"STUDY OF CLINICAL SPECTRUM IN PATIENTS OF DENGUE FEVER AND FACTORS PREDICTING COMPLICATIONS IN PATIENTS ATTENDING A RURAL TERTIARY CARE HOSPITAL IN SOUTH INDIA"

By

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DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF MEDICINE

IN

GENERAL MEDICINE

Under the guidance of

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DECLARATION BY THE CANDIDATE

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Dr. SRIKANTH RAMMOHAN T

ABSTRACT

INTRODUCTION:

Dengue is a rapidly spreading mosquito-borne viral disease & is emerging as a leading infectious disease in urban and periurban regions. 2005 World Health Assembly resolution quantifies Dengue as a disease which may constitute a public health emergency of international concern.

The spectrum of manifestations in Dengue varies widely from being totally asymptomatic to a complicated infection presenting with shock & haemorrhage. Our study enables to correlate the spectrum of manifestations, severity, lab investigations and radiological means to determine the predictors of complications in Dengue fever.

MATERIALS & METHODS :

The Study group included 107 inpatients of R L Jalappa Hospital, Kolar. It was a prospective study done between April 2012 to August 2013. The subjects were enrolled after taking consent for the study.

INCLUSION CRITERIA:

1. Patients with history of fever & tested positive by Lab Tests.(Dengue – NS1Ag, IgM & IgG)
2. Age > 18yrs.

EXCLUSION CRITERIA:

1. Patients with mixed infections- such as those tested positive for malaria, leptospirosis along with dengue.
2. Those with bleeding diathesis due to other causes such as DIC, ITP, and hemophilia were excluded from the study.

RESULTS:

55% of the patients belonged to the age group of 18- 35 years. 62.6% subjects tested positive for IgM by serological methods. Most common symptom was fever seen in all cases. Petechiae was seen in 11.2% of the study population. Pleural effusion was seen in 8 and ascites in 9 patients. 82.2% patients had thrombocytopenia, seen in 82.2% of the study population. Mean platelet count was 78,336 cells/mm^3. 34.5% patients had leucopenia. 32.7% patients had PCV > 45%. Four fold rise in SGOT values & 2 fold rise in SGPT values were seen in comparison with the normal population. No significant statistical correlation was present between symptoms & investigations. Significant positive statistical correlation was present between Hb & PCV with 'p' value less than 0.01. Negative statistical correlation between Hb & platelet count was noted with 'p' value of 0.04. There was a significant positive correlation between total protein & albumin.

CONCLUSION

The determining factor in dengue is severity & extent of plasma leakage. Complications and recovery are determined by the extent of plasma leakage and are commonly seen at the end of febrile phase. Clinical monitoring should be based on extent of hydration, general wellbeing & regular monitoring of blood counts. Adequate hydration should be the corner stone in the management of dengue & haematocrit should be used as a tool in assessing the extent of plasma leakage & management.

LIST OF ABBREVIATIONS

ADE	Antibody Dependent Enhancement
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
CBC	Complete Blood Counts
CD4	Cluster of Differentiation 4, T Helper cell surface glycoprotein
CD8	Cluster of Differentiation 8, T cell co-receptor transmembrane glycoprotein
DEN	Dengue
DENV	Dengue virus
DF	Dengue Fever
DHF	Dengue Haemorrhagic Fever
DNA	Deoxyribonucleic acid
DSS	Dengue Shock syndrome
ELISA	Enzyme linked Immunosorbent Assay
F_C - receptor	Fragment, crystallisable region, a cell receptor
HI	Haemagglutination Inhibition
Ig M	Immunoglobulin M
Ig G	Immunoglobulin G
MAC – ELISA	Ig M antibody capture enzyme linked immunosorbent assay
NS	Non Structural protein
PCR	Polymerase Chain reaction
RNA	Ribonucleic acid
T cells	A group of Lymphocytes important for cell mediated immunity

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INTRODUCTION

INTRODUCTION

Dengue is a rapidly spreading mosquito-borne viral disease & is emerging as a leading infectious disease in urban and periurban regions accounting for 50 million infections annually.[1,2] 2005 World Health Assembly resolution quantifies Dengue as a disease which may constitute a public health emergency of international concern.[3] It has been responsible for many outbreaks of epidemics globally including India.[1]

The spectrum of manifestations in Dengue varies widely from being totally asymptomatic to a complicated infection presenting with shock & haemorrhage.[4] There have been many studies which have been conducted globally & over India which have focused in predicting the number of cases associated with outbreak.[3] Warning signs include persistent vomiting, abdominal pain, lethargy or restlessness, oliguria, refusal of oral intake & postural hypotension.[5] Our study enables to correlate the spectrum of manifestations, severity, lab investigations and radiological means to determine the predictors of complications in Dengue fever.

OBJECTIVES

OBJECTIVES OF THE STUDY

1. To Determine the Clinical spectrum & Investigate patients with Dengue fever.

2. To correlate Clinical Spectrum & Investigations with Complications.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

HISTORICAL PERSPECTIVE:-

The name "dengue" is derived from the Swahili *ki denga pepo*, meaning a sudden seizure by a demon. The term 'break-bone fever' was coined during the Philadelphia epidemic in 1780. DEN 1 was first isolated from Hawaii in 1944, DEN 2 from New Guinea in 1944 and DEN 3 and 4 from the Philippines in 1956.[6]

BURDEN OF DISEASE:

Dengue fever (DF) and its Severe forms – Dengue haemorrhagic fever (DHF) and Dengue shock syndrome (DSS) - have become major international public health concerns. Over the past three decades, there has been dramatic global increase in the frequency of dengue fever, DHF and DSS and their epidemics. It is found in tropical and subtropical regions around the world, predominantly in urban and semi-urban areas, and are now spreading to rural areas.[7]

2.5 billion People i.e. two fifth of the world's population in tropical and subtropical countries are at risk of the disease. An estimated 50 million dengue infections occur worldwide annually and about 5,00,000 people with DHF require hospitalization each year. Approximately 90 per cent of them are children aged less than five years, and about 2.5 per cent of those affected die. During epidemics, infection rate among those who have not been previously exposed to the virus are often 40 to 50 per cent, but can also reach 80 to 90 per cent [8].Cocirculation of multiple serotypes/genotypes is evident.

Dengue and DHF is endemic in more than 100 countries in the WHO regions of Africa, the Americas, Eastern Mediterranean, South East Asia and Western Pacific. The South East Asia and Western pacific regions are most seriously affected. Detection of all four serotypes has now rendered the countries hyper endemic. The countries of South-East Asia region are divided into 3 categories [8]. India falls under category one where it is a

a. Major public health problem;

b. Leading cause of hospitalization and death among children;

c. Hyperendemicity with all 4 serotypes circulating in urban areas; and

d. Spreading to rural areas.

DENGUE IN INDIA:-

Dengue was initially confined to the east coast of India and has caused epidemics, sometimes along with the Chikungunya virus, as in 1963 when extensive out breaks affected Calcutta and Madras. Subsequently it has spread westwards and in the 1990s Surat and Delhi had major epidemics with deaths due to DHF and DSS. All four types of dengue virus are present in this country. Occasionally, more than one type of the virus has been isolated from the same patient.[6]

In India, the risk of dengue has shown an increase in recent years due to rapid urbanization, lifestyle changes and deficient water management including improper water storage practices in urban, peri-urban and rural areas, leading to proliferation of mosquito breeding sites. The disease has a seasonal pattern i.e. the cases peak after monsoon, and it is not

uniformly distributed throughout the year. However, in the southern states and Gujarat the transmission is perennial.[9]

Dengue is endemic in 31 states and Union Territories. During 2011, about 18,059 cases were reported with 119 deaths. The case fatality rate was 0.65 per cent. The highest number of cases was reported from Punjab followed by Tamil Nadu, Gujarat, Kerala and Andhra Pradesh.[10] All the four serotypes i.e. dengue 1, 2, 3 and 4 have been isolated in India but at present DENV1 and DENV2 serotypes are widespread.[11]

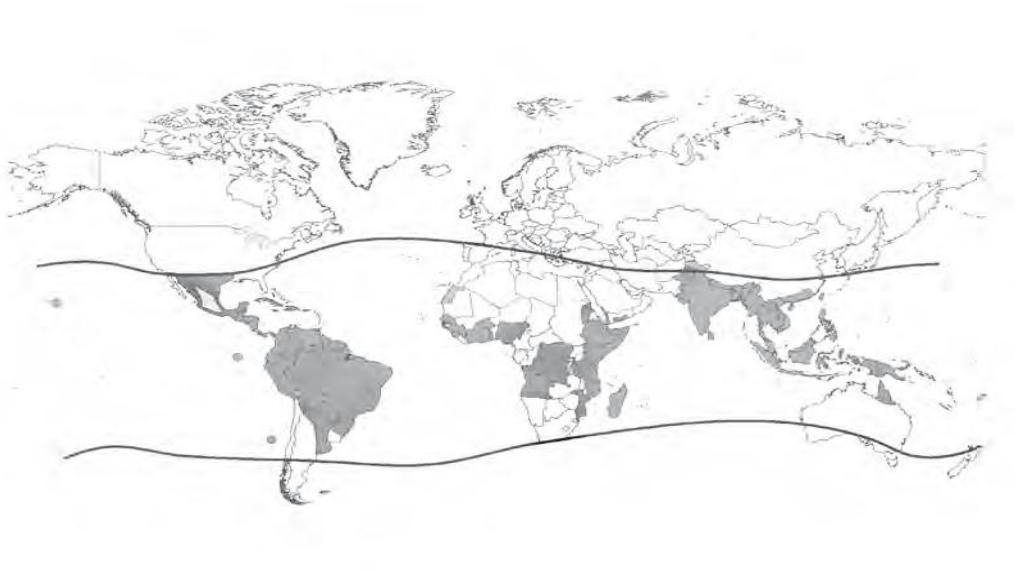


Figure 1: Countries / Areas at Risk of Dengue Transmission

Dengue virus is widely distributed throughout the tropics and subtropics. Dengue fever is clinically similar to the illness caused by the Chikungunya and O'nyong –nyong viruses. Immunity is type specific so that it is possible for a person to have four separate episodes of dengue fever.

VECTOR:-

- Dengue virus (DEN) is a small single-stranded RNA virus comprising four distinct serotypes (DEN 1 to 4). These closely related serotypes of the dengue virus belong to the genus Flavivirus & Family Flaviviridae.
- The mature particle of the dengue virus is spherical with a diameter of 50nm containing multiple copies of the three structural proteins, a host-derived membrane bilayer and a single copy of a positive-sense, single-stranded RNA genome. The genome is cleaved by host and viral proteases in three structural proteins (capsid, C, prM, the precursor of membrane, M, protein and envelope, E) and seven nonstructural proteins (NS).
- Distinct genotypes or lineages have been identified within each serotype, highlighting the extensive genetic variability of the dengue serotypes. "Asian" genotypes of DEN-2 and DEN-3 are frequently associated with severe disease accompanying secondary dengue infections.[12-14] Intra-host viral diversity (quasispecies) has also been described in human hosts.

