS	50.0%	50.0%	100.0%	
Total	No	35	65	100	
	% within DIAGNOSIS	35.0%	65.0%	100.0%	

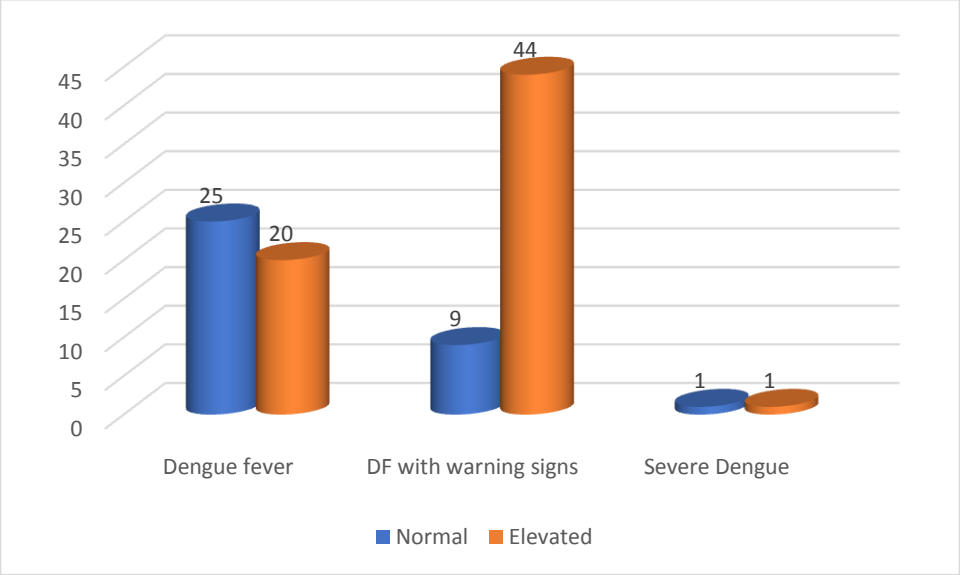


Figure. 32. SGPT in dengue

ALT elevation was seen in 65 (65%) patients. 20 (44.4%) had dengue fever, 44 (83%) in dengue fever with warning signs, 1 (50%) patient in severe dengue.

There is a significant differences between these groups and there is a strong association between elevated liver enzymes and dengue severity (p value = 0.000)

ALP:

Table.29 : ALP in dengue among study population

DIAGNOSIS		ALP		Total	P value
		Normal	Elevated		
Dengue fever	No	42	3	45	0.056
	% within DIAGNOSIS	93.3%	6.7%	100.0%	
DF with warning signs	No	42	11	53	
	% within DIAGNOSIS	79.2%	20.8%	100.0%	
Severe Dengue	No	1	1	2	
	% within DIAGNOSIS	50.0%	50.0%	100.0%	
Total	No	85	15	100	
	% within DIAGNOSIS	85.0%	15.0%	100.0%	

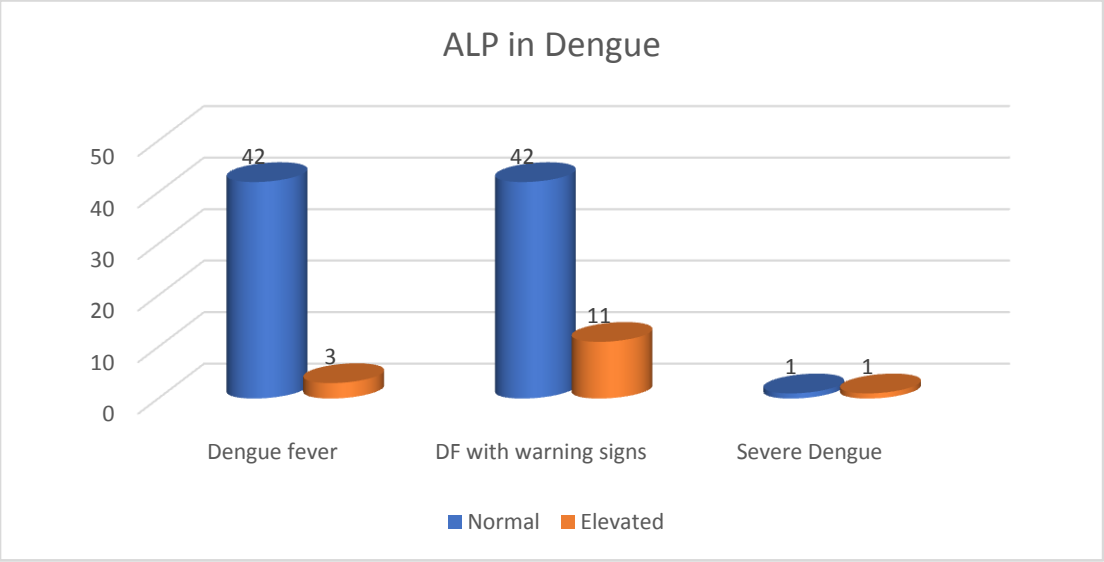


Figure.33:ALP in Dengue among study population

ALP elevated in 15(15%) of patients, in which 3 (6.7%) had dengue fever, 11 (20.8%) had dengue fever with warning signs, 1(50%) had severe dengue.

There is no significant difference between these group and there is no association between dengue severity and elevation of liver enzymes.

GGT:

Table. 30: GGT in dengue among study population

DIAGNOSIS		GGT		Total	P value
		Normal	Elevated		
Dengue fever	No	32	13	45	0.008
	% within DIAGNOSIS	71.1%	28.9%	100.0%	
DF with warning signs	No	21	32	53	
	% within DIAGNOSIS	39.6%	60.4%	100.0%	
Severe Dengue	No	1	1	2	
	% within DIAGNOSIS	50.0%	50.0%	100.0%	
Total	No	54	46	100	
	% within DIAGNOSIS	54.0%	46.0%	100.0%	

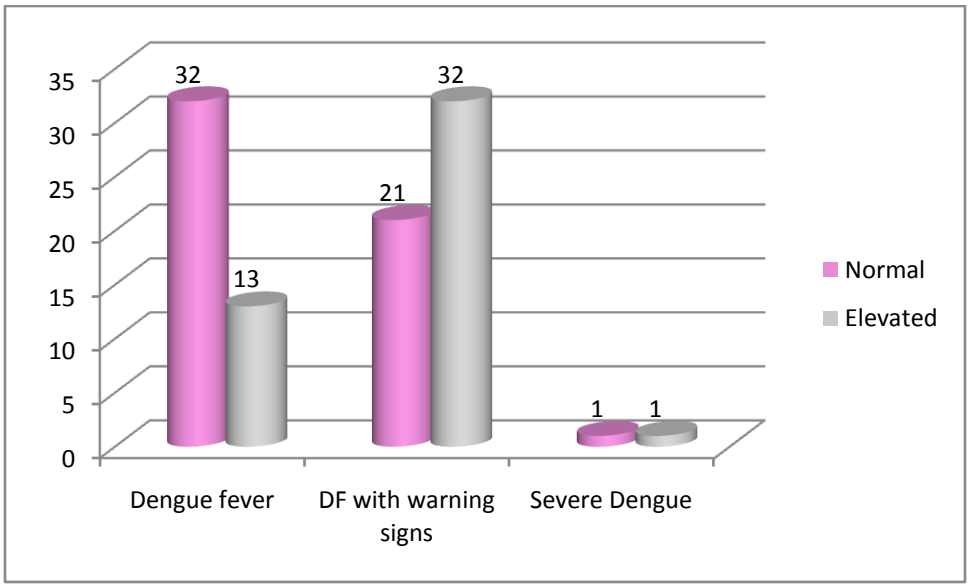


Figure .34:GGT in Dengue among study population

GGT elevation seen in 46 patients, in which 13 (28.9%) had dengue fever, 32 s(60.4%) had dengue fever with warning signs, 1 (50%) patient had severe dengue. There is a significant difference between these groups and there is a strong association between GGT elevation and dengue severity (p value= 0.008)

Table:31. Gall bladder wall thickening in dengue among study population

DIAGNOSIS		GB Thickened And Edematous		Total	P value
		Yes	No		
Dengue fever	No	13	32	45	0.000
	% within DIAGNOSIS	28.9%	71.1%	100.0%	
DF with warning signs	No	38	15	53	
	% within DIAGNOSIS	71.7%	28.3%	100.0%	
Severe Dengue	No	2	0	2	
	% within DIAGNOSIS	100.0%	.0%	100.0%	
Total	No	53	47	100	
	% within DIAGNOSIS	53.0%	47.0%	100.0%	

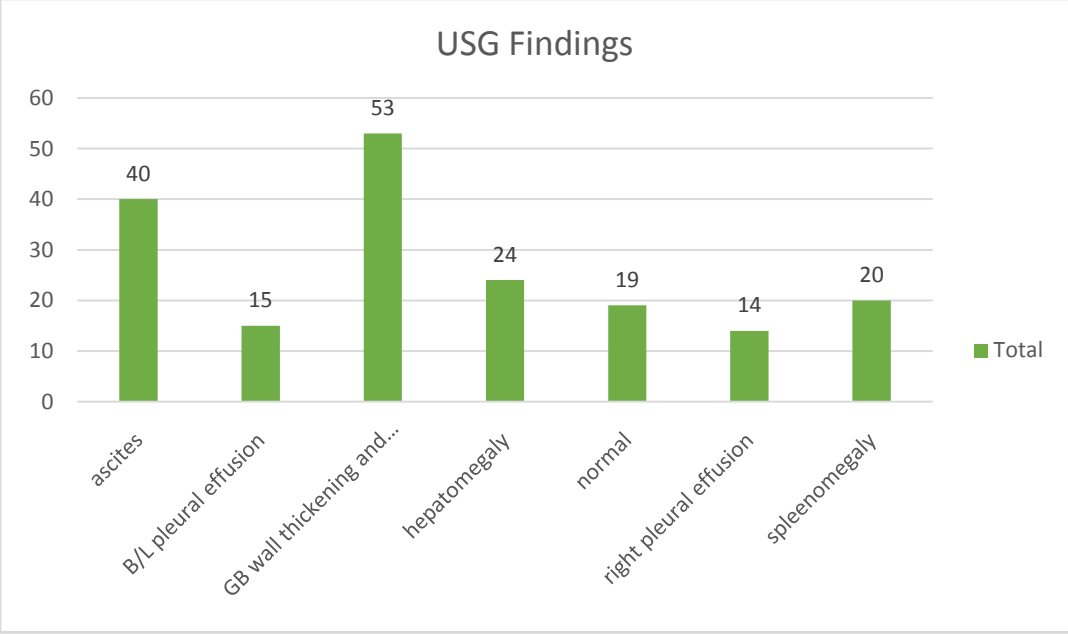
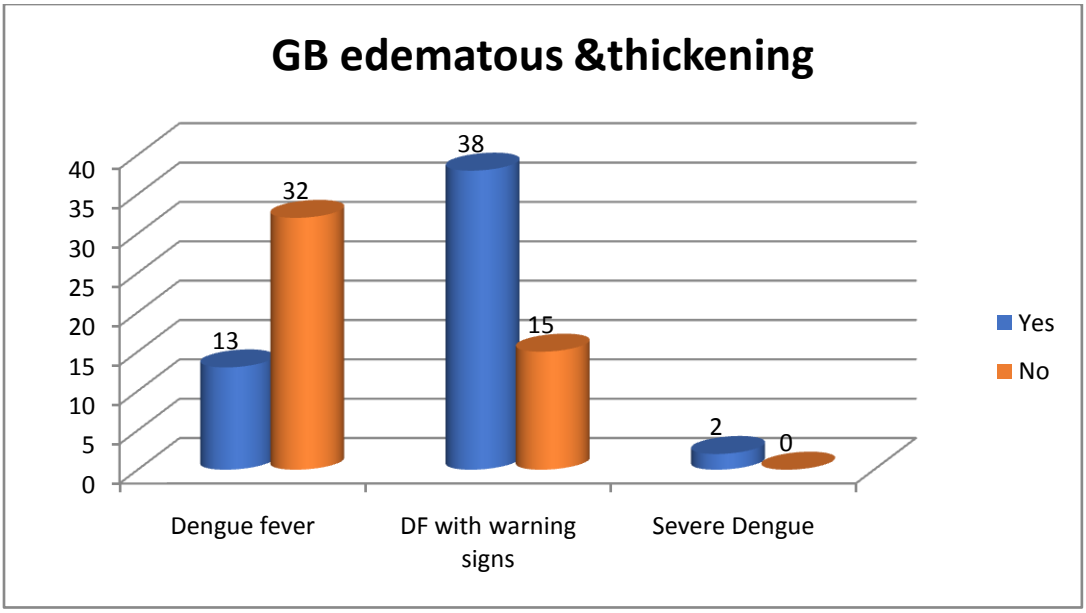


Figure: 35.Ultrasound findings in dengue among study population

Gall bladder wall thickening and edematous gall bladder was seen in 53 (53%) patients.

Figure.36: Gall bladder wall thickening in dengue



In these 53 patients, 13 (28.9%) had dengue fever, 38 (71.7%) had dengue fever with warning signs, 2 (100%) had severe dengue fever. There is a statistical difference between these groups (p value – 0.000).

In 100 patients, 40 (40%) patients had ascites.

Table.32: Ascites in dengue among study population

DIAGNOSIS		ASCITES		Total	P value
		Yes	No		
Dengue fever	No	0	45	45	0.000
	% within Diagnosis	.0%	100.0%	100.0%	
DF with warning signs	No	38	15	53	
	% within Diagnosis	71.7%	28.3%	100.0%	
Severe Dengue	No	2	0	2	
	% within diagnosis	100.0%	.0%	100.0%	
Total	No	40	60	100	
	% within Diagnosis	40.0%	60.0%	100.0%	

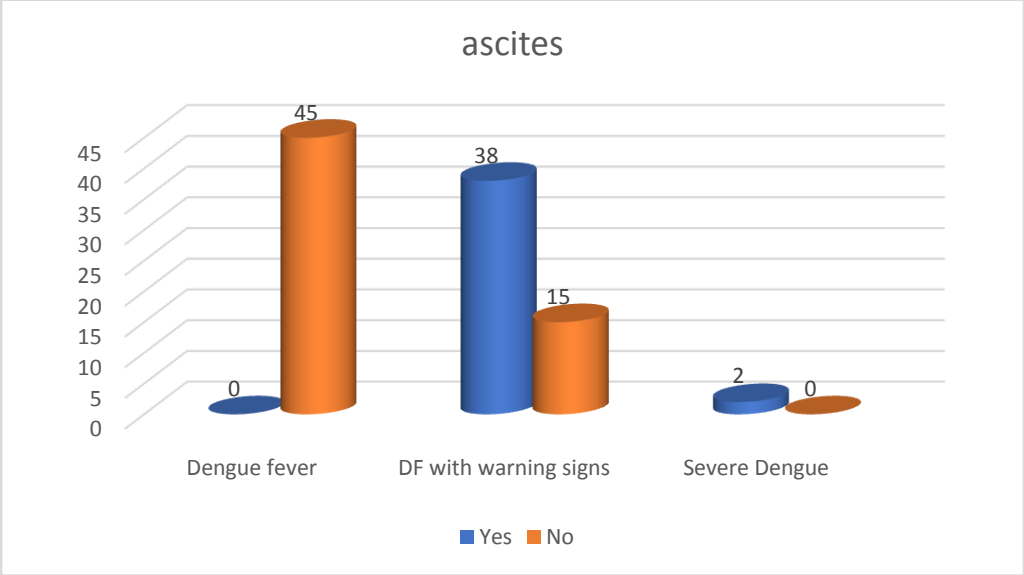


Figure.37: Ascites in dengue among study population

In these 40 patients, 38 (71.7%) patients had dengue fever with warning signs, 2 (100%) patients had severe dengue.

Right pleural effusion was seen in 14 (14%) patients.

Table.33: Right plueral effusion among study population

DIAGNOSIS		Right Pleural Effusion		Total	P value
		Yes	No		
Dengue fever	No	0	45	45	0.001
	% within Diagnosis	.0%	100.0%	100.0%	
DF with warning signs	No	14	39	53	
	% within Diagnosis	26.4%	73.6%	100.0%	
Severe Dengue	No	0	2	2	
	% within Diagnosis	.0%	100.0%	100.0%	
Total	No	14	86	100	
	% within Diagnosis	14.0%	86.0%	100.0%	

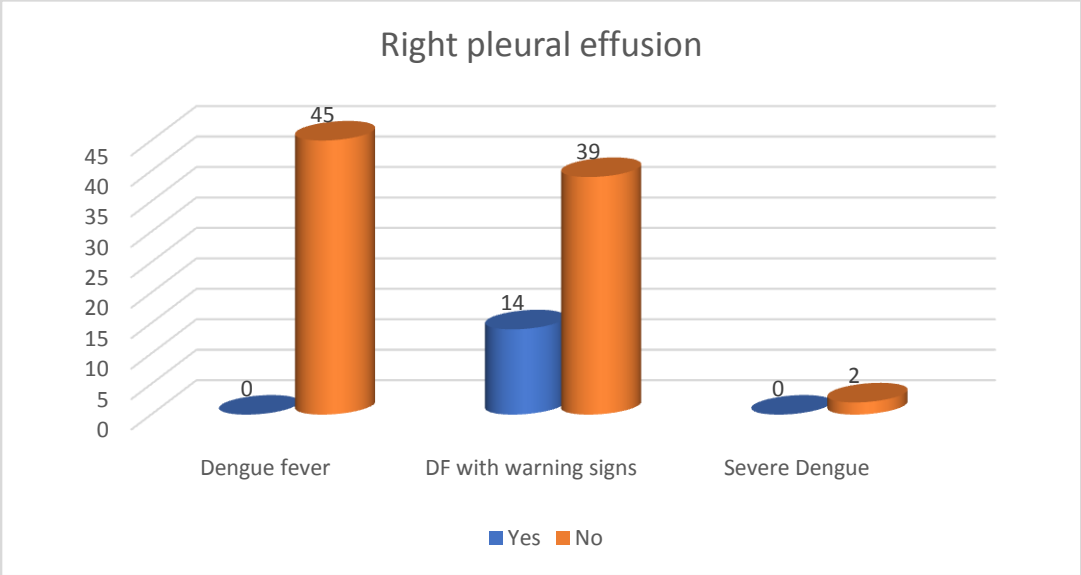


Figure. 38:Right plueral effusion among study population

In these 14 patients, all 14 (26.4%) patients had dengue fever with warning signs. There is a statistical difference between these groups (p value 0.001)

Table.34: B/L pleural effusion in dengue among study population

DIAGNOSIS		B/L Pleural Effusion		Total	P value
		Yes	No		
Dengue fever	No	0	45	45	0.000
	% within Diagnosis	.0%	100.0%	100.0%	
DF with warning signs	No	14	39	53	
	% within Diagnosis	26.4%	73.6%	100.0%	
Severe Dengue	No	1	1	2	
	% within Diagnosis	50.0%	50.0%	100.0%	
Total	No	15	85	100	
	% within Diagnosis	15.0%	85.0%	100.0%	

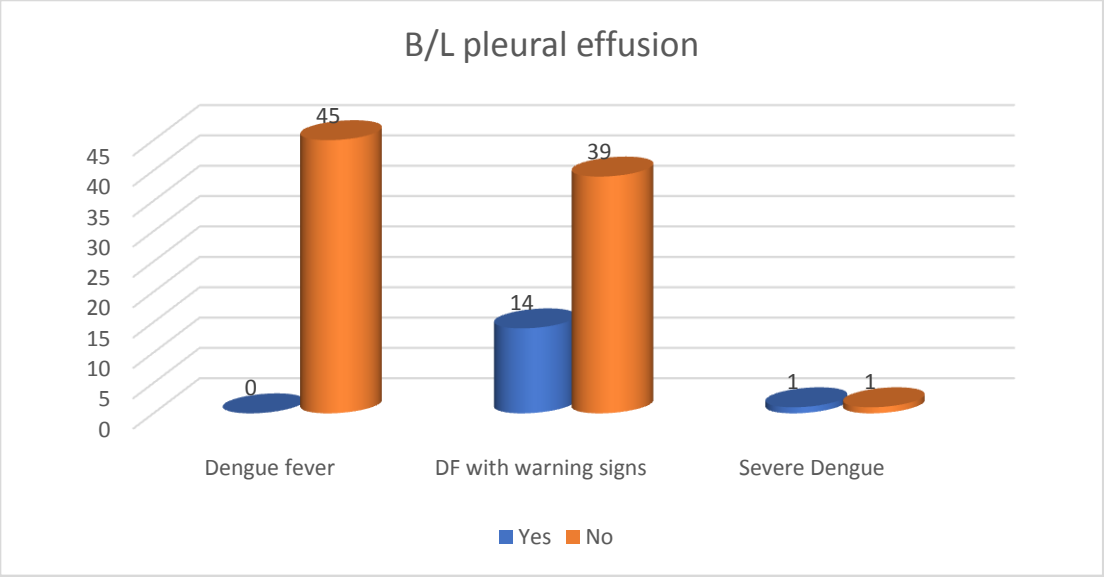


Figure.39 : B/L pleural effusion among study population

15 patients had bilateral pleural effusion, in which 14 (26.4%) had dengue fever with warning signs, 1 (50%) patient had severe dengue. There is a statistical difference between these groups (p value 0.000).