- The various serotypes of the dengue virus are transmitted to humans through the bites of infected *Aedes* mosquitoes, principally *Ae.aegypti*. This mosquito is a tropical and subtropical species widely distributed around the world, mostly between latitudes 35 ^{0}N and 35 ^{0}S .[15]

- *Aedes aegypti* and *Aedes albopictus* are the two most important vectors of dengue. They both carry high vectorial competency for dengue virus, i.e., high susceptibility to infecting virus, ability to replicate the virus and ability to transmit the virus to another

host. Aedes aegypti is a highly domesticated, strongly anthropophilic, nervous feeder (i.e., it bites more than one host to complete one blood meal) and is a discordant species (i.e., it needs more than one feed for the completion of the gonotropic cycle). This habit results in the generation of multiple cases and the clustering of dengue cases in the cities. On the contrary, *Ae.albopictus* partly invades peripheral areas of urban cities. It is an aggressive feeder and concordant species, i.e., the species can complete its blood meal in one go on one person and also does not require a second blood meal for the completion of the gonotropic cycle. [7]

- The immature stages are found in water-filled habitats, mostly in artificial containers closely associated with human dwellings and often indoors. Studies suggest that most female *Ae.aegypti* may spend their lifetime in or around the houses where they emerge as adults. This means that people, rather than mosquitoes, rapidly move the virus within and between communities. Dengue outbreaks have also been attributed to *Aedes albopictus*, *Aedes polynesiensis* and several species of the *Aedes scutellaris* complex. Each of these species has a particular ecology, behaviour and geographical distribution. In recent decades *Aedes albopictus* has spread from Asia to Africa, the Americas and Europe, notably aided by the international trade in used tyres in which eggs are deposited.[15]

OVERVIEW OF DENGUE:-

After an incubation period of 4-10 days, infection by any of the four virus serotypes can produce a wide spectrum of illness, although most infections are asymptomatic or subclinical. Primary infection is thought to induce lifelong protective immunity to the infecting serotype.[16] Individuals suffering an infection are protected from clinical illness with a different serotype within 2-3 months of the primary infection but with no long-term cross-protective immunity.

Individual risk factors determine the severity of disease and include secondary infection, age, ethnicity and possibly chronic diseases. Young children in particular may be less able than adults to compensate for capillary leakage and are consequently at greater risk of dengue shock.

Seroepidemiological studies in Cuba and Thailand consistently support the role of secondary heterotypic infection as a risk factor for severe dengue, although there are a few reports of severe cases associated with primary infection.[17-20] The time interval between infections and the particular viral sequence of infections may also be of importance. A higher case fatality rate was observed in Cuba when DEN2 infection followed a DEN1 infection after an interval of 20 years compared to an interval of four years. Severe dengue is also regularly observed during primary infection of infants born to dengue-immune mothers. Antibody-dependent enhancement (ADE) of infection has been hypothesized as a mechanism to explain severe dengue in the course of a secondary infection and in infants with primary infections.[21,22] According to it non-neutralizing, cross-reactive antibodies raised during a primary infection, or acquired passively at birth, bind to epitopes on the surface of a

heterologous infecting virus and facilitate virus entry into Fc-receptor-bearing cells. The increased number of infected cells is predicted to result in a higher viral burden and induction of a robust host immune response that includes inflammatory cytokines and mediators, some of which may contribute to capillary leakage. During a secondary infection, cross-reactive memory T cells are also rapidly activated, proliferate, express cytokines and die by apoptosis in a manner that generally correlates with overall disease severity. Host genetic determinants might influence the clinical outcome of infection, though most studies have been unable to adequately address this issue.[23,24] Studies in the American region show the rates of severe dengue to be lower in individuals of African ancestry than those in other ethnic groups.[25]

The dengue virus enters via the skin while an infected mosquito is taking a blood meal. During the acute phase of illness the virus is present in the blood and its clearance from this compartment generally coincides with defervescence. Humoral and Cellular immune responses are considered to contribute to virus clearance via the generation of neutralizing antibodies and the activation of CD4+ and CD8+ T lymphocytes. In addition, innate host defense may limit infection by the virus. After infection, serotype specific and cross-reactive antibodies and CD4+ and CD8+ T cells remain measurable for years.

Plasma leakage, haemoconcentration and abnormalities in homeostasis characterize severe dengue. The mechanisms leading to severe illness are not well defined but the immune response, the genetic background of the individual and the virus characteristics may all contribute to severe dengue.

Recent data suggest that endothelial cell activation could mediate plasma leakage.[26,27] Plasma leakage is thought to be associated with functional rather than

destructive effects on endothelial cells. Activation of infected monocytes and T cells, the complement system and the production of mediators, monokines, cytokines and soluble receptors may also be involved in endothelial cell dysfunction.

Thrombocytopenia may be associated with alterations in megakaryocytopoieses by the infection of human haematopoietic cells and impaired progenitor cell growth, resulting in platelet dysfunction (platelet activation and aggregation), increased destruction or consumption (peripheral sequestration and consumption). Haemorrhage may be a consequence of thrombocytopenia and associated platelet dysfunction or disseminated intravascular coagulation. In summary, a transient and reversible imbalance of inflammatory mediators, cytokines and chemokines occurs during severe dengue, probably driven by a high early viral burden, and leading to dysfunction of vascular endothelial cells, derangement of the haemocoagulation system then to plasma leakage, shock and bleeding.

TRANSMISSION OF THE DENGUE VIRUS:-

Humans are the main amplifying host of the virus. Dengue virus circulating in the blood of viraemic humans is ingested by female mosquitoes during feeding. The virus then infects the mosquito mid-gut and subsequently spreads systemically over a period of 8-12 days. After this extrinsic incubation period, the virus can be transmitted to other humans during subsequent probing or feeding. The extrinsic incubation period is influenced in part by environmental conditions, especially ambient temperature. Thereafter the mosquito remains infective for the rest of its life. *Ae.aegypti* is one of the most efficient vectors for arboviruses because it is highly anthropophilic, frequently bites several times before completing oogenesis, and thrives in close proximity to humans. Vertical transmission (transovarial transmission) of dengue virus has been demonstrated in the laboratory but rarely in the field. The significance of vertical transmission for maintenance of the virus is not well understood. Sylvatic dengue strains in some parts of Africa and Asia may also lead to human infection, causing mild illness. Several factors can influence the dynamics of virus transmission - including environmental and climate factors, host pathogen interactions and population immunological factors. Climate directly influences the biology of the vectors and thereby their abundance and distribution; it is consequently an important determinant of vector-borne disease epidemics.

SPECTRUM AND STAGES OF DISEASE:-

Dengue infection is a systemic and dynamic disease. It has a wide clinical spectrum that includes both severe and non-severe clinical manifestations. After the incubation period, the illness begins abruptly and is followed by the three phases - Febrile, Critical and Recovery.