Table.35 :Spleenomegaly among study population

DIAGNOSIS		Spleenomegaly		Total	P value
		Yes	No		
Dengue fever	No	4	41	45	0.032
	% within Diagnosis	8.9%	91.1%	100.0%	
DF with warning signs	No	15	38	53	
	% within Diagnosis	28.3%	71.7%	100.0%	
Severe Dengue	No	1	1	2	
	% within Diagnosis	50.0%	50.0%	100.0%	
Total	No	20	80	100	
	% within Diagnosis	20.0%	80.0%	100.0%	

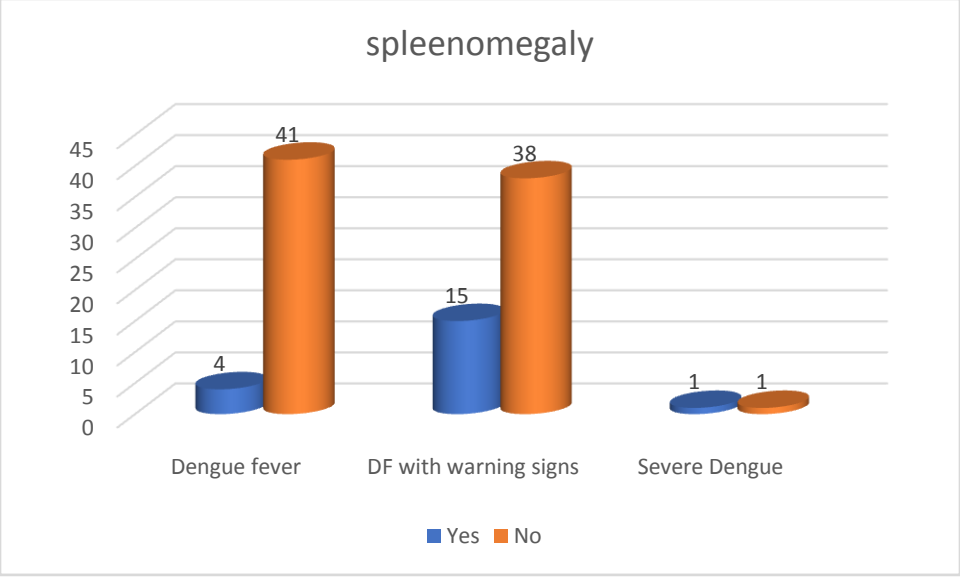


Figure. 40: Spleenomegalyamong study population

20 patients had splenomegaly, in which 4 (8.9%) patients had dengue fever, 15 (28.3%) patients had dengue fever with warning signs and 1(50%) patient had severe dengue. There is a statistical difference of p value 0.032.

Table.36: hepatomegaly in dengue among study population

DIAGNOSIS		Hepatomegaly		Total	P value
		Yes	No		
Dengue fever	No	12	33	45	0.650
	% within Diagnosis	26.7%	73.3%	100.0%	
DF with warning signs	No	12	41	53	
	% within Diagnosis	22.6%	77.4%	100.0%	
Severe Dengue	No	0	2	2	
	% within Diagnosis	.0%	100.0%	100.0%	
Total	No	24	76	100	
	% within Diagnosis	24.0%	76.0%	100.0%	

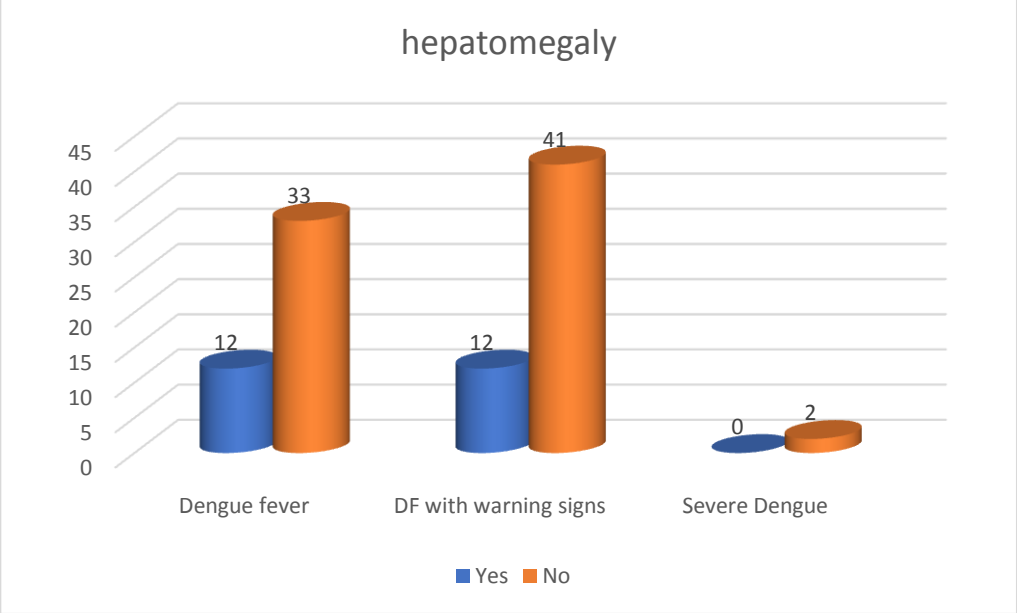


Figure .41: hepatomegaly in dengue among study population

Hepatomegaly was seen in 24 patients, 12 (26.7%) in dengue fever and 12 (22.6%) in dengue fever with warning signs. There is no statistical difference between these groups (p value 0.650).

OUTCOME

In present study, no mortality was recorded in dengue fever in 2015. All the patients had good recovery.

DISCUSSION

During the period of 1st January 2018 to 31st December 2018 , 100 patients admitted in PSG IMSR hospital with positive dengue serology (NS1 or Ig M or IgG)admitted were included in this study.

In 100 patients, most of the cases 39% occurred in the age group of 21- 30 years , followed by 22% in the age group of 31 – 40 years, 18% in less than 20 years of age, 9% in 41-50 years of age, 7 % in 51 – 60 years of age and 5 % cases in above 60 years of age.

The mean age, in our study, was 32.31 ± 14.03 years. Youngest was 16 years and the eldest was 86 years. Similar studies by Sharma et al observed 65.81% in 11-30 years of age group, by Modi TN et alobserved 300 cases (81.3%) were in the age group of 12 to 30 years of age.

There is no stastically significant differences between different age groups and dengue severity. (p value = 0.057)

Out of 100 patients admitted with dengue, 59 were males and 41 were females. In the present study males (59) were more affected than females (41) with ratio of 1.43:1. Similar observation was observed by Modi TN et alwith a ratio of 2.35:1, by Shekar and Amaravadiet al with a ratio 1.13.(table-37) This studies showed an increased occuranceof dengue infection among males. This because due to more outdoor activities and more environmental exposure that causes dengueseen among males.

Table.37: comparison of sex distribution with other studies

Author	Year	Male : Female ratio
Modi TN et al	2015	2.35:1
Shekar and Amaravadi et al	2016	1.13:1
Present study	2017- 18	1.43:1

Thereis no statistical difference between sex and severity of dengue fever.(p value= 0.15) NS1 antigen assay was done in 82 patients, in which 68 (82.9%) patients were positive & 14 (17.07%) patients were negative for dengue NS1 antigen.

Dengue IgM&IgG serology was done in all patients. 54 (54%) patients had primary dengue infection. 44 (44%) patients had secondary dengue infection. 2 (2%) patients had recent dengue infection. In primary infection. In primary infection, more than half (55.5%) of patients had dengue fever without warning signs. In secondary infection, more than half (65.9%) of patients had dengue fever with warning signs.

In the present fever was present in all patients (100, 100%). Mean duration of fever was 4.24 ±1.38 days, followed by headache was observed in 72 (72%) cases, joint pain in 68 (68%) cases, myalgia was observed in 52 (52%) cases, myalgia (52%). Other sypmtoms observed in descending order of frequency were: vomiting (43%),retro orbital pain (36%), erythematous skin rashes (15%), abdominal pain (14%), diarrhea (14%), malena

(11%), petechiae (11%), bleeding gums (7%), excessive bleeding per vaginum (6%), hematuria (2%), epistaxis (2%).

Other observations by Modi TN et alshowed fever (100%) and headache (73.98%), followed by myalgia (71.81%) were the most presenting symptoms.

In present study only one patient had severe microcytic hypochromic anemia. Mean haemoglobin in present study was 14.18 g/dl ranged from 5.3 g/dl to 19.2 g/dl, and mean haematocrit was 41.3% ranged from 29.7 % to 58.5%. Haemoglobin and haematocrit was not significant in our study. Similar observation was seen with Shekar and Amaravadiet al mean hemoglobin and haematocrit of 13.1 g/dl and 38.8%, respectively and not significant.

Leucopenia was observed in 50.16% of cases. Mean leucocyte count was 4,845 cells/ cu mm , varied from 1000 cells/ cu mm to 15,300 cells / cu mm. Leucopenia was seen 53.3% of patients in dengue fever without warning signs, 47.2% and 50% of patients in dengue fever with warning signs and in severe dengue respectively, but there is no statistically significant leucopenia between these groups. Similar observation was seen by Shekar and Amaravadiet al.

Activated lymphocytes was seen in 53 (53%) patients, and there was no statistical significance between these groups.

Thrombocytopenia was observed in all patients (100%). 91(91%) patients had platelet count of <1 lakh / cu mm as per WHO criteria. 9 patients had platelet count of > 1 lakh / cu mm but< 1.5 1 lakh / cu mm Mean platelet count in this study was 65,295 cells /cu

mm. similar findings observed by Modi TN et al (92.68%) and 90 % by Daniel et al study.

In dengue fever without warning signs only one patient had severe thrombocytopenia, 13 and 23 patients had moderate and mild thrombocytopenia respectively.

In dengue fever with warning signs, 32 patients had severe dengue, 15 and 5 patients had moderate and mild thrombocytopenia respectively.

In severe dengue one patient had severe thrombocytopenia and one patient had moderate thrombocytopenia.

There was a stastically significant difference in mean platelet count between these groups (p value= 0.00).

There was a negative correlation between mean platelet count and haematocrit (r = -0.72) and was insignificant.

Platelet count and bleeding manifestations:

39 of 100 patients developed bleeding manifestations during course of illness. Petechiae was seen in 11 patients at a mean platelet count of 14272 cu mm^3, malena seen in 11 patients at a mean platelet count of 20636 cu mm^3, followed by bleeding gums in 7 patients at a mean platelet count of 20428 cu mm^3, increased bleeding per vagina in 6 patients at a mean platelet count of 19833 cu mm^3, epistaxis seen in 2 patients and hematuria seen in 2 patients at a mean platelet count of 15500 cu mm^3 and 39000 cu mm^3 respectively.

In this study bleeding manifestations were seen in 39 (39%) patients. Major bleeding manifestations in this study were petechiae(11%) and malena (11%) , followed by bleeding gums, which was similar to other studies studies by Modi TN et al observed 42.81% and Karoli et al observed 40% .

In microcirculation, approximately a platelet count of 5,000 – 10,000 cu mm^3 is required to maintain the vascular integrity. If the platelet count were markedly decreased, petechiae usually appears first especially in the areas of increased venous pressure.

Petechiae indicates there is a decreased number of platelets and doesn't indicates platelet dysfunction. Petechiaes are non blanching pin point haemorrhages.

In 39 patients, 27 patients had bleeding manifestation occurred with severe thrombocytopenia, 11 patients had bleeding manifestation with moderate thrombocytopenia, 1 patient had bleeding manifestation with mild thrombocytopenia.