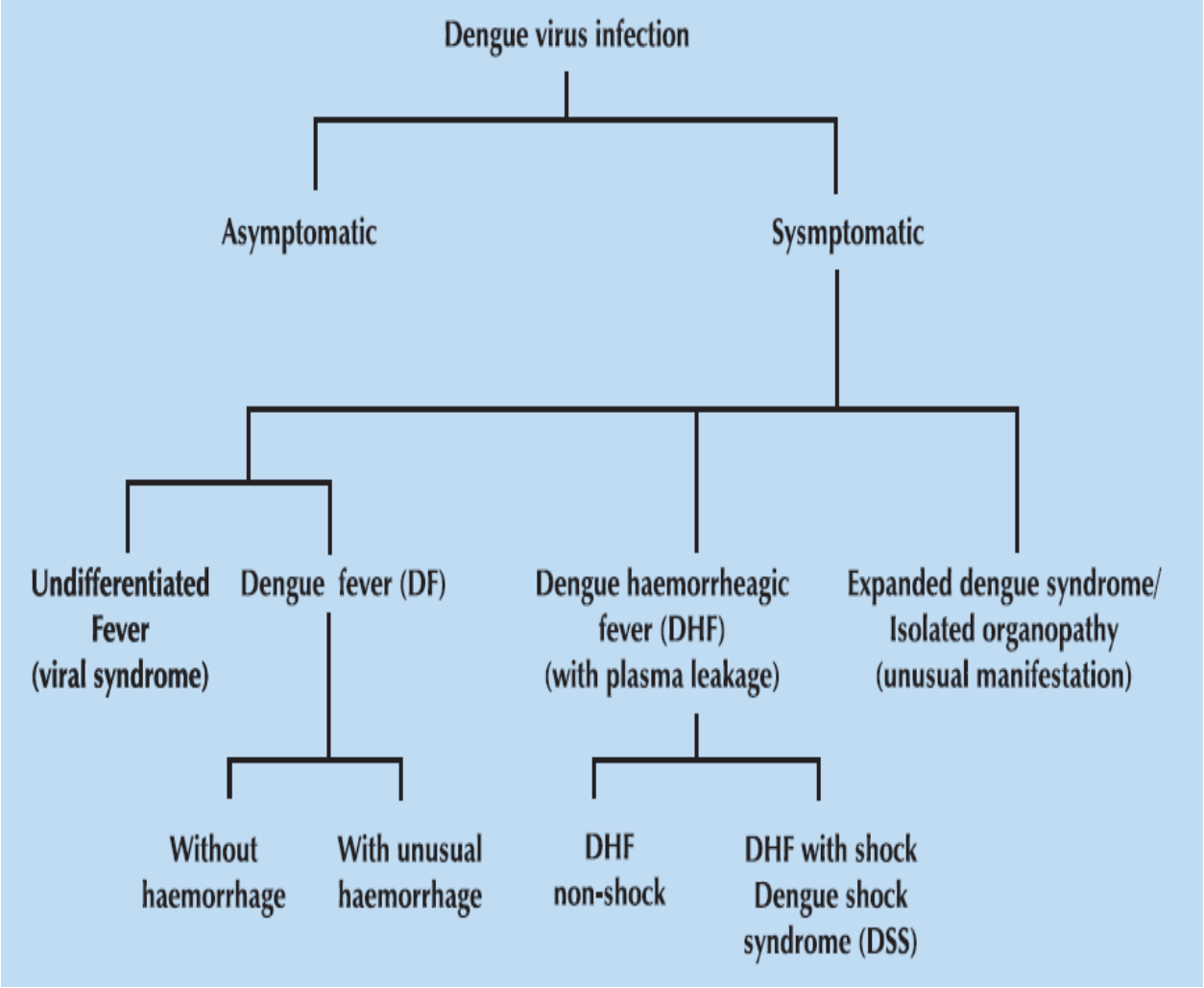


Table No 1 – Clinical Spectrum In Dengue Fever

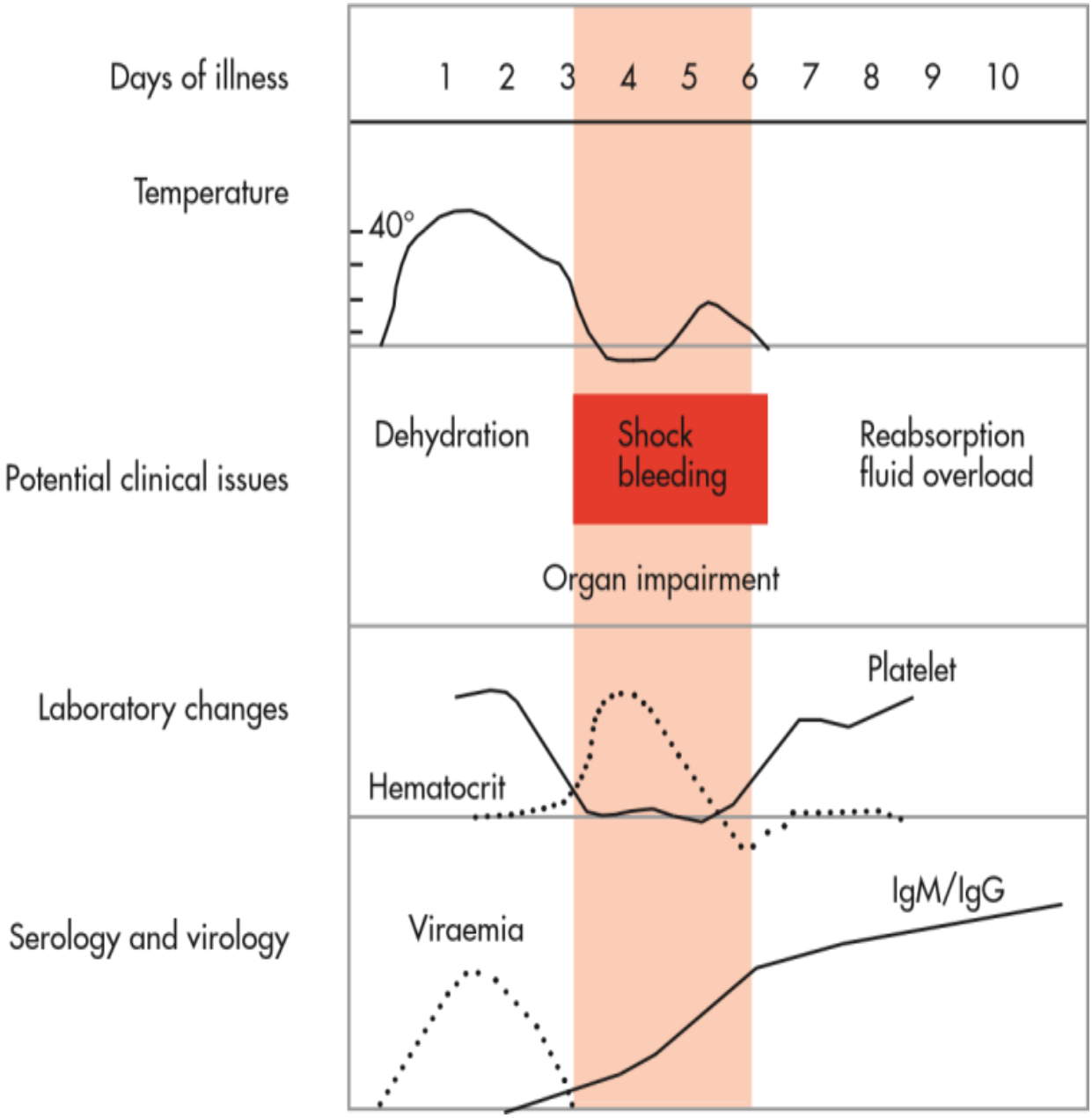


Figure 2 - Course in Dengue Fever

For a disease that is complex in its manifestations, management is relatively simple, inexpensive and very effective in saving lives so long as correct and timely interventions are instituted. The key is early recognition and understanding of the clinical problems during the different phases of the disease, leading to a rational approach to case management and a good clinical outcome. An overview of good and bad clinical practices is given below.

	Good practice	Bad practice
1	Assessment and follow-up of patients with non-severe dengue and careful instruction of warning signs to watch out for	Sending patients with non-severe dengue home with no follow-up and inadequate instructions
2	Administration of paracetamol for high fever if the patient is uncomfortable	Administration of acetylsalicylic acid (aspirin) or ibuprofen
3	Obtaining a haematocrit level before and after fluid boluses	Not knowing when haematocrit levels are taken with respect to fluid therapy
4	Clinical assessment of the haemodynamic status before and after each fluid bolus	No clinical assessment of patient with respect to fluid therapy
5	Interpretation of haematocrit levels in the context of fluid administered and haemodynamic assessment	Interpretation of haematocrit levels independent of clinical status
6	Administration of intravenous fluids for repeated vomiting or a high or rapidly rising haematocrit	Administration of intravenous fluids to any patient with non-severe dengue
7	Use of isotonic intravenous fluids for severe dengue	Use of hypotonic intravenous fluids for severe dengue
8	Giving intravenous fluid volume just sufficient to maintain effective circulation during the period of plasma leakage for severe dengue	Excessive or prolonged intravenous fluid administration for severe dengue
9	Avoiding intramuscular injections in dengue patients	Giving intramuscular injections to dengue patients
10	Intravenous fluid rate and frequency of monitoring and haematocrit measurement adjusted according to the patient's condition	Fixed intravenous fluid rate and unchanged frequency of monitoring and haematocrit measurement during entire hospitalization for severe dengue
11	Close monitoring of blood glucose, i.e. tight glycaemic control	Not monitoring blood glucose, unaware of the hyperglycaemic effect on osmotic diuresis and confounding hypovolaemia
12	Discontinuation or reducing fluid therapy once haemodynamic status stabilizes	Continuation and no review of intravenous fluid therapy once haemodynamic status stabilizes

Table No.2 – Good & Bad Clinical Practices in Dengue

FEBRILE PHASE:-

Patients typically develop high-grade fever suddenly. This acute febrile phase usually lasts 2–7 days and is often accompanied by facial flushing, skin erythema, generalized body ache, myalgia, arthralgia and headache.[28] Some patients may have sore throat, injected pharynx and conjunctival suffusion. Anorexia, nausea and vomiting are common. It can be difficult to distinguish dengue clinically from non-dengue febrile diseases in the early febrile phase. A positive tourniquet test in this phase increases the probability of dengue.[29-30] In addition, these clinical features are indistinguishable between severe and non-severe dengue cases. Therefore monitoring for warning signs and other clinical parameters is crucial to recognizing progression to the critical phase. The warning signs are tabulated as below.

Clinical	Abdominal pain or tenderness Persistent vomiting Clinical fluid accumulation Mucosal bleed Lethargy, restlessness Liver enlargement >2 cm
Laboratory	Increase in HCT concurrent with rapid decrease in platelet count

Table No. 3 – Warning Signs in Dengue

Mild haemorrhagic manifestations like petechiae and mucosal membrane bleeding (e.g. nose and gums) may be seen[29-31]. Massive vaginal bleeding (in women of childbearing age)

and gastrointestinal bleeding may occur during this phase but is not common[31]. The liver is often enlarged and tender after a few days of fever[31]. The earliest abnormality in the full blood count is a progressive decrease in total white cell count, which should alert the physician to a high probability of Dengue.

CRITICAL PHASE:-

Around the time of defervescence, when the temperature drops to 37.5–38^{o}C or less and remains below this level, usually on days 3–7 of illness, an increase in capillary permeability in parallel with increasing haematocrit levels may occur.[32,33] This marks the beginning of the critical phase. The period of clinically significant plasma leakage usually lasts 24–48 hours.

Progressive leucopenia followed by a rapid decrease in platelet count usually precedes plasma leakage. At this point patients without an increase in capillary permeability will improve, while those with increased capillary permeability may become worse as a result of lost plasma volume[29]. The degree of plasma leakage varies. Pleural effusion and ascites may be clinically detectable depending on the degree of plasma leakage and the volume of fluid therapy. Hence chest x-ray and abdominal ultrasound can be useful tools for diagnosis. The degree of increase above the baseline haematocrit often reflects the severity of plasma leakage.

Shock occurs when a critical volume of plasma is lost through leakage. It is often preceded by warning signs. The body temperature may be subnormal when shock occurs. With prolonged shock, the consequent organ hypoperfusion results in progressive organ impairment, metabolic acidosis and disseminated intravascular coagulation. This in turn leads to severe

hemorrhage causing the haematocrit to decrease in severe shock. Instead of the leucopenia usually seen during this phase of dengue, the total white cell count may increase in patients with severe bleeding. In addition, severe organ impairment such as severe hepatitis, encephalitis or myocarditis and/or severe bleeding may also develop without obvious plasma leakage or shock.[34]

Those who improve after defervescence are said to have non-severe dengue. Some patients progress to the critical phase of plasma leakage without defervescence and, in these patients, changes in the full blood count should be used to guide the onset of the critical phase and plasma leakage.

Those who deteriorate will manifest with warning signs. This is called dengue with warning signs. Cases of dengue with warning signs will probably recover with early intravenous rehydration. Some cases will deteriorate to severe dengue.

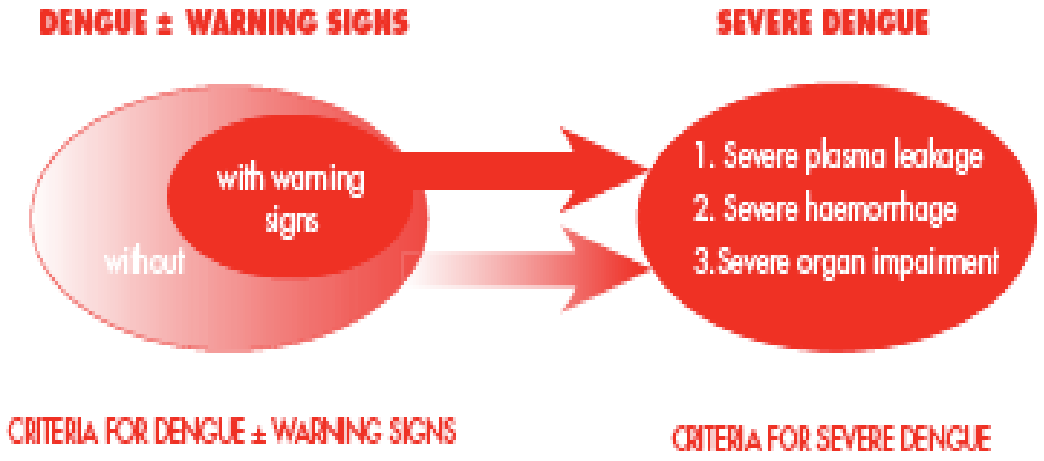


Figure No.3 – Relation between Dengue, Warning Signs & Severe Dengue

RECOVERY PHASE:-

If the patient survives the 24–48 hours of critical phase, a gradual reabsorption of extravascular compartment fluid takes place in the following 48–72 hours. General well-being improves, appetite returns, gastrointestinal symptoms abate, hemodynamic status stabilizes and diuresis ensues. Some patients may have a rash of "isles of white in the sea of red"[35]. Some may experience generalized pruritus. Bradycardia and electrocardiographic changes are common during this stage.