In the present study, there is a raised AST, ALT at frequency of 86%, 65% respectively. Other studies by Modi TN et alreported elevated liver enzymes (AST, ALT) in 295(79.94%) cases, Nimmagadda et al observed raised AST of 92.7% and raised ALT of 85.3% respectively.A conclusion by Smith et al, there is a liver involvement in the pathobiology of dengue infection supports the study. There is significant elevation of AST when compared to ALT.

In the present study, in ultrasound abdomen and chest findings, gall bladder wall thickening and edematous gall bladder wall was the most common finding seen in 53

(53%) patients, followed by ascites (40%) seen in 40 patients and 24 patients had hepatomegaly (24%). Other findings seen on ultrasound were in decreasing order: spleenomegaly (20%) seen in 20 cases, bilateral pleural effusion (15%) was seen in 15 patients, right pleural effusion (14%) was seen in 14 patients. Similar study by Modi TN et al observed Pericholecystic oedema (48.23%) was the common sonographic finding.

Table.38: comparison of USG findings with other studies

	Present study (100)	**Modi TN et al (369)**
USG findings	No of patients (%)	No of patients (%)
Pericholecysticedema	53 (53)	178 (48.23)
GB thickening		141(38.21)
Ascites	40 (40)	45 (12.19)
Hepatomegaly	24 (24)	247 (66.93)
Splenomegaly	20 (20)	82 (22.22)
B/L plueral effusion	15 (15%)	39 (10.56)

In the present study only 2 patients had severe dengue, both patients had hypotension and required inotropic support. In both increased bleeding per vaginum was the bleeding manifestation. In both patients hypotension and bleeding PV occurred when patients had moderate thrombocytopenia, platelet count does not correlate with severity of disease. And both were transfused with packed red blood cells and platelets.

Platelet transfusion done in 32 patients, 29 patients were in dengue fever with warning signs, 2 patients were in severe dengue and 1 patient got transfusion in dengue fever.

CONCLUSION

- To conclude the study, dengue was most prevalent among young males.
- In this study, dengue fever with warning signs is the most common followed by dengue fever without warning signs and severe dengue.
- Clinically presented with classical features of dengue such as fever, headache and joint pain as the common presenting symptoms. Petechiae, malena, bleeding gums are the most common bleeding manifestation.
- Thrombocytopenia, Leucopenia and raised haematocrit (hematological profile), deranged liver enzymes (biochemical profile), sonographic findings such as gall bladder wall edema and thickening, ascites, plureal effusion are all seen in prima facie of dengue fever, and all features individually or in combination indicates a provisional diagnosis of dengue infection.
- Bleeding risk increases if the platelet count goes below 20,000 cells/ cumm.
- Thrombocytopenia does not have any correlation with bleeding manifestations and severity of dengue infection.
- Treatment of dengue infection is mainly supportive care.
- Early diagnosis and adequate fluid management plays a important role in disease outcome.
- Blood pressure, platelets, haematocrit should be monitored closely to evaluate the progress of disease.

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PSG Institute of Medical Sciences & Research
Institutional Human Ethics Committee

Recognized by The Strategic Initiative for Developing Capacity in Ethical Review (SIDCER)
POST BOX NO. 1674, PEELAMEDU, COIMBATORE 641 004, TAMIL NADU, INDIA
Phone : 91 422 - 2598822, 2570170, Fax : 91 422 - 2594400, Email : ihec@psgimsr.ac.in

To
Dr V Kanchanadevi
Postgraduate
Department of General Medicine
Guide/s: Dr K Jayachandran
PSG IMS & R
Coimbatore

Ref: Project No. **17/402**

Date: December 29, 2017

Dear Dr Kanchanadevi,

Institutional Human Ethics Committee, PSG IMS&R reviewed and discussed your application dated 14.12.2017 to conduct the research study entitled *"A study on clinical, biochemical and imaging profile in dengue fever: A prospective observational study"* during the IHEC meeting held on 22.12.2017.

.The following documents were reviewed and approved:

1. Project submission form
2. Study protocol (Version 1 dated 14.12.2017)
3. Informed consent forms (Version 1 dated 14.12.2017)
4. Data collection tool (Version 1 dated 14.12.2017)
5. Permission letter from concerned Head of Department
6. Current CVs of Principal investigator, Co-investigator
7. Budget

The following members of the Institutional Human Ethics Committee (IHEC) were present at the meeting held on 22.12.2017 at IHEC Secretariat, PSG IMS & R between 10.00 am and 11.00 am:

Sl. No.	Name of the Member of IHEC	Qualification	Area of Expertise	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
1	Mr R Nandakumar (Chairperson, IHEC)	BA., BL	Legal Expert	Male	No	Yes
2	Dr D Vijaya (Member – Secretary, IHEC)	M Sc., Ph D	Basic Medical Sciences (Biochemistry)	Female	Yes	Yes
3	Dr S Shanthakumari	MD	Pathology, Ethicist	Female	Yes	Yes
4	Dr Sudha Ramalingam	MD	Epidemiologist, Ethicist Alt. member-Secretary	Female	Yes	Yes
5	Dr G Subhashini	MD	Epidemiologist	Female	Yes	Yes

The study is approved in its presented form. The decision was arrived at through consensus. Neither PI nor any of proposed study team members were present during the decision making of the IHEC. The IHEC functions in accordance with the ICH-GCP/ICMR/Schedule Y guidelines. The approval is valid until one year from the date of sanction. You may make a written request for renewal / extension of the validity, along with the submission of status report as decided by the IHEC.

SECRETARY
PSG IMS&R
COIMBATORE-641004.
INSTITUTIONAL HUMAN ETHICS COMMITTEE

PSG Institute of Medical Sciences & Research
Institutional Human Ethics Committee

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Following points must be noted:

1. IHEC should be informed of the date of initiation of the study
2. Status report of the study should be submitted to the IHEC every 12 months
3. PI and other investigators should co-operate fully with IHEC, who will monitor the trial from time to time
4. At the time of PI's retirement/intention to leave the institute, study responsibility should be transferred to a colleague after obtaining clearance from HOD, Status report, including accounts details should be submitted to IHEC and extramural sponsors
5. In case of any new information or any SAE, which could affect any study, must be informed to IHEC and sponsors. The PI should report SAEs occurred for IHEC approved studies within 7 days of the occurrence of the SAE. If the SAE is 'Death', the IHEC Secretariat will receive the SAE reporting form within 24 hours of the occurrence
6. In the event of any protocol amendments, IHEC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b. Alteration in the budgetary status should be clearly indicated and the revised budget form should be submitted
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval
   d. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented
   e. If there are any amendments in the trial design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the IHEC and only then can they be implemented
   f. Any deviation-Violation/waiver in the protocol must be informed to the IHEC within the stipulated period for review
7. Final report along with summary of findings and presentations/publications if any on closure of the study should be submitted to IHEC

Kindly note this approval is subject to ratification in the forthcoming full board review meeting of the IHEC.

Thanking You,

Yours Sincerely,

SECRETARY
PSG IMS&R
COIMBATORE-641004

Dr Sudha Ramalingam
Alternate Member - Secretary
Institutional Human Ethics Committee

CASE PROFORMA

A Study of clinical, biochemical and imaging profile in dengue fever in PSG IMS&R, Coimbatore: A Prospective Observational Study

Dr. V. Kanchanadevi, Prof.Dr. K. Jayachandran

Patient name: IP/OP no:

Age/Gender: Address:

Contact number:

Height: Weight: BMI:

Occupation :

Ethnicity (Religion) :

History of Presenting Illness :

Past History:

Personal History:

Smoking/Alcohol -

Diet -

Menstrual History:

LMP:

Family History:

Examination:

General examination:

Vitals:

Pulse:

Blood pressure:

Respiratory rate:

SpO_2:

Temperature:

Systemic examination:

CVS:

RS:

P/A:

CNS:

DIAGNOSIS :

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Hb							

Hematocrit							
Total count							
Platelet							
LFT S.Bilirubin (T/D/IN)							
SGOT							
SGPT							
GGT							
Alkaline phosphatase							
RFT B.Urea							
S.Creatinine							
S.Electrolytes							
Peripheral smear							

USG Abdomen							
Chest x ray If needed							
Echo If needed							
MRI Brain If needed							
ECG If needed							
Platelet transfusion If any							
Blood products transfusion If any							

ABBREVATIONS

DENV 1	-	Dengue virus 1
DENV 2	-	Dengue virus 2
DENV 3	-	Dengue virus 3
DENV 4	-	Dengue virus 4
prM	-	Precursor protein
NS protein	-	Non structural protein
TLR 4	-	Toll like receptor 4
FcR	-	Fc gamma R
IL 2	-	Interleukin 2
IL 6	-	Interleukin 6
IL 5	-	Interleukin 5
IL4	-	Interleukin 4
IL12	-	Interleukin 12
IL 13	-	Interleukin 13
IL 18	-	Interleukin 18
IFN- c	-	Interferon c
RT-PCR	-	Reverse transcriptase polymerase chain reaction
HIA	-	Hemagglutination Inhibition Assay
SGOT/AST	-	Serum glutamic oxaloacetic transaminase / Aspartate transaminase
SGPT/ALT	-	Serum glutamate pyruvate transaminase / Alanine transaminase
GGT	-	Gamma glutamyltransferase
ALP	-	Alkaline phosphatase

PSG Institute of Medical Science and Research, Coimbatore

Institutional Human Ethics Committee

INFORMED CONSENT FOR RESEARCH PROJECTS

I **Dr. V. Kanchanadevi** am carrying out a study on the topic**: A Study of clinical, biochemical and imaging profile in dengue fever, in PSG IMS&R, Coimbatore : A Prospective Observational Study**as part of my research project being carried out under the aegis of the Department of General Medicine.

My research guide is**: Prof. Dr. K. Jayachandran**

The justification for this studyis:

- Dengue is one of the major public health problem in India.
- Complications secondary to dengue and mortality is increasing in trend.

The results may help in risk stratification and may also guide early identification of complications associated with dengue infection thereby reducing morbidity and mortality.

The objectives of this study are:

Primary Objective:

To evaluate the clinical, biochemical and imaging profile of 100 patients with Dengue NS1 positive / Dengue IgM / Ig G positive cases.

Secondary Objective:

- Toevaluate the complications secondary to dengue infection
- To evaluate the need for platelet transfusion

Sample size: 100 patients

Study participants:

Patients aged more than 16 years who admitted in medical wards, IMCU , MICU with dengue NS1/ IgM/ IgG positive cases .

Location:

Department of General Medicine , PSG Hospital, Coimbatore

We request you to kindly cooperate with us in this study. We propose to collect background information and other relevant details related to this study. We will be carrying out:

Initial interview: 10 to 15 minutes.

Data collected will be stored for a period of three years. We will / will not use the data as part of another study.

Blood sample collection: 4 ml directly from patient , these collected samples will not be used for any other purposes

No. of times it will be collected: **daily (**for daily platelet count and hematocrit values)

Whether blood sample collection is part of routine procedure or for research (study) purpose: **Routine procedure**

Specify **purpose**, discomfort likely to be felt and side effects, if any: **To look for Complete blood picture, liver function test, renal function test, PT/INR,aPTT. minimal discomfort (during blood collection).**

Whether blood sample collected will be stored after study period**: No**

Case details and data will be stored for 3 yrs

Whether blood sample collected will be sold: **No**

Whether blood sample collected will be shared with persons from another institution: **No**

Medication given, if any, duration, side effects, purpose, benefits**: No medications**

Benefits from this study: we can detect secondary complications earlier, and can reduce dengue associated morbidity and mortality.