The haematocrit stabilizes or may be lower due to the dilutional effect of reabsorbed fluid. White blood cell count usually starts to rise soon after defervescence but the recovery of platelet count is typically later than that of white blood cell count.

Respiratory distress from massive pleural effusion and ascites will occur at any time if excessive intravenous fluids have been administered. During the critical and/or recovery phases, excessive fluid therapy is associated with pulmonary oedema or congestive heart failure.

The various clinical problems during the different phases of dengue can be summarized as below.

1	**Febrile phase**	Dehydration; high fever may cause neurological disturbances and febrile seizures in young children
2	**Critical phase**	Shock from plasma leakage; severe haemorrhage; organ impairment
3	**Recovery phase**	Hypervolaemia (only if intravenous fluid therapy has been excessive and/or has extended into this period)

Table No.4 - Different phases in Dengue Fever

SEVERE DENGUE:-

Severe dengue is defined by one or more of the following:-

(i) Plasma leakage that may lead to shock (dengue shock) and/or fluid accumulation, with or without respiratory distress, and/or

(ii) Severe bleeding, and/or

(iii) Severe organ impairment.

As dengue vascular permeability progresses, hypovolaemia worsens and results in shock. It usually takes place around defervescence, usually on day 4 or 5 (range days 3–7) of illness, preceded by the warning signs. During the initial stage of shock, the compensatory mechanism

which maintains a normal systolic blood pressure also produces tachycardia and peripheral vasoconstriction with reduced skin perfusion, resulting in cold extremities and delayed capillary refill time. Uniquely, the diastolic pressure rises towards the systolic pressure and the pulse pressure narrows as the peripheral vascular resistance increases. Patients in dengue shock often remain conscious and lucid. The inexperienced physician may measure a normal systolic pressure and misjudge the critical state of the patient. Finally, there is decomposition and both pressures disappear abruptly. Prolonged hypotensive shock and hypoxia may lead to multi-organ failure and an extremely difficult clinical course.

The patient is considered to have shock if the pulse pressure (i.e. the difference between the systolic and diastolic pressures) is $\leq$ 20 mm Hg in children or has signs of poor capillary perfusion (cold extremities, delayed capillary refill, or rapid pulse rate). In adults, the pulse pressure of $\leq$ 20 mm Hg may indicate a more severe shock. Hypotension is usually associated with prolonged shock which is often complicated by major bleeding.

Patients with severe dengue may have coagulation abnormalities, but these are usually not sufficient to cause major bleeding. When major bleeding does occur, it is almost always associated with profound shock since this, in combination with thrombocytopenia, hypoxia and acidosis, can lead to multiple organ failure and advanced disseminated intravascular coagulation. Massive bleeding may occur without prolonged shock in instances when acetylsalicylic acid (aspirin), ibuprofen or corticosteroids have been taken.

Parameters	Stable circulation	Compensated shock	Hypotensive shock
Hypotensive shock	Clear and lucid	Clear and lucid (shock can be missed if you do not touch the patient)	Change of mental state (restless, combative)
Capillary refill time	Brisk (<2 sec)	Prolonged (>2 sec)	Very prolonged, mottled skin
Extremities	Warm and pink extremities	Cool peripheries	Cold, clammy extremities
Peripheral pulse volume	Good volume	Weak and thready	Feeble or absent
Heart rate	Normal for age	Tachycardia	Severe tachycardia with bradycardia in late shock
Blood pressure	Normal for age Normal pulse pressure for age	Normal systolic pressure but rising diastolic pressure Narrowing pulse pressure Postural hypotension	Narrowed pulse pressure (<20 mmHg) Hypotension (see definition below) Unrecordable blood pressure
Respiratory rate	Normal for age	Tachypnoea	Metabolic acidosis hyperpnoea/ Kussmaul's breathing

Table No.5 –Haemodynamic changes in Dengue

Unusual manifestations, including acute liver failure and encephalopathy, may be present, even in the absence of severe plasma leakage or shock. Cardiomyopathy and encephalitis are also reported in a few dengue cases. However, most deaths from dengue occur in patients with profound shock, particularly if the situation is complicated by fluid overload.

Severe dengue should be considered if the patient is from an area of dengue risk presenting with fever of 2–7 days plus any of the following features:

- There is evidence of plasma leakage, such as:
  - high or progressively rising haematocrit;
  - pleural effusions or ascites;
  - circulatory compromise or shock (tachycardia, cold and clammy extremities, capillary refill time greater than three seconds, weak or undetectable pulse, narrow pulse pressure or, in late shock, unrecordable blood pressure).
- There is significant bleeding.
- There is an altered level of consciousness (lethargy or restlessness, coma, convulsions).
- There is severe gastrointestinal involvement (persistent vomiting, increasing or intense abdominal pain, jaundice).[36]

AETIOLOGY AND PATHOGENESIS:-

All four dengue serotypes are capable of causing dengue fever or DHF, depending on the immune status and probably age of the host, as DHF occurs almost exclusively in children under the age of 16 years and is associated with secondary dengue infection. A strong association between DHF and secondary dengue infection has led to Halstead's proposed concept of two sequential infections. Based on his in vitro and monkey studies, an antibody dependent immune enhancement theory has been hypothesized by Halstead[37]. It is suggested that during the second infection with a heterotypic dengue virus which differs from the first one, pre-existing antibody from the first infection fails to neutralize and may instead enhance viral uptake and replication in the mononuclear phagocytes. Such infected cells may then become the target of an immune elimination mechanism which can trigger the production of mediators of complement and the clotting cascade and eventually produce DHF [37.]

Studies over the last 40 years have demonstrated transmission of all four dengue serotypes, with dengue type 2 as the predominating serotype up to 1990.[38,39] The studies and experience in Thailand, as well as in Cuba, confirmed the suggestion that the interval between the two dengue infections and the sequences of infecting dengue serotypes, i.e. secondary infection with DENV2 following DENV1 infection may be important factors in determining the occurrence and severity of DHF.[37,40] The interval between the two infections was first suggested to be 1-5 years following Cuban experience with the first outbreak of DHF with DENV2 in 1981 which followed the outbreak of dengue fever with DENV1 in 1977. The second outbreak of DHF in Santiago, Cuba in 1977 with DENV2 after a period of apparent elimination of vectors and dengue virus for 16 years led to two important observations:

(1) Immune enhancement could occur after a long duration of 20 years.

(2) Primary DENV2 infection in children under 16 years did not cause DHF.[41]

A study by Vaughn et al revealed that increased dengue disease severity (dengue vs DHF) correlated with high viremia titre, secondary dengue infection and DENV2 serotype.[42] The most recent study on the role of T cells in the pathogenesis of DHF has described a phenomenon of original antigenic sin.[46] The group has found a paradoxical T cell response in that many of the T cells had a relatively low affinity for the current infecting DENV serotype but showed higher affinity for serotypes which had been encountered before. This phenomenon resulted in delayed elimination of the secondary infecting serotype, allowing further proliferation and high viral load.[43]

Other theories involving a virulent strain of dengue virus and genetic differences in the hosts have been proposed.[44-46] The association of the introduction of a specific (south-east Asian) genotype of DENV2 and the appearance of DHF in America suggested that a certain genotype has potential to cause severe dengue (DHF).[47] The finding that the same DENV 2 genotype may cause dengue fever of DHF in Thailand suggested that both virus genotype and secondary infection are important contributing factors in the pathogenesis of DHF.[48]

PATHOPHYSIOLOGY:

The pathophysiological hallmarks of DHF are plasma leakage and abnormal haemostasis. Evidence supporting plasma leakage includes a rapid rise in hematocrit, pleural effusion and ascites, hypoproteinemia and reduced plasma volume. A significant loss of plasma leads to hypovolemic shock and death. The acute onset of shock and the rapid and often dramatic clinical

recovery when the patient is treated properly, together with the absence of inflammatory vascular lesions, suggest a transient functional increase in vascular permeability that results in plasma leakage.

A disorder in haemostasis involves all major components.[49]

(1) Vascular changes including capillary fragility changes that lead to a positive tourniquet test and easy bruisability;

(2) Thrombopathy with impaired platelet function and moderate to severe thrombocytopenia;

(3) Coagulopathy, acute-type disseminated intravascular clotting (DIC) is documented in severe cases, often with prolonged shock and responsible for the severe bleeding. Evidence for DIC includes hypofibrinogenemia and the presence of fibrinogen degradation products (FDP) and D-dimer. The clotting factors II, V, VIII, IX and XII are low.

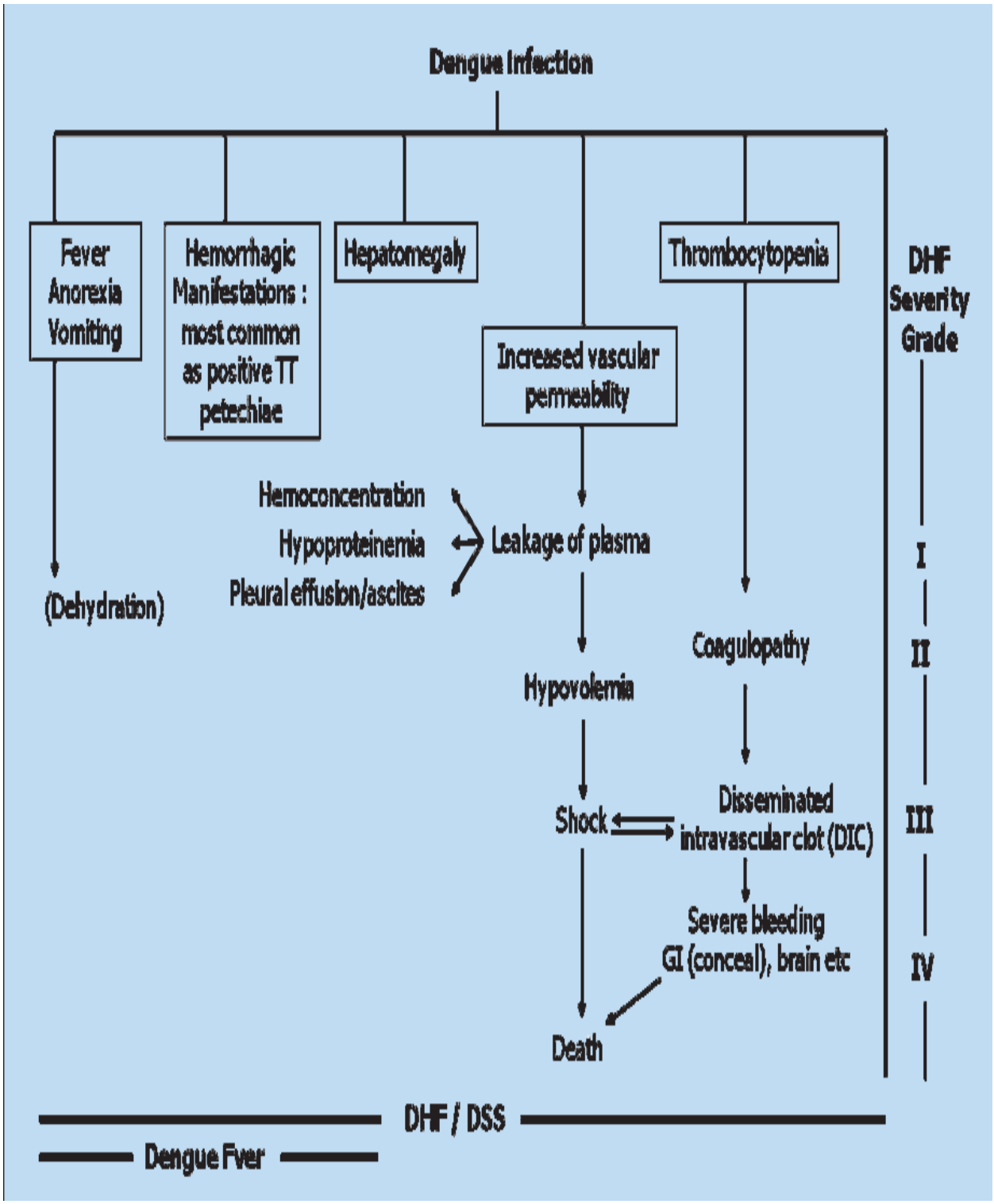


Table No.6 – Manifestations / Pathophysiological changes in DHF

(4) Bone marrow changes include depression of all marrow elements, with maturation arrest of megakaryocytes during the early phase of the illness, which is readily reversed when the fever subsides and during the stage of shock.

Kidney studies in non-fatal cases show changes similar to glomerulonephritis but these are usually mild and transient.[50,51]

Postmortem studies show that serous effusions with high protein content, mostly found in pleural and peritoneal cavities, and widespread petechial haemorrhages in many organs are constant findings.[51] The sites of common hemorrhage include gastrointenstinal tract, skin, heart, pleura and lungs, soft tissue, periadrenal tissue.[51]

HISTOLOGICAL CHANGES:

Significant changes are found in major organ systems:

- Vascular changes include vasodilatation, congestion, perivascular haemorrhage and oedema of arterial walls
- Proliferation of reticuloendothelial cells with accelerated phagocytic activity is observed frequently
- The lymphoid tissues show increasing activity of the B lymphocyte system with active proliferation of plasma cells and lymphoblastoid cells
- In the liver there is focal necrosis of the hepatic and kupffer cells, with formation of councilman-like bodies.[50,51]

Dengue virus antigen is found predominantly in cells of the spleen, thymus and lymph nodes, in kupffer cells and in the sinusoidal lining cells of liver and alveolar lining cells of the lung.

The pathogenetic mechanism of DHF is presumed to be immunological, involving both humoral and cell-mediated immune modulation. A constant finding in DHF is activation of the complement system with profound depression of C3 and C5 levels.[50] Immune complexes have been described in DHF cases associated with secondary infection, and they may contribute to complement activation. The C3a and C5a anaphylatoxins are released and their association with the time of leakage, shock and disease severity has been demonstrated.[52] They are the most likely vascular permeability increasing mediators.

A most recent study in Thailand on the role of non-structural protein NS1 and complement in the pathogenesis of plasma leakage revealed that complement activation mediated by NS1 led to local and systemic generation of anaphylatoxin C5a and the terminal SC5b-9 complex. The plasma levels of NS1 and SC5b-9 complexes correlated with disease severity and they were present in the pleural fluid from patients with dengue shock syndrome (DSS). This is a novel finding that implicates the major role of NS1 as an important trigger for complete complement activation and the role of the terminal SC5b-9 complex in the pathogenesis of plasma leakage.[53] Notably, it was also shown in this study and by Libraty et al. that high circulating levels of NS1 that can be detected early in dengue illness are correlated with the development of DHF.[54]

CLINICAL FEATURES OF DENGUE FEVER:

The clinical features of dengue fever are age dependent. Infants and children infected with dengue virus for the first time (i.e. primary dengue infection) usually develop a simple fever or undifferentiated febrile illness; dengue fever is most common in adults and older children and may be benign or may be a classical incapacitating disease (classical dengue fever) with severe muscle, joint and bone pain (break bone fever)[53].

Typically, after an incubation period of 5-8 days following an infective mosquito bite, the disease in adults begins with a sudden onset of fever with severe headache, and any of the following: chills, pain behind the eyes – particularly on eye movement or eye pressure-photophobia, backache, and pain in the muscles, bone and joints of the extremities.

The temperature is usually high (39-40° C); the fever may be sustained for 5-6 days and may occasionally have a biphasic course. As the disease progresses, the patient becomes anorexic and may show marked weakness and prostration. Other common symptoms include sore throat, altered taste sensation, colicky pain and abdominal tenderness, constipation, dragging pain in the inguinal region and general depression. A relative bradycardia is common during the febrile phase. Symptoms vary in severity and usually persist for several days.

Several types of skin rash have been described. Initially, diffuse flushing, mottling or fleeting pinpoint eruptions may be observed on the face, neck and chest. These are transient in nature. A second type of skin rash is a conspicuous rash that may be maculopapular or scarlatiniform and appears on approximately the third or fourth day. This rash starts on the chest and trunk and spreads to the extremities and face and may be accompanied by itching and dermal hyperasthesia.

There is generalized enlargement of the lymph nodes but the liver and spleen are not usually palpable. A positive tourniquet test and petechiae on extremities are not uncommon.

Towards the end of the febrile period or immediately after defervescence, the generalized rash fades and localized clusters of petechiae may appear over the dorsum of the feet and on the legs, hands and arms. This confluent petechial rash is characterized by a scattered pale round area of normal skin.

Convalescence may be rapid and uneventful but is often prolonged in adults, sometimes taking several weeks, and may be accompanied by pronounced asthenia and depression. Bradycardia is common during this period. Loss of hair has been reported during convalescence.

Haemorrhagic complications such as epistaxis, gum bleeding, gastrointestinal Haemorrhage, haematuria and hypermenorrhoea have been reported in many epidemics of dengue fever and on rare occasions severe bleeding has caused deaths in some epidemics.[55,56]

Dengue fever with encephalitic signs but with normal cerebrospinal fluid has been reported in some epidemics[57]. Reye's syndrome associated with dengue infection is not uncommon.[57] Recently there has been an increase in reported cases of dengue encephalitis which was confirmed either by demonstration of virus, antigen or anti-dengue IgM antibody in cerebrospinal fluid.[58]

The most significant laboratory finding during the acute illness is leucopenia, which is usually noted 2-3 days after onset and lasts throughout the febrile phase. Mild to moderate thrombocytopenia is occasionally observed.[59]

CLINICAL FEATURES OF DHF:

DHF is a severe form of dengue infection that is accompanied by haemorrhagic diathesis and a tendency to develop fatal shock (Dengue shock syndrome: DSS) as a consequence of plasma leakage selectively into pleural and peritoneal cavities. The clinical course could be divided into febrile, critical and convalescence phases.

Typically, the disease begins with the febrile phase with an abrupt onset of high fever, accompanied by facial flush and headache. Some patients with an injected pharynx may complain of sore throat but rarely have rhinitis or cough. Anorexia, vomiting and abdominal pain are common. During the first few days of the febrile phase, which usually lasts for 2-7 days, the illness resembles dengue fever in many respects but a maculopapular rash and myalgia are less common. Occasionally the body temperature may be as high as $40\text{-}41^0$ C and febrile convulsions may occur.

A haemorrhagic diathesis commonly presents in the febrile phase as scattered petechiae on extremities, axilla, trunk and face. A positive tourniquet test and/or tendency to bruise at venepuncture sites are invariably present. Bleeding from the nose, gums and gastrointestinal tract are less common. Haematuria is extremely rare.

The liver is often enlarged, soft and tender but jaundice is not observed. Splenomegaly is rarely observed in small infants. Generalized lymphadenopathy is noted in about half of the cases.

The Critical phase, which is the period of plasma leakage, is reached near or by the time the fever subsides. Accompanying or shortly after, a rapid drop in the temperature there are

varying degrees of circulatory disturbance. The patient is often sweating and restless and has cool extremities. In less severe cases (Grades I&II) the changes in vital signs are minimal and transient; the patient recovers spontaneously or after a brief period of therapy. In more severe cases shock ensues. The skin is cold and clammy and the pulse pressure becomes narrow (≤ 20 mmHg) with a slight elevation of diastolic level, e.g. 100/80 mmHg. The course of shock is brief and stormy. If no treatment is given, the patient deteriorates rapidly into the stage of profound shock with an imperceptible pulse and blood pressure and dies within 12-24 h. prolonged shock is often complicated by metabolic acidosis and severe bleeding, which indicates a poor prognosis. However, if the patient is properly treated before irreversible shock has developed, rapid, often dramatic recovery is the rule. Infrequently, encephalitic signs associated with metabolic or electrolyte disturbances, intracranial haemorrhage or hepatic failure (a form of Reye's-like syndrome) occur and give rise to a more complicated course and grave prognosis.[57] The critical phase usually lasts 24-48 h.

The convalescence phase is usually short and uneventful. Sinus bradycardia is common. A characteristic confluent petechial rash with scattered round areas of pale skin, as described in dengue fever, which is frequently observed on the lower extremities, is found in about 20-30%. The course of the illness is about 7-10 days in most uncomplicated cases.