Risks involved by participating in this study: **No risks**

How the **results** will be used: the results will be used for **further researches and publications**

If you are uncomfortable in answering any of our questions during the course of the interview / biological sample collection, **you have the right to withdraw from the interview / study at anytime.** You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered nor would it attract any penalty. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be used for approved research purposes only. You will be informed about any significant new findings - including adverse events, if any, – whether directly related to you or to other participants of this study, developed during the course of this research which may relate to your willingness to continue participation.

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s. Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements).

Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the Interviewer with date: Witness:

Contact no: 9790886016

பூ. சா. கோ மருத்துவக் கல்லூரி மற்றும் ஆராய்ச்சி நிறுவனம், கோவை

மனித நெறிமுறைக் குழு

ஒப்புதல் படிவம்

தேதி:

மரு. வே. காஞ்ணாதேவி, ஆகிய நான் பூ. சா. கோ மருத்துவக் கல்லூரியின் / மருத்துவமனையின் **பொது மருத்துவத்** துறையின் கீழ், **"டெங்கு காய்ச்சலால் ஏற்படும் பாதிப்புகளை மருத்துவ பரிசோதனை ரீதியாக, இரத்தப்பரிசோதனை ரீதியாக, வயிற்று ஸ்கேன் ரீதியாக அறிதல்"** என்ற தலைப்பில் ஆய்வு மேற்கொள்ள உள்ளேன்.

என் ஆய்வு வழிகாட்டி: மரு. K. ஜெயச்சந்திரன்

ஆய்வு மேற்கொள்வதற்கான அடிப்படை:

டெங்கு காய்ச்சலால் ஏற்படும் பாதிப்புகளை மருத்துவ பரிசோதனை ரீதியாக, இரத்தப்பரிசோதனை ரீதியாக, வயிற்று ஸ்கேன் ரீதியாக அறிதல்.

ஆய்வின் நோக்கம்:

1. டெங்கு காய்ச்சலால் ஏற்படும் பின்விளைவுகளை பற்றி அறிதல்.
2. இரத்த தட்டணுக்களின் தேவையை அறிதல்.

ஆய்வில் பங்கு பெறும் நபர்களின் எண்ணிக்கை: 100

ஆய்வில் பங்கு பெறுவோர் மற்றும் வயது: 18 வயதுக்கு மேற்பட்ட மற்றும் டெங்கு காய்ச்சலால் பதிக்கப்பட்டோர்கள்.

ஆய்வு மேற்கொள்ளும் இடம்: பூ. சா. கோ. மருத்துவக்கல்லூரி மருத்துவமனை, கோயம்புத்தூர்.

இந்த ஆய்வில் எங்களுடன் ஒத்துழைக்குமாறு கேட்டுக்கொள்கிறோம். நாங்கள் சில தகவல்களை இந்த ஆய்விற்காக சேகரிக்க உள்ளோம்.

ஆய்வு செய்யப்படும் முறை:

முதன்மை நேர்காணல்: 10-15 நிமிடங்கள்

இந்த ஆய்வில் கிடைக்கும் தகவல்கள் **3 வருடங்கள்** பாதுகாக்கப்படும். இந்த தகவல்கள் வேறு ஆய்விற்குப் பயன்படுத்தப் பட மாட்டாது.

சுகாதாரக் கல்வி: அமர்வுகள் **ஒரு** முறை ஒரு அமர்வுக்கான நேரம்: **10** நிமிடங்கள்

இரத்த மாதிரி சேகரிப்பு: 4 மில்லி, தினமும்

இரத்த மாதிரி எடுப்பது வழக்கமான சிகிச்சைக்காகவோ அல்லது இந்த ஆய்விற்காகவோ: வழக்கமான சிகிச்சைக்காக

இதனால் ஏற்படக் கூடிய அசௌகரியங்கள் / பக்க விளைவுகள்: இரத்தம் எடுக்கும்போது சிறிதளவு வலி ஏற்படும்.

இரத்த மாதிரிகள் ஆய்விற்குப் பின் பாதுகாத்து வைக்கப்படுமா? ஆம் / இல்லை, அழிக்கப்படும்: **இல்லை அழிக்கப்படும்**

சேகரிக்கப்பட்ட இரத்தம் விற்கப்படுமா? ஆம் / இல்லை **இல்லை**

சேகரிக்கப்பட்ட இரத்தம் வேறு நிறுவனத்துடன் பகிர்ந்து கொள்ளப்படுமா? ஆம் / இல்லை: **இல்லை**

மருந்துகள் ஏதேனும் கொடுக்கப்படவிருந்தால் அவை பற்றிய விவரம் (கொடுக்கப்படும் காரணம், காலம், பக்க விளைவுகள், பயன்கள்): **பொருந்தாது**

மருந்துகள் கொடுக்கப்படுவது வழக்கமான சிகிச்சை முறையா?: ஆம் / இல்லை (இல்லை என்றால் கொடுக்கப்படும் காரணம்) **பொருந்தாது**

கொடுக்கப்படும் மருந்துகளுக்கு மாற்று உள்ளதா?: ஆம் / இல்லை (ஆம் என்றால் இந்த குறிப்பிட்ட மருந்து கொடுக்கப்படும் காரணம்) **பொருந்தாது**

ஆய்வில் பங்குபெறுவதால் ஏற்படும் பலன்கள்:
டெங்கு காய்ச்சலால் ஏற்படும் பின்விளைவுகளை எளிதில் கண்டறியலாம்

ஆய்வில் பங்கேற்பதால் ஏற்படும் அசௌகரியங்கள் / பக்க விளைவுகள்: இந்த ஆய்வினால் தங்களுக்கு எந்த விதமான அபாயங்களும் அசௌகரியங்களும் ஏற்படாது.

ஆய்வின் முடிவுகள் எந்த முறையில் பயன்படுத்தப்படும்?
ஆய்வின் முடிவுகள், அடுத்தகட்ட ஆராய்ச்சிகளுக்கும், மருத்துவ ஆய்வு பத்திரிக்கைகளில் வெளியிடுவதற்கும் பயன்படுத்தப்படும்.

இந்த ஆய்வின் கேள்விகளுக்கு பதிலளிப்பதோ, இரத்த மாதிரிகள் அல்லது திசு மாதிரிகள் எடுப்பதிலோ உங்களுக்கு ஏதேனும் அசௌகரியங்கள் இருந்தால், எந்த நேரத்தில் வேண்டுமானாலும் ஆய்விலிருந்து விலகிக்கொள்ளும் உரிமை உங்களுக்கு உண்டு. ஆய்விலிருந்து விலகிக்கொள்வதால் உங்களுக்கு அளிக்கப்படும் சிகிச்சை முறையில் எந்த வித பாதிப்பும் இருக்காது என்று உங்களுக்கு உறுதியளிக்கிறோம். மருத்துவ மனையில் நோயாளிகளுக்கு அளிக்கப்படும் சேவைகளை நீங்கள்

தொடர்ந்து பெறலாம். இந்த ஆய்வில் பங்கேற்க ஒப்புக்கொள்ளுவதால் வேறு எந்த விதமான கூடுதலான பலனும் உங்களுக்குக் கிடைக்காது. நீங்கள் அளிக்கும் தகவல்கள் இரகசியமாக வைக்கப்படும். ஆய்வில் பங்கேற்பவர்கள் பற்றியோ அவர்கள் குடும்பத்தைப் பற்றியோ எந்தத் தகவலும் எக்காரணம் கொண்டும் வெளியிடப்படாது என்று உறுதியளிக்கிறோம். நீங்கள் அளிக்கும் தகவல்கள் / இரத்த மாதிரிகள் / திசு மாதிரிகள் அங்கீகரிக்கப்பட்ட ஆய்விற்கு மட்டுமே பயன்படுத்தப்படும். இந்த ஆய்வு நடைபெறும் காலத்தில் குறிப்பிடத்தகுந்த புதிய கண்டுபிடிப்புகள் அல்லது பக்க விளைவுகள் ஏதும் ஏற்பட்டால் உங்களுக்குத் தெரிவிக்கப்படும். இதனால் ஆய்வில் தொடர்ந்து பங்கு பெறுவது பற்றிய உங்கள் நிலைப்பாட்டை நீங்கள் தெரிவிக்க ஏதுவாகும்.

ஆய்வுக்குட்படுபவரின் ஒப்புதல்: இந்த ஆய்வைப் பற்றிய மேற்கூறிய தகவல்களை நான் படித்து அறிந்து கொண்டேன் / ஆய்வாளர் படிக்கக் கேட்டுத் தெரிந்து கொண்டேன். ஆய்வினைப் பற்றி நன்றாகப் புரிந்து கொண்டு இந்த ஆய்வில் பங்கு பெற ஒப்புக்கொள்கிறேன். இந்த ஆய்வில் பங்கேற்பதற்கான எனது ஒப்புதலை கீழே கையொப்பமிட்டு, கை ரேகை பதித்து நான் தெரிவித்துக் கொள்கிறேன்.

பங்கேற்பாளரின் பெயர், முகவரி:

பங்கேற்பாளரின் கையொப்பம் / கை ரேகை / சட்டப்பூர்வ பிரதிநிதியின் கையொப்பம்:

தேதி :

ஆய்வாளரின் கையொப்பம்:

தேதி :

ஆய்வாளரின் தொலைபேசி எண்: 9790886016

மனித நெறிமுறைக் குழு அலுவலகத்தின் தொலைபேசி எண்: 0422-4345818

LIST OF TABLES

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MASTER CHART

								CBC				LFT					RFT								
S.No	NAME	AGE	Sex	IP No	DAY OF ILLNESS	NS1	IgM/IgG	HB	Ht	WBC	Plt	Bilirubin	SGOT	SGPT	ALP	GGT	S.urea	s.creatinine	Electrolytes	PS	USG abdomen	others	Plt Transfusion	Blood Transfusion	Diagnosis
1	Ashok	35	Male	I18000177	6	Not done	P/N	14.6	43.1	2.9	34000	0.4/0.2/0.2	447	515	93	119	19	1.1	136/3.8/102/20.6	NN, Leukopenia, Thrombocytopenia, activated lymphocytes	Diffuse edematous GB, mild ascites		4		DF WITH WARNING SIGNS
2	Kowsalya	23	Female	I18000981	4	Positive	P/N	13.4	40.9	4.4	43000	0.5/0.2/0.3	50	21	84	45	15	0.8	133/4.1/100/23.4	NN , Thrombocytopenia	GB Wall thickness & edematous/ mild splenomegaly		10		DF WITH WARNING SIGNS
3	Amala .s	23	Female	I18000979	4	Not done	P/P	11.2	33.5	2.2	87000	0.3/0.1/0.2	127	113	49	56	13	0.7	138/4.2/102/24	Leukopenia, Thrombocytopenia, monocytosis	Mild splenomegaly				DF WITH WARNING SIGNS
4	Kalidas.N	21	Male	I18002265	4	Positive	P/N	19.1	58.5	2.2	9000	0.4/0.1/0.3	217	123	53	104	11	0.8	136/3.8/101/22.6	NN, Leukopenia, Thrombocytopenia, monocytosis, activated lymphocytes	GB Wall thickness & edematous/ mild splenomegaly		10		DF WITH WARNING SIGNS
5	Navaneetha Krishnan	33	Male	I18000943	6	Not done	P/P	14.4	43.2	7.1	21000	0.5/0.2/0.3	79	57	57	47	11	0.7	133/3.8/96/21	NN, relative lymphocytosis, severe thrombocytopenia	Mild splenomegaly, Minimal Ascites, Pleural effusion				DF WITH WARNING SIGNS
6	Thangaraj	39	Male	I18000112	3	Not done	P/P	16.5	49.6	7.3	7000	2.9/2.7/0.2225	225	111	150	420	14	0.78	135/4.71/104/21.3	NN, severe thrombocytopenia	Edematous wall thickness of GB, Moderate Ascites, B/L Mild pleural effusion, mild hepatomegaly		6		DF WITH WARNING SIGNS
7	Mohammed Arief	18	Male	I18005524	6	Not done	P/P	17	49.2	3.1	42000	0.8/0.4/0.4	107	76	63	17	26	0.86	131/3.74/95/21.8	NN, Leukopenia, Thrombocytopenia	Normal study				DENGUE FEVER
8	Shankar Ganesh	16	Male	I18000921	4	Positive	P/N	14.8	44.2	2	76000	0.3/0.2/0.1	290	154	62	24	12	0.7	139/4.4/105/23.4	NN, Leukopenia, Thrombocytopenia	GB Wall thickness & edematous		6		DF WITH WARNING SIGNS
9	Tamilarasu. M	18	Male	I18005556	5	Negative	P/P	18.2	54.7	4.6	8000	0.7/0.3/0.4	201	149	77	50	19	0.85	137/4.02/103/19.9	NN, relative lymphocytosis, severe thrombocytopenia	Mild hepatomegaly/edematous GB wall thickening/moderate spleenomegaly/mild ascites/mild pl.effusion		4		DF WITH WARNING SIGNS
10	Porameshwari	50	Female	I17054956	4	Negative	P/P	14.4	43.7	2.7	10000	0.7/0.2/0.5	329	246	168	254	17	0.7	139/4/104/20	NN, blood pictrue, Thrombocytopenia, Acivated lymphocytes	Fatty liver, mod. Ascites, mild to mod. Pleural effusion		4		DF WITH WARNING SIGNS
11	Sivaranjini	21	Female	I18000544	5	Not done	P/N	13.8	42.3	5.3	119000	0.3/0.2/0.1	30	35	47	34	8	0.64	140/5/101/23.6	NN A, Mild Thrombocytopenia	NAD				DENGUE FEVER
12	Firuthouriya	21	Female	I18002645	6	Positive	P/P	12.9	39	6.2	23000	0.3/0.1/0.2	204	111	53	142	5	0.68	137/4.02/102/23.7	NN A, relative lymphocytosis, activated lymphocytes, mod. Thrombocytopenia	Mod. Ascites, B/L pleural effusion				DF WITH WARNING SIGNS
13	Sathya. V	33	Female	I18001415	6	Positive	P/N	14.7	44.3	4.7	13000	0.3/0.2/0.1	79	55	56	41	97	0.52	138/3.8/104/19	NN, Blood pictrue, relative lymphocytosis, Thrombocytopenia	thickening GB wall, Mild ascites		8		DF WITH WARNING SIGNS
14	Kaliappa Gounder	86	Male	I18024033	5	Positive	P/N	14.6	44.3	6.9	21000	3.2/2.7/3.2	266	184	142	106	31.78	1.51	136/4.27/102/18.5	NN, activated lymphocytes, thrombocytopenia	Mild Hepatomegaly, Mild free fluid, mild enlargement of prostate		5		DF WITH WARNING SIGNS
15	Vignesh	21	Male	I18024129	1	Positive	P/N	14	43	8.1	270000	0.6/0.3/0.3	23	18	77	22	9.8	1.06	135/3.22/97/20	Mild anisocytosis, NN	No Sonological abnormality				DENGUE FEVER
16	Narayanasamy	73	Male	I18003569	5	Positive	P/N	15.6	45.5	3.3	111000	0.7/0.5/0.2	42	25	58	17	25	1.26	136/3.7/101/17.7	NN, Leukopenia, thrombocytopenia & activated lymphocytes	Normal				DENGUE FEVER
17	Muruganantham	46	Male	I18026637	1	Positive	P/N	16.8	51.2	4.6	22000	0.8/0.5/0.3	93	71	212	686	13	0.92	139/3.78/100/25.4	NN, Thrombocytopenia, activated lymphocytes	Mildly thickness and trabeculated gall bladder wall, minnimal, ascites, minimal pleural effusion				DF WITH WARNING SIGNS
18	Bharathi prasanth	22	Male	I18027799	6	Not done	P/N	14.3	42.7	4.4	172000	0.6/0.3/0.3	82	80	80	41	18	1.16	133/3.9/98/19	NN	Mild spleenomegaly, increased periportal echogenicity in liver probale hepatits				DENGUE FEVER
19	Muthukumaran	19	Male	I18028137	4	Negative	P/P	16.4	49.3	3.3	15000	0.6/0.2/0.4	77	37	83	47	12	0.72	136/3.8/97/24.8	NN, LP, activated lymphocytes, Thrombocytopenia	Mild spleenomegaly, mild pleural effusion minimal free fluid in abdomen				DF WITH WARNING SIGNS
20	Poorani	18	Female	I18028552	5	Negative	P/N	13.9	42.5	3.1	49000	0.2/0.1/0.1	54	16	48	13	7	0.52	140/3.8/104/21	NN, lp, activated lymphocytes, thrombocytopenia	Diffuse edematous wall thickness in Gall bladder, mild ascites, Right minimal pleural effusion				DF WITH WARNING SIGNS
21	Neeraja	61	Female	I18030785	3	Negative	P/P	9.8	29.7	4.6	107000	0.3/0.2/0.1	15	11	60	16	27	0.88	113/3.1/81/17.6	NN,thrombocytopenia, relative neutrophilia, activated lymphocytes	Fatty liver/Hepatomegdy				DENGUE FEVER
22	Mohammed Sulaiman khan	25	Male	I18030906	5	Negative	P/P	17.9	53.6	7.4	10000	0.6/0.4/0.2	187	123	102	135	23	1.1	134/6/106/23	NN, monocytosis, activated lymphocytes & Thrombocytopenia	Fatty changes in liver, Mild thickned GB wall, minimal free fluid in abdomen, minimal B/L pleural effusion		6		DF WITH WARNING SIGNS
23	Vishnu Chander	25	Male	I18031273	3	Positive	P/N	15.4	47.3	3.3	150000	o.4/0.2/0.2	21	6	62	22	22	0.8	136/4.1/102/23	NN, Mild TP	Normal				DENGUE FEVER
24	Punitha	27	Female	I18031477	3	Positive	P/P	12.1	37.4	2.6	187000	03./0.2/0.1	39	13	46	15	17	0.76	138/3.4/102/22.5	NN, activated lymphocytes, tp,lp	hemmorrhagic right ovarian cyst				DENGUE FEVER
25	Ruthira Kumar	28	Male	I18032373	5	Positive	P/N	13.3	40.9	1.9	118000	0.4/0.2/0.2	69	19	59	26	15	0.96	138/3.9/100/23.6	NN, LP, Thrombocytopenia	nad				DENGUE FEVER
26	Derek Goel	18	Male	I18033570	2	Positive	P/N	15.6	47.2	4.3	166000	0.4/0.2/0.2	23	29	82	16	14	0.96	139/3.71/102/18.7	NN, LP, TP, activated lymphocytes lymphocytosis	Mild spleenomegaly				DENGUE FEVER
27	Abhirama sundari	26	Female	I18033978	3	Positive	P/P	12.4	37.7	2	47000	0.6/0.3/0.3	80	44	38	60	10	0.65	134/3/97/20	NN, LP, Ac lymp, TP	Fatty liver, mild ascites, B/L Mild pleural effusion		6		DF WITH WARNING SIGNS
28	Ambika	25	Female	I18034207	3	Positive	P/N	10.6	32.4	4.3	52000	0.2/0.1/0.1	17	9	47	7	6	0.55	138/3.5/106/20	NN, LP, TP, AL	Live fetrn 16-17 wks matarity mildly dilated extra renal peln, prominent calyces on both sides				DENGUE FEVER
29	Suresh Kumar	37	Male	I18034252	3	Positive	P/P	15.1	45.6	2.8	75000	0.5/0.3/0.2	56	24	40	16	15	1.01	134/3.2/97/23.2	NN,rl,al,tp	Diffue GB wall thickness, mild ascites				DF WITH WARNING SIGNS
30	Govindaraj	59	Male	I19017857	5	Positive	P/N	15.7	41.6	5.2	79000	0.4/0.1/0.3	18	26	44	32	16	0.8	137/4.2/104/23.2	NN,lp,tp	nad				DENGUE FEVER
31	Elaiyabharathi	40	Male	I18021366	4	Positive	P/P	13.5	39.5	1.7	67000	0.5/0.3/0.2	161	111	49	54	13	0.69	135/3.5/102/13.5	NN, LP, AL, TP	Fatty liver				DENGUE FEVER
32	Prabhujith Eswar	18	Male	I18020784	5	Positive	P/N	13.8	41.8	1	97000	0.5/0.3/0.2	41	24	53	29	22	1.12	133/3.8/97/20.6	NN, LP, TP, monocytosis	Mild spleenomegaly				DENGUE FEVER
33	Vivek	23	Male	I18011843	5	Negative	P/N	14.5	43.2	1.9	46000	2.5/2.0/0.5	366	245	218	322	25	0.99	134/3.9/96/22.8	NN, leukopenia, relative lymphocytosis, TP, activated lymphocytes	mild splenomegaly, minimal right plureal effusion				DF WITH WARNING SIGNS