A normal white blood count or leucopenia is common and neutrophils may predominate initially. Towards the end of the febrile phase there is a reduction in the number of total leucocytes and neutrophils shortly before or simultaneously with a relative increase in lymphocytes with the presence of atypical lymphocytes. The leucopenia usually reaches a nadir shortly before the temperature and platelets drop. This observation is valuable in predicting the end of the febrile period and the beginning of the critical phase. Thrombocytopenia and

haemoconcentration occur simultaneously with the haematocrit rise (≥20%) and both changes occur before the subsidence of fever and before onset of shock. Clotting abnormalities are usually found, especially in severe cases with shock. Other changes include hypoproteinemia, hypoalbuminemia, hyponatremia and mildly elevated alanine aminotransferase/aspartate aminotransferase levels.[60]

Disease severity is arbitrarily classified as 'non-shock' cases (grades I and II – grade II is more severe than grade I with the presence of spontaneous haemorrhage) and 'shock' cases (grades III and IV-the latter is a profound shock with imperceptible pulse and/or blood pressure).[50]

DF/ DHF	Grade	Signs and Symptoms	Laboratory
DF		Fever with two of the following: • Headache. • Retro-orbital pain. • Myalgia. • Arthtralgia/bone pain. • Rash. • Haemorrhagic manifestations. • **No evidence of plasma leakage**.	• Leucopenia (wbc ≤5000 cells/mm³). • Thrombocytopenia (Platelet count <150 000 cells/mm³). • Rising haematocrit (5% – 10%). • No evidence of plasma loss.
DHF	I	Fever and haemorrhagic manifestation (positive tourniquet test) and **evidence of plasma leakage**	Thrombocytopenia <100 000 cells/ mm³; HCT rise ≥20%
DHF	II	As in Grade **I plus** spontaneous bleeding.	Thrombocytopenia <100 000 cells/mm³; HCT rise ≥20%.
DHF#	III	As in Grade **I or II plus** circulatory failure (weak pulse, narrow pulse pressure (≤20 mmHg), hypotension, restlessness).	Thrombocytopenia <100 000 cells/mm³; HCT rise ≥20%.
DHF#	IV	As in Grade **III** plus profound shock with undetectable BP and pulse	Thrombocytopenia < 100 000 cells/mm³; HCT rise ≥20%.

Table No. 7 - Staging of Dengue Haemorrhagic Fever

System	Unusual or atypical manifestations
Neurological	Febrile seizures in young children. Encephalopathy. Encephalitis/aseptic meningitis. Intracranial haemorrhages/thrombosis. Subdural effusions. Mononeuropathies/polyneuropathies/Guillane-Barre Syndrome. Transverse myelitis.
Gastrointestinal/hepatic	Hepatitis/fulminant hepatic failure. Acalculous cholecystitis. Acute pancreatitis. Hyperplasia of Peyer's patches. Acute parotitis.
Renal	Acute renal failure. Hemolytic uremic syndrome.
Cardiac	Conduction abnormalities. Myocarditis. Pericarditis.
Respiratory	Acute respiratory distress syndrome. Pulmonary haemorrhage.
Musculoskeletal	Myositis with raised creatine phosphokinase (CPK). Rhabdomyolysis.
Lymphoreticular/bone marrow	Infection associated haemophagocytic syndrome. IAHS or Haemophagocytic lymphohistiocytosis (HLH), idiopathic thrombocytopenic purura (ITP). Spontaneous splenic rupture. Lymph node infarction.
Eye	Macular haemorrhage. Impaired visual acuity. Optic neuritis.
Others	Post-infectious fatigue syndrome, depression, hallucinations, psychosis, alopecia.

Table No 8 – Unusual / Atypical Manifestations in Dengue Fever

DIAGNOSIS:-

The clinical features of DHF are rather stereotyped; thus it is possible to make a correct clinical diagnosis based on the major characteristic manifestations as described. The world Health organization established criteria for clinical diagnosis[50,60]. High continuous fever for 2-7 days; a haemorrhagic diathesis; hepatomegaly and shock; together with two laboratory changes: thrombocytopenia (≤100 000/mm³) with concurrent haemoconcentration (haematocrit elevation of 20% or more). The time course relationship between the drop in platelet count and a rapid rise in haematocrit appears to be unique in DHF. These changes, which represent the major pathophysiological hallmarks of DHF, i.e. abnormal haemostasis and plasma leakage, clearly distinguish DHF from dengue fever and other diseases. Evidences of plasma leakage could be confirmed by chest X-ray at the right lateral decubitus position or by ultrasound to detect pleural effusion/ascites. A normal or low erythrocyte sedimentation rate (ESR) observed in DHF and DSS helps in differentiating DSS from septic shock[61.]

Diagnosis of dengue fever and dengue haemorrhagic fever[k]

Dengue fever

Probable diagnosis:

Acute febrile illness with two or more of the following[l]:

- headache,
- retro-orbital pain,
- myalgia,
- arthralgia/bone pain,
- rash,
- haemorrhagic manifestations,
- leucopenia (wbc ≤5000 cells/mm³),
- thrombocytopenia (platelet count <150 000 cells/mm³),
- rising haematocrit (5 – 10%);

and at least one of following:

- supportive serology on single serum sample: titre ≥1280 with haemagglutination inhibition test, comparable IgG titre with enzyme-linked immunosorbent assay, or tasting positive in IgM antibody test, and
- occurrence at the same location and time as confirmed cases of dengue fever.

Confirmed diagnosis:

Probable case with at least one of the following:

- isolation of dengue virus from serum, CSF or autopsy samples.
- fourfold or greater increase in serum IgG (by haemagglutination inhibition test) or increase in IgM antibody specific to dengue virus.
- detection of dengue virus or antigen in tissue, serum or cerebrospinal fluid by immunohistochemistry, immunofluorescence or enzyme-linked immunosorbent assay.
- detection of dengue virus genomic sequences by reverse transcription-polymerase chain reaction.

Dengue haemorrhagic fever

All of following[m]:

- acute onset of fever of two to seven days duration.
- haemorrhagic manifestations, shown by any of the following: positive tourniquet test, petechiae, ecchymoses or purpura, or bleeding from mucosa, gastrointestinal tract, injection sites, or other locations.
- platelet count ≤100 000 cells/mm³
- objective evidence of plasma leakage[n] due to increased vascular permeability shown by any of the following:
  - Rising haematocrit/haemoconcentration ≥20% from baseline or decrease in convalescence, or evidence of plasma leakage such as pleural effusion, ascites or hypoproteinaemia/ albuminaemia.[39]

Dengue shock syndrome

Criteria for dengue haemorrhagic fever as above with signs of shock including:

- tachycardia, cool extremities, delayed capillary refill, weak pulse, lethargy or restlessness, which may be a sign of reduced brain perfusion.
- pulse pressure ≤20 mmHg with increased diastolic pressure, e.g. 100/80 mmHg.
- hypotension by age, defined as systolic pressure <80 mmHg for those aged <5 years or 80 to 90 mmHg for older children and adults.

Table No – 9 Criteria for Diagnosis of Dengue fever, DHF & DSS

VIROLOGICAL DIAGNOSIS:

Etiological diagnosis can be confirmed by Serological testing and virus detection by isolation or molecular technique from the blood during the early febrile phase. Antibodies to dengue virus antigens increase rapidly in patients with secondary dengue infection. A diagnostic (four-fold) increase in dengue antibody by the haemagglutination inhibition test can usually be demonstrated from paired sera obtained early in the febrile phase or on admission, and 3-5 days later. A third specimen 2-3 weeks after onset is, however required to confirm diagnosis of primary dengue infection.[53]

Serological diagnosis by detection of anti-dengue IgM and IgG by enzyme-linked immunosorbent assay (ELISA) is now widely used to document primary and secondary infection. IgM antibody capture (MAC)-ELISA is a relatively new test. It is specific in distinguishing dengue from other flavivirus infection and has the advantage over the haemagglutination test in that a definite diagnosis can be made from an acute blood specimen alone, with a sensitivity of about 78%; when convalescent sera are tested the sensitivity is >97%.[62]Recently an ELISA assay for dengue NS1 antigen detection has been developed and commercial test kits are now available.

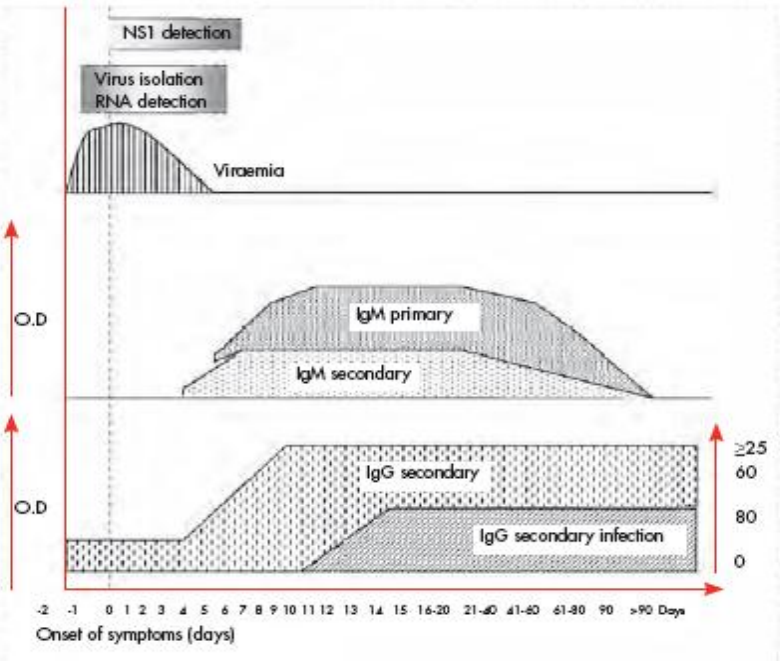


Figure No –4 Relation between Viremia, Detection of Antigen & Formation of Antibodies

MANAGEMENT

The management of DHF is entirely symptomatic and supportive and is principally aimed towards replacement of plasma loss during the period of active leakage of about 24-48 h. Prognosis depends on early clinical recognition and frequent monitoring for a drop in platelet count and rise in haematocrit. Early volume replacement when the haematocrit rises sharply (≥20%) as plasma leaks out can prevent shock and/or modify severity.

The management of DHF during the febrile phase is similar to that of dengue fever. Usually DHF cannot be distinguished from dengue fever until platelets drops, with a concurrent rise in haematocrit as plasma leakage starts by the end of the febrile phase. Therefore patients or care takers should be advised to observe for the warning signs of circulatory disturbance and bring the patients to the hospital for proper treatment. The Warning signs include:

- Refusal of food or drinking water
- Become drowsy or restless
- Protracted vomiting
- Acute abdominal pain
- Oliguria /thirst
- Worsening of general condition when temperature drops
- Any bleeding.

Antipyretics may be needed to control high fever; aspirin and ibuprofen must not be used (to avoid gastric irritation and severe bleeding and as a precaution to prevent Reye's syndrome

associated with dengue infection). Oral fluid and electrolyte therapy are recommended for patients who have anorexia and vomiting.

The critical period when plasma leakage occurs and shock may develop is at the transition from the febrile to the afebrile phase, which is varied according to the duration of febrile phase (2-7 days). Shock could develop as early as on the third day of illness in a patient whose febrile phase is two days. A drop in the platelet count to 1,00,000 cells/mm^3 or less usually precedes a rise in the haematocrit. A rise in haematocrit of 20% or more (e.g. from baseline 35% to 42% or more) indicates significant plasma loss and intravenous fluid therapy is indicated. In mild to moderately severe cases (grades I and II) fluid therapy can be given for a period of 12-24 h at an out-patient clinic where there are facilities to monitor vital signs and haematocrit. Patients who continue to have high haematocrit or present with any warning signs should be admitted to the hospital.