34	Raghul	19	Male	I18015307	3	Positive	P/N	13.6	40.4	4.7	180000	0.8/0.1/0.7	36	26	54	18	14	0.94	140/4.21/99/23.9	NN, Thrombocytopenia	Mild Spleenomegaly				DF WITH WARNING SIGNS
35	Kevin idiculla	24	Male	I18016187	3	Positive	P/N	13.9	40.8	3.7	144000	0.5/0.3/0.2	42	19	72	12	9	0.92	140/3.3/104/18.6	NN, leukopenia, monocytosisns, activated lymphocytes lymphocytosis, large platelets	normal				DENGUE FEVER
36	Metilda Jennifer	29	Female	I18017633	3	Positive	P/N	11.9	35.9	1.8	138000	0.3/0.2/0.1	76	84	102	124	13	0.72	139/4.4/106/25.2	NN, LP, AL, thrombocytopenia, gian platelet, platelet clumps	Diffue GB wall thickness, mild ascites				DF WITH WARNING SIGNS
37	Gnanasekaran	47	Male	I18018183	5	positive	P/P	12.6	37.3	4.6	90000	0.3/0.1/0.2	32	17	44	25	14	0.79	133/3.8/99/23.1	NN, AL, TP, Small Clumps	Mild spleenomepaly, mild dilated portal vain				DENGUE FEVER
38	Deepa	18	Female	I18008280	4	Negative	P/N	12.8	37.3	2.7	62000	0.3/0.1/02	193	146	54	40	4.67	0.54	139/3.2/103/21	NN, LP, TP, AL	Gall bladder calculi & wall thickness				DENGUE FEVER
39	Kowsika	19	Female	I18005342	4	Positive	P/P	11.4	35.1	6.9	246000	0.1/0.3/0.7	44	72	87	140	8.41	0.52	136/3.82/101/21	NN	No abnormal				DENGUE FEVER
40	Ranganathan	70	Male	I18019090	2	Positive	P/P	13.7	39.2	3.7	95000	0.4/0.2/0.2	56	25	40	19	47	1.08	129/3.6/95/19.9	NN, LP, TP, AL	Fatty liver				DENGUE FEVER
41	Mr. Nachimuthu. R	54	Male	I18020012	7	Negative	P/N	16.8	51	4.7	107000	0.9/0.4/0.5	51	50	83	184	23	0.7	130/4.17/95/21.4	NN blood picture wih relative lymplocytosis, activated lymphocytes, Thrombocytopenia	Cholelithiasis, Prominent, CBD, Mild Prostatomegaly				DENGUE FEVER
42	Venkatesh. M	31	Male	I18020513	5	Negative	P/N	16.5	48	2.5	40000	0.4/0.3/0.1	172	187	48	102	16	1.05	139/3.51/100/26.1	NN, Blood picture with gythrocytosis, leucopenia, thrombocytopenia	Mild splenomegaly, GB edematous wall thickening				DF WITH WARNING SIGNS
43	Surya	18	Male	I18019995	5	Not done	P/P	14.2	43.2	3.3	92000	1/0.3/0.7	150	238	119	107	21	1.06	135/2.7/98/21	NN, Blood Picture with leukopenia, relative lymphocytosis & thrombocytopenia	Mesentric lymphadenopathy, small non-mobile hyperchogenic focus in neck of GB				DENGUE FEVER
44	Sulakshana	34	Female	I18004126	2	Negative	P/P	14	42.1	7	13000	2.1/2/0.1	434	180	295	312	10.75	0.74	136/4.2/111/20	NN, activated lymphocytes & Thrombocytopenia	gb wall thickening, mild ascites, minimal b/l plueral effusion		11	1	SEVERE DENGUE
45	Elango. C	24	Male	I18004508	5	Positive	P/N	16.6	49.9	7	21000	0.7/0.3/0.4	193	90	43	43	16	0.8	138/4.3/101/24.2	NN, Thrombocytopenia, activated lymphocytes lymphocytosis	Normal				DENGUE FEVER
46	Shandhi	48	Female	I18018526	6	Negative	P/N	11.6	35.8	2.7	71000	0.3/0.2/0.1	72	42	101	53	18	0.67	135/3.5/99/22	NN, LP, AL, TP, large plts	gb wall thickening, mild ascites, minimal b/l plueral effusion				DF WITH WARNING SIGNS
47	Karthik	32	Male	I18022701	3	Positive	P/P	18.8	56.1	3.9	7000	1/0.5/0.5	231	169	122	320	17	0.9	139/3.8/103/21.5	NN, TP, activated lymphocytes	GB midly thickned minima pleural effusion		5		DF WITH WARNING SIGNS
48	Kumar	44	Male	I18021541	4	Positive	P/P	16.4	49.5	6.6	33000	1.1/0.5/0.6	665	408	106	253	18	1.06	136/4.1/99/23	NN, blood picture with thrombocytopenia, activated lymphocytes	Mild hepatomegaly with fatty mfilvation, gall bladder wall appears mildly thickness edematous		6		DF WITH WARNING SIGNS
49	Ganesh. K	58	Male	I18022519	1	Positive	P/N	12.7	38.5	5.2	161000	0.4/0.2/0.2	15	18	44	22	9.8	1.19	135/3.92/98/25	NN, Blood Picture with leukopenia, activated lymphocytes lymphocytosis & thrombocytopeni	Mild prostatomegaly				DENGUE FEVER
50	Dhanya kamatchi	25	Female	I18019038	6	NOT DONE	P/P	13.9	41.9	11.1	49000	0.2/0.1/0.1	150	124	68	56	11.68	0.57	137/4/104/19	NN,AL,TP, RELATIVE lymphocytosis	hepatomegaly, gall bladder wall thickening				DENGUE FEVER
51	Ranjith	28	Male	I18018537	5	Negative	P/N	14.6	44.9	15.3	56000	1.8/0.3/2.1	269	264	397	147	16	1.02	137/4.7/101/22.3	NC	Mild ascites and GB Thickned		6		DF WITH WARNING SIGNS
52	Ryan	18	Male	I18034319	6	Not done	N/P	15.1	46.8	4.4	50000	0.4/0.3/0.1	86	62	104	75	9	0.62	140/4.21/102/23.1	NN, activated lymphocytes, TP	Edematom GB wall, Mild ascites				DF WITH WARNING SIGNS
53	Dhanabal	33	Male	I18037399	6	Not done	P/P	16.1	48.8	6.2	40000	1/0.5/0.5	87	85	96	190	18	1.15	136/4.2/103/24.1	NN, AL, TP	Fatty liver, Mild spleenomegaly, Mild pleural effusion				DF WITH WARNING SIGNS
54	Sarika	36	Female	I18037341	2	Positive	P/P	12.1	36.8	4.7	13000	0.3/0.2/0.1	46	20	47	30	10	0.6	138/3.66/104/19.7	NN, lymphocytosis, AL, TP	Diffuse Gbwall thickening, B/L minimal pleural effusion		4		DF WITH WARNING SIGNS
55	Deepa	37	Female	I18036352	2	Positive	P/P	11.8	37.4	11.1	28000	0.3/0.1/0.2	168	119	57	178	15	0.49	139/4.6/101/25.3	NN, monocytosissis, AL, TP	Diffuse Gbwall thickening, B/L minimal pleural effusion		5		DF WITH WARNING SIGNS
56	Karitha. S	36	Female	I18036101	3	Positive	P/P	12.7	39	9.2	18000	0.8/0.3/0.5	107	42	123	156	9	0.44	140/3.6/106/20.7	NN, Relating monocytosisns, AL, TP	gb wall thickening, mild ascites		4		DF WITH WARNING SIGNS
57	Munna yadhav	29	Male	I18034498	5	Positive	P/N	15.4	46.1	4.8	68000	0.3/0.1/0.2	69	46	50	20	17	0.66	137/3.7/101/20.5	NN, activated lymphocytes, TP	gb wall thickening, mild ascites, minimal b/l plueral effusion		6		DF WITH WARNING SIGNS
58	Anish	20	Male	I18034472	5	Positive	P/P	16.1	47.2	4.4	41000	0.6/0.2/0.4	64	43	59	34	24	0.77	134/3.61/101/15.3	NN, AL, Lymphocytes, TP	Mild ascites, Mild pleural effusion				DF WITH WARNING SIGNS
59	Dharun Kumar	17	Male	I18023863	4	Positive	P/N	14.6	44.1	2.6	112000	0.5/0.1/0.4	39	16	102	11	18	0.91	137/4.4/99/21	NN, blood picture with mild leukoponia, thrombocytopenia	Increased periportal echogenicity both lobes of liver, edema/inflammatony, no other abnormality detected				DENGUE FEVER
60	Deivanai	45	Female	I18023568	3	positive	P/P	13.9	42.7	13.7	37000	0.3/0.1/0.2	62	64	158	155	24	0.47	139/3.97/101/22.9	Lymphocytosis with presence of many activated lymphocytes & Thrombocytopenia	Diffuse gall bladder wall thickness moderate fatty liver				DENGUE FEVER
61	Selvi	49	Female	I18022709	3	Negative	P/P	13.9	41	5.4	12000	4/3.9/0.1	511	208	459	450	26	1.15	133/3.72/100/20.7	NN, Blood picture with relative lymphocytosis & Thrombocytopenia	gb wall thickening, mild ascites, minimal b/l plueral effusion		2		DF WITH WARNING SIGNS
62	Karuppusamy	38	Male	I18002192	4	Positive	P/N	13.8	39.9	1.8	151000	0.1/0.5/0.6	103	94	69	54	11.68	0.8	137/4.43/98/27.2	NN, anemia crelatne neutrophilia	Normal				DENGUE FEVER
63	Kanishka	40	Female	I18001718	4	Positive	P/N	12.6	38.5	2.8	72000	0.2/0.1/0.1	28	14	63	52	14	0.49	135/3.09/101/20.8	NN blood picture wih relative lymplocytosis, activated lymphocytes, Thrombocytopenia	Gall bladder calculi & wall thickness, minimal ascities				DF WITH WARNING SIGNS
64	Karthik. B	29	Male	I18001658	4	Positive	P/N	13.9	41.4	4.3	97000	0.4/0.2/0.2	161	95	64	88	12	0.76	137/4.3/102/24.1	NN blood picture wih relative lymplocytosis, activated lymphocytes, Thrombocytopenia	Gall bladder wall thickness, minimal ascinese		4		DF WITH WARNING SIGNS
65	Sathyanarayanan	25	Male	I18001552	3	Positive	P/N	16.8	50.4	4.6	118000	1.1/0.5/0.6	88	132	80	188	32	0.89	137/4.48/103/1.189	NN	FATTY LIVER		6		DENGUE FEVER
66	Kala. G	52	Female	I18000759	3	Positive	P/N	12.1	36.9	3	55000	0.4/0.3/0.1	203	102	217	186	7.48	0.59	124/3.86/94/19.5	Leucopenia & Thrombocytopenia,	Gall bladder wall thickness, MOderate ascities	RBBB	4		DF WITH WARNING SIGNS
67	Pavithra	24	Female	I19019531	6	Not done	P/P	12	36.2	2.4	86,000	0.3/0.1/0.2	447	382	54	98	9	0.62	138/2.88/102/20.2	NN leukopenia, Thrombocytopenia	Mild hepatonegaly fathy infilltration small left ovaron cyst				DENGUE FEVER
68	Elayaraja. L	35	Male	I19019534	5	Positive	P/N	16.6	50.8	31	196000	0.5/0.2/0.3	24	13	43	24	19	0.77	138/3.64/100/21.1	NN blood picture leukopenia	Small echoganidesion in Rt lobe flves incely hemagioma				DENGUE FEVER