As there is active and continuous leakage of plasma into the pleural and peritoneal cavities during the critical period, judicious volume replacement is mandatory.

Guiding principles for volume replacement in DHF:

- Intravenous fluid replacement is indicated when plasma leakage occurs, as indicated by rising haematocrit with concurrent thrombocytopenia.
- The type of fluid used should be isotonic solution that has an electrolyte composition similar to plasma, e.g. 5% dextrose in normal saline solution (DNS) or Ringer's lactate solution. In case of massive leakage colloidal solution, e. g. Dextran 40 or other plasma expander may be needed

- The volume should be just sufficient to maintain effective circulation, which could be guided by vital signs, urine output and haematocrit level. The total volume needed during the period of leakage is approximately maintenance plus 5-6% deficit (similar to mild or moderate dehydration)
- The rate of the fluid infusion must be adjusted according to the rate and extent of plasma leakage, which is more rapid during the 6-12 hours around the time temperature drops.
- The need for intravenous replacement usually lasts for no longer than 48h, the time by which plasma leakage stops. Fluid replacement must be stopped when the haematocrit and vital signs become stable and return to normal and a diuresis ensues.

When shock has developed, satisfactory results have been obtained with the following regimen.

1. Immediately and rapidly correct hypovolemia from plasma loss with isotonic salt solution at the rate of 10-20 ml/kg per hour until improvement in vital signs in apparent. In cases of profound shock with no blood pressure / or pulse perceptible, a bolus of 10 ml/kg (1-2 liters bolus) should be given.
2. Continue to replace further plasma losses to maintain effective circulation for a period of 24-48 h. The rate of infusion should be reduced after initial resuscitation and adjusted according to rate of plasma leakage.
3. Correct metabolic and electrolyte disturbance e.g. metabolic acidosis, hypoglycemia, hyponatremia.
4. Blood transfusion is indicated in cases with significant clinical bleeding, most often with haematemesis and malaena. Fresh whole blood is preferable and should be given only in volume to achieve a normal red cell concentration. Blood components, e.g. concentrated platelets are rarely needed.

Apart from the fact that SGOT levels were raised in all patients, nearly 85% patients had SGOT levels more than twice the upper limit of normal. Although most patients presented after 3-4 days of fever, in those who came early, there was a rise of SGOT levels on day two and three itself. The presence of vomiting in 80% patients from day one may indicate hepatic dysfunction early on. The mechanism of liver involvement in dengue infection is not clear and may involve a direct injury to liver cells or an immunological response. Ascites in dengue has been attributed to plasma leakage. However there is one study which attributes portal hypertension in addition to plasma leakage for development of ascites. Leucopenia has been reported in dengue and has been attributed to transient marrow suppression by the virus.

MATERIALS & METHODS

MATERIALS & METHODS

SOURCE OF DATA:

The Study group was selected from inpatients of R L Jalappa Hospital attached to Sri Devaraj Urs Medical College, Tamaka, Kolar. It was a prospective study done over one year 4 months duration between April 2012 to August 2013. It included 107 subjects who presented to the Hospital in the above said period. The subjects were enrolled after taking informed consent for the study.

The Criteria of Inclusion & Exclusion for the study are mentioned below:

INCLUSION CRITERIA:

1. Patients with history of Fever & Tested positive by Lab Tests.(Dengue – NS1Ag, IgM &Ig G)
2. Age > 18yrs.

EXCLUSION CRITERIA:

1. Patients with mixed infections- such as those tested positive for malaria, leptospirosis along with dengue.

2. Those with bleeding diathesis due to other causes such as DIC, ITP, and hemophilia were excluded from the study.

METHOD OF COLLECTION OF DATA:

1. Patients admitted to hospital with complaints of fever & tested positive for Dengue serological Tests – NS1Ag, IgM & IgG were included in the study after they met the Inclusion criteria.
2. Informed Consent was obtained from the patients prior to their enrolment.
3. Thorough history was taken & detailed clinical Examination was performed on all the patients.
4. The results of the clinical findings were recorded in a proforma sheet (ANNEXURE 1) & the patients were followed during their hospital Stay.
5. Investigations performed on all patients included complete Blood Counts (Hb, PCV, TLC, DLC, PBS), chest X ray, electrocardiogram, ultrasonography (USG), liver Function Tests (LFT), coagulation Profile was done on patients in whom it was considered significant based on the clinical findings.
6. Serial haematological parameters performed during Hospital stay were noted.
7. The results obtained from the study were analyzed according to symptoms, signs, lab investigations (haematological parameters) & any association between the clinical spectrum & laboratory investigations was analysed.
8. The results obtained were analysed through statistical analysis & appropriate tests of significance using SPSS Software.

STATISTICAL ANALYSIS:

Data was entered into Microsoft excel after coding and analyzed using SPSS 11 software. Proportions and Frequencies were computed for qualitative data. Correlation was computed quantitative data. Chi-square was the test of significance for categorical data. $p < 0.05$ is considered as statistically significant.

RESULTS

OBSERVATIONS & RESULTS

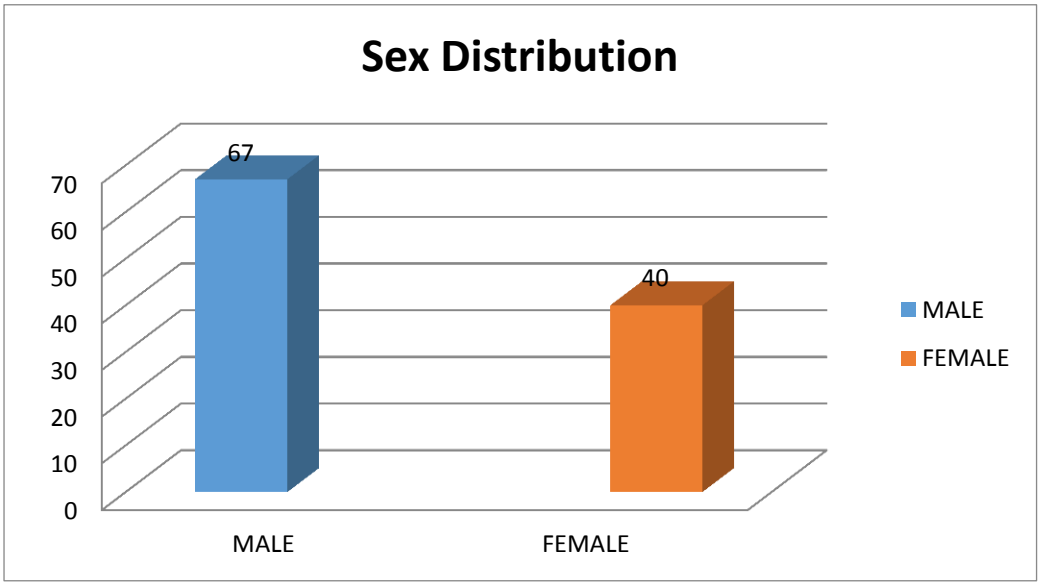
The study was done on 107 patients who were tested positive for Dengue serological tests. Thorough history & detailed clinical examination was performed on all patients. The results obtained in the study are tabulated in the form of Tables, graphs & charts as mentioned below.

Sex Distribution

Table No.10 – Sex Distribution

SEX	FREQUENCY	PERCENTAGE
MALE	67	62.6
FEMALE	40	37.4

Graph No 1 – Sex Distribution

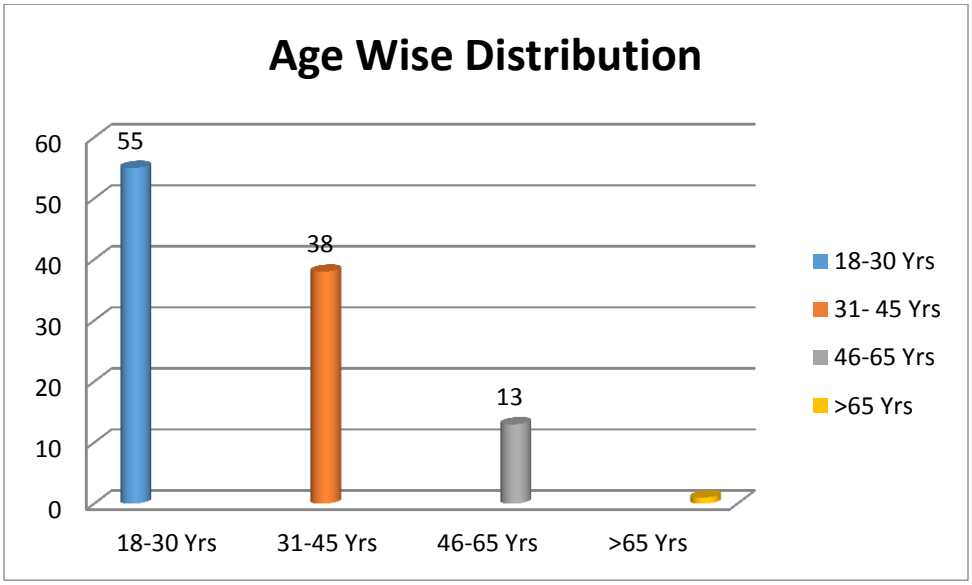


Age Wise Distribution

Table No 11 – Age Wise Distribution

AGE RANGE	FREQUENCY	PERCENTAGE
18 - 30 Yrs	55	51.4
31 – 45 Yrs	38	35.6
46 – 65 Yrs	13	12.1
>65 Yrs	1	0.9

Graph No 2 – Age Wise Distribution

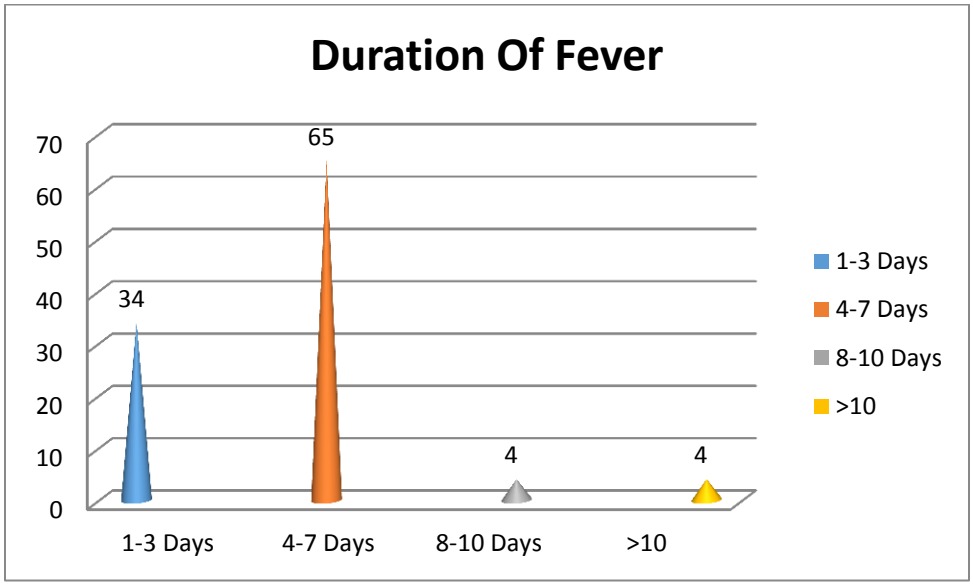


Duration of Fever

Table No 12 - Duration of Fever

DURATION	FREQUENCY	PERCENTAGE
1-3 Days	34	31.8
4-7 Days	65	60.8
8- 10 Days	4	3.7
>10 Days	4	3.7