69	Pravin. V	28	Male	I19017517	4	Positive	P/N	14	42.2	3.6	133000	0.6/0.3/0.3	58	35	57	24	11.2	1.15	136/3.13/96/22.7	NN blood picture leukopenia, relative neutropilia	GB wall thickness				DENGUE FEVER
70	Hari Prasath. S	24	Male	I19020422	3	Positive	P/N	16.5	51.3	6.8	75000	0.5/0.2/0.3	47	20	65	72	12	0.81	141/3.49/105/22.5	NN blood picture wih relative lymphocytosis, activated lymphocytes, Thrombocytopenia	Fatty lver, thickness gall baldder wall				DENGUE FEVER
71	Dev Nithin	17	MALE	I19019976	4	Positive	P/P	15.6	46.6	1.8	86000	0.3/0.2/0.1	54	34	54	19	7.01	1.13	141/4.6/106/24.9	NN blood picture wih relative lymplocytosis, activated lymphocytes, Thrombocytopenia	Gall bladder wall thickness, minimal ascinese	SINUS BRADY	4		DF WITH WARNING SIGNS
72	Chandran	51	Male	I18002198	7	NOT DONE	N/P	15.7	46.6	9.3	51000	0.4/0.1/0.3	136	50	56		8.8	0.87	130/3.95/100/20.9	NN blood picture, Thrombocytopenia	Normal USG abdomen				DENGUE FEVER
73	Dhanalakshmi.M	36	Female	I19018921	6	Positive	P/N	7.4	23	1.5	55000	0.4/0.1/0.3	118	147	155	99	6.54	0.66	136/4.6/101/21.8	NN blood picture wih relative lymplocytosis, activated lymphocytes, Thrombocytopenia	cholelithiasis, mild ascites				DF WITH WARNING SIGNS
74	Ramaraj. P	67	Male	I19018412	6	Not done	P/N	15.5	47.5	5.5	129000	1.0/0.3/0.7	31	13	51	13	49	1.68	134/3.9/98/20.9	NN blood picture wih relative lymplocytosis, activated lymphocytes, Thrombocytopenia	Mild fatty liver, B/L Midly moreased renal cortisal echoes, B/L few simple renal cotical cysts	SINUS BRADY			DENGUE FEVER
75	Hariharan	23	Male	I19020389	3	Positive	P/P	16.6	49.4	3.5	89000	0.5/0.2/0.3	67	53	73	31	9	0.69	139/4.3/103/23	NN blood picture leukopenia, THROMBOCYTOPENIA	GB thickening, minimal ascites				DF WITH WARNING SIGNS
76	Pavithra. M	23	Female	I19021008	7	Positive	P/P	13.7	42.1	5	32000	0.4/0.2/0.2	442	321	60	118	13	0.58	137/4.16/104/20	NN blood picture relative lymplocytes & thrombocytopenia	NAD				DENGUE FEVER
77	Banu sri	20	Female	I19020456	5	Positive	P/N	11.8	35.5	1.2	60000	0.7/0.2/0.2	92	53	30	12	13	0.64	135/3.32/101/21.1	NN ohenia leukopenia, lyaplocytes & thrombocytopenia	No signtreat abnomally deteeted				DENGUE FEVER
78	Revathy. K	27	Female	I19020764	4	Positive	P/N	11.2	35.1	3.6	50000	0.3/0.1/0.2	768	541	67	218	7	0.63	134/4.38/109/12.8	NN ohenia, throbocyloptia, plateless are in aggregrates	Acule akalcalous cholestirs, polycystic ovakes				DENGUE FEVER
79	Savitha Karpagam. S	37	Female	I19020710	5	Positive	P/N	11.8	37	2.6	110000	0.9/0.1/0.1	28	21	43	22	18	0.65	136/4.6/102/19.9	nn , Thrombocytopenia, activated lymphocytes +	normal				DENGUE FEVER
80	Senthil Kumar	42	Male	I19021209	3	Positive	P/N	14.8	45.8	5.8	98000	0.7/0.4/0.3	112	88	90	233	11	0.79	134/3.68/99/25.8	NN blood picture wih relative lymplocytosis, activated lymphocytes, Thrombocytopenia	edematous gb thickening, mild ascites,mild spleenomegaly				DF WITH WARNING SIGNS
81	M. Saheen	51	Male	I19025349	4	Positive	P/N	17.5	52.4	4.2	123000	0.3/0.1/0.2	28	24	79	22	21	1.01	139/4.5/106/23.7	NN blood picture wih relative lymplocytosis, activated lymphocytes, Thrombocytopenia	large exphytic ujst in kidney prominent prostatd				DENGUE FEVER
82	Amirtharaj Vijay. S	35	Male	I19023070	6	not done	P/P	13.4	40.5	2.9	62,000	0.7/0.4/0.3	103	99	55	116	14	0.92	135/3.7/101/24.6	NN blood picture wih relative lymplocytosis, activated lymphocytes, Thrombocytopenia	Hepatomeyaly fatty infillration, mild splenomesaly, minimal ascites B/L minimal flevial effusion		6		DF WITH WARNING SIGNS
83	Jayasudha	38	Female	I19021995	4	Positive	P/P	14.4	42.1	2.8	39,000	0.6/0.3/0.3	158	62	58	81	16	0.79	132/3.12/18.4/0.95	Leukopenia activated lymphocytes eymphocytese thrombolytopenia normocytic norchromic	Fatty liver, Mild ascites, small umblical hernia, B/L mild pleural effusion		3		DF WITH WARNING SIGNS
84	Chinnathal. V	55	Female	I19022374	7	Not done	P/P	12.8	40	10	55000	0.3/0.1/0.2	68	58	12	79	51	0.92	137/3.43/104/22.2	NN blood picture with leucocytosis, lymphocytosis activated lymphocytes thrombocytopenia	Cholelithiasis	SHORT PR interval			DENGUE FEVER
85	Nishana	24	Female	I19023233	5	Positive	P/N	5.3	18.7	3.5	38000	0.7/0.3/0.4	72	39	48	34	10	0.6	137/3.5/23.5	Moderate anisopoikilocytosis, Microcytic, hypochromic, macrocytes, elliptocytes, spherocyte	Edematous wall thickning in gall bladder, moderate splenomegaly, mild ascites		4	2	SEVERE DENGUE
86	Rajkumar. M	33	Male	I19023632	3	positive	P/P	13.3	39.6	4.1	101000	0.5/0.2/0.3	97	151	78	61	19	0.9	135/3.24/97/21.3	NN WITH THROMBOCYTOPENIA	Fatty liver & edematous gall bladder wall thickening		6		DF WITH WARNING SIGNS
87	aruna	29	Female	I19001521	4	Positive	P/N	14.8	45	4.4	45000	0.4/0.2/0.2	116	45	63	72	14	0.68	133/3.54/98/18.8	NN leucopenia with thrombocytopenia activated lymphocytes	minimal pleuel effsion				DF WITH WARNING SIGNS
88	Sornalatha	24	Female	I19001490	3	Positive	P/N	11	34.1	2.1	30000	0.5/0.1/0.4	141	78	119	55	16	0.49	136/3.9/100/21	NN , leucopenia , thrombocytopenia	GB wall thickness, mild splenoegals	sinus brady	4		DF WITH WARNING SIGNS
89	Prabakaran	27	Male	I19001435	6	Not done	P/P	15.1	45.8	3	28000	0.6/0.3/0.3	75	33	45	50	12	0.9	139/4.05/102/24.4	NN Thrombocytoenia activated lymphocytes	Mild GB wall thickness				DENGUE FEVER
90	Sajitha	31	Female	I19001260	6	Not done	P/P	14.5	43.9	11.9	69000	0.2/0.1/0.1	118	95	93	199	14	0.67	138/4.96/97/24.2	NN activated lymphocytes, Thrombytopia	GB wall edema, mild ascites, mild pleural ethrion				DF WITH WARNING SIGNS
91	Dinesh Kanna	30	Male	I19001155	5	Positive	P/P	15.9	47.5	4.8	18000	0.5/0.2/0.3	78	58	78	89	19	0.72	135/3.84/100/20	NN thrombocytopenia & activated lymphocytes	Edematom GB wall, minimal ascites, minimal b/c pleual effision		6		DF WITH WARNING SIGNS
92	Tamillarasan	24	Male	I19000949	5	Positive	P/P	17.5	53.6	6.5	22000	1.6/0.6/1	283	213	62	118	19	0.91	133/4.22/97/25.8	NN severe thromocytopenia activated lymphocytes lymophocyties giant plates	Mild hepatomepaly fatty inhltrohon, mild splemomegaly, moderate ascites mod. Bilteral pleural effision		4		DF WITH WARNING SIGNS
93	Varsha	25	Female	I19000789	3	Positive	P/P	13.8	41.5	1.9	124000	0.2/0.1/0.1	40	36	83	16	11	0.82	136/4.5/103/24	nn blood picture, leucopenia, activated lymphocytes, thrombocytopenia	mild GB wall thickness				DENGUE FEVER
94	Raja	23	Male	I19002830	5	Positive	P/N	15.6	46.4	2.6	80000	0.6/0.3/0.3	266	207	69	271	22	0.67	137/3.84/97/25.6	NN blood pichre leucopenia thrombocytopenia activated lymphocytes	Minimal GB wall thickening+				DENGUE FEVER
95	Nivedhasri	19	Female	I19020900	4	Positive	P/P	14.9	45.5	10.1	15000	0.4/0.2/0.2	195	91	92	122	18	0.94	132/3.4/96/22.3	NN blood Picture actived lymphocytes & Thromobytopia	GB wall thickness/mod ascites/pleurel effission		4		DF WITH WARNING SIGNS
96	Sri hari	29	Male	I19026058	3	Positive	P/N	15.6	45.9	2.2	189000	0.8/0.4/0.4	77	177	156	169	22	1.15	135/3.9/98/21	activated lymphocytes/giant platelets	Minimal GB wall thickening, minimal ascites				DF WITH WARNING SIGNS
97	Sasikala	43	Female	I19026084	4	Positive	P/P	10.3	31.6	2.1	154000	0.4/0.3/0.1	146	130	113	111	15	1.06	139/3.38/103/23	nn, leucopenia with activated lymphocytes, thrombocytopenia	Mild fatty liver, Edemalone gall bladder wall reactive, mild splenonegaly, mild ascites, mild plaeral effcision				DF WITH WARNING SIGNS
98	Rehitha	24	Female	I19026871	3	Positive	P/N	12.6	36.2	3.9	169000	0.3/0.1/0.2	278	220	59	38	9	0.6	138/4.2/101/24.6	NN , leucopenia , thrombocytopenia	NAD				DENGUE FEVER
99	shri sudharsini	18	Female	I19026414	3	Positive	P/P	13.2	39.5	2.7	91000	0.3/0.1/0.2	90	30	55	14	14	0.76	139/4.73/106/19.6	nn anemia, thrombocytopenia, lymphocytosis	Edematom GB wall thickness, moderate ascites, moderate pleural effrs, minimal pleural effission				DF WITH WARNING SIGNS
100	Aswanth manoharan	21	Male	I19021511	4	Positive	P/N	16.4	48.7	3.4	154000	1.2/0.9/0.3	43	18	56	11	15	0.6	135/4.1/99/24.1	NN , leucopenia , thrombocytopenia	Mild hepatomegaly				DENGUE FEVER