Graph No 3 – Age Wise Distribution

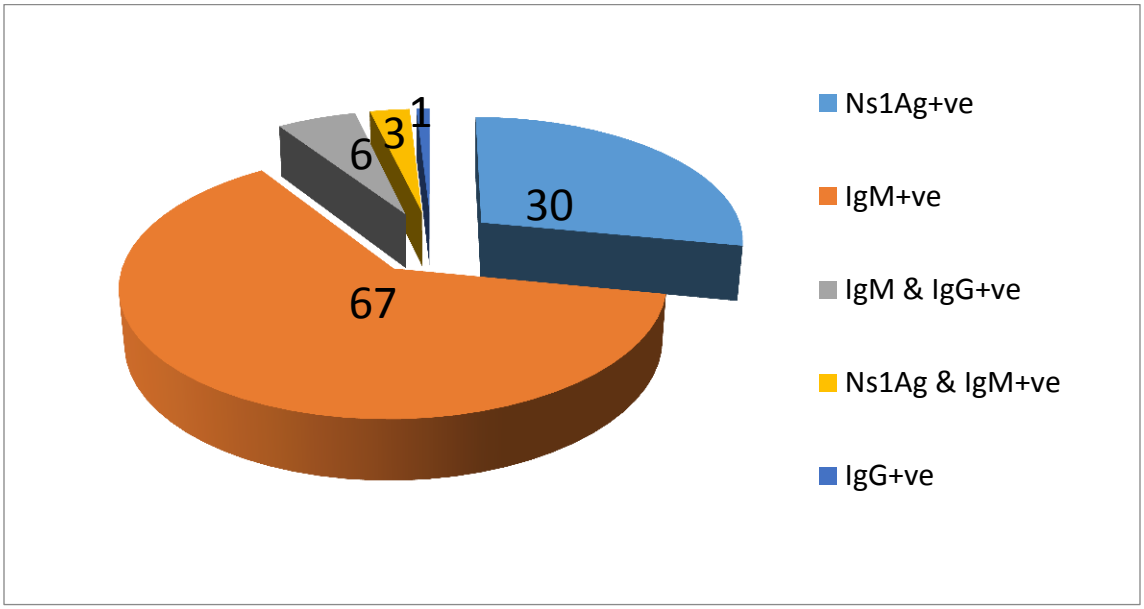


Serology Results

Table No 13 - Serology Results

SEROLOGY	FREQUENCY	PERCENTAGE
NS1Ag +ve	30	28.1
IgM+ve	67	62.6
NS1Ag+ve & IgM +ve	3	2.8
IgM+ve & IgG+ve	6	5.6
IgG+ve	1	0.9

Graph No 4 - Serology Results

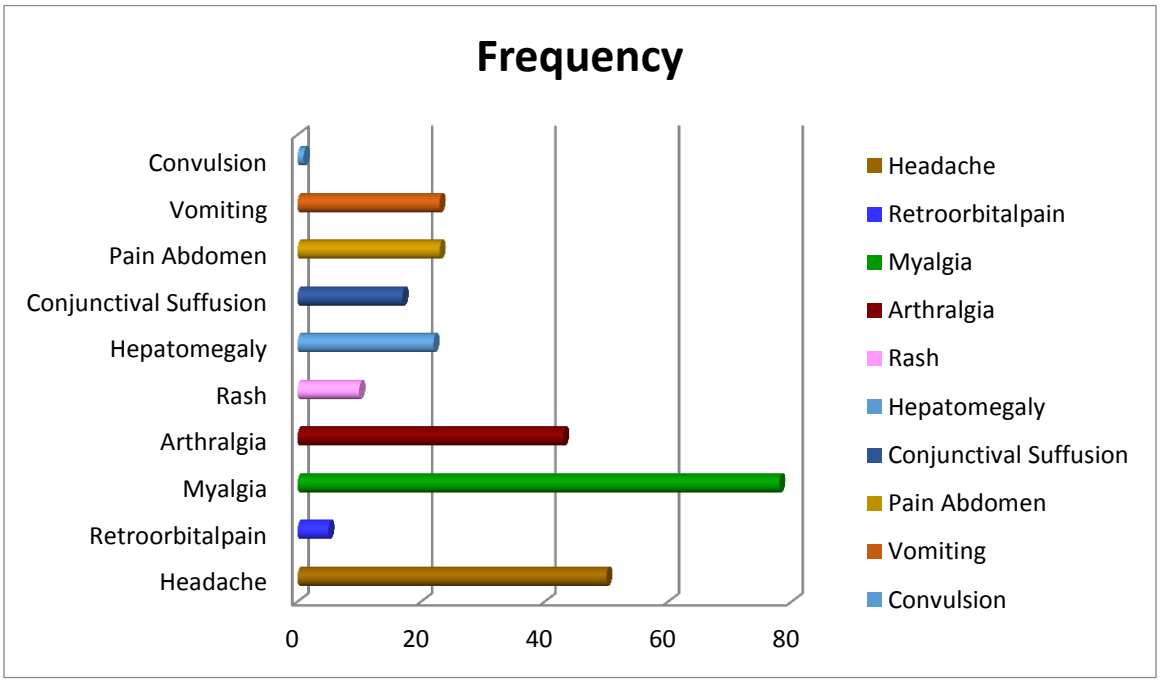


Symptoms in Study Population

Table No.14 – Symptoms in study population

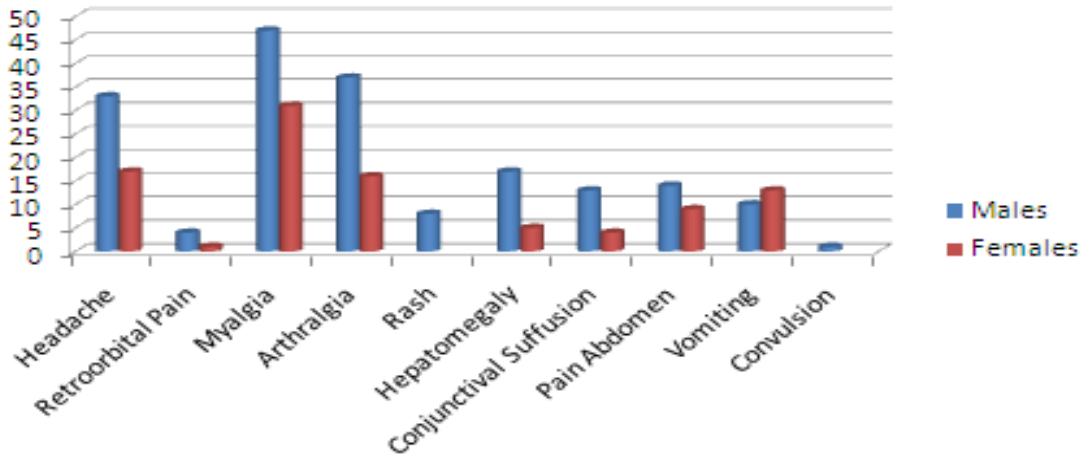
SYMPTOMS	FREQUENCY	PERCENTAGE
Headache	50	46.7
Retroorbital pain	5	4.7
Myalgia	78	72.9
Arthralgia	43	40.2
Rash	10	9.3
Hepatomegaly	22	20.6
Conjunctival Suffusion	17	15.8
Pain Abdomen	23	18.6
Vomiting	23	18.6
Convulsion	1	0.9

Graph No 5 – Prevalence of Symptoms in study population



Graph No 6 – Symptoms & its Relation to Sex Distribution

SYMPTOMATOLOGY-ITS RELATION TO SEX DISTIBUTION

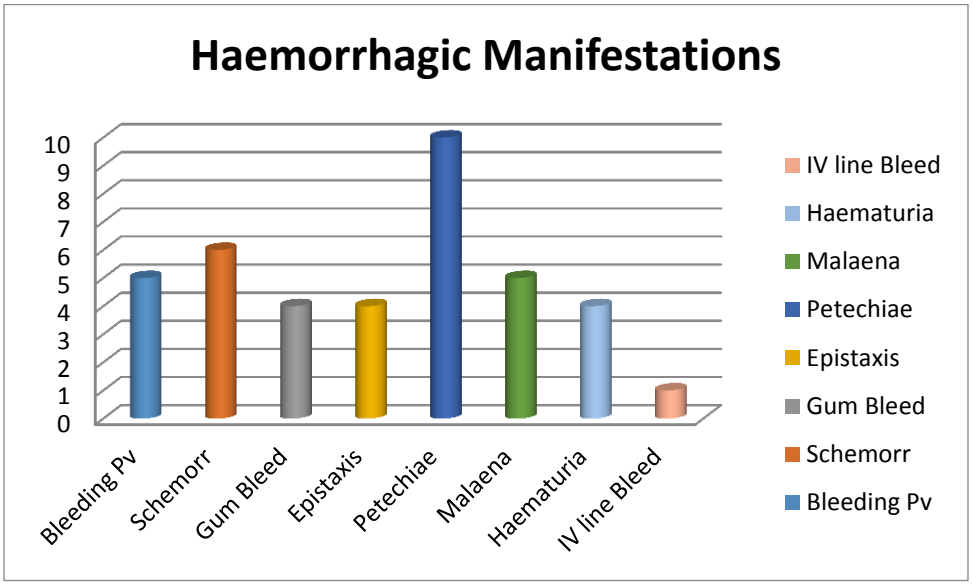


Haemorrhagic Manifestations in Study Population

Table No – 15 Haemorrhagic Manifestations

Haemorrhagic Manifestation	Frequency	Percentage
Bleeding PV	5	4.7
Sub Conjunctival Haemorrhage	6	5.6
Gum Bleeding	4	3.7
Epistaxis	4	3.7
Petechiae	12	11.2
Malaena	5	4.7
Haematuria	4	3.7
IV Line Bleed	1	0.9

Graph No – 7 Haemorrhagic Manifestations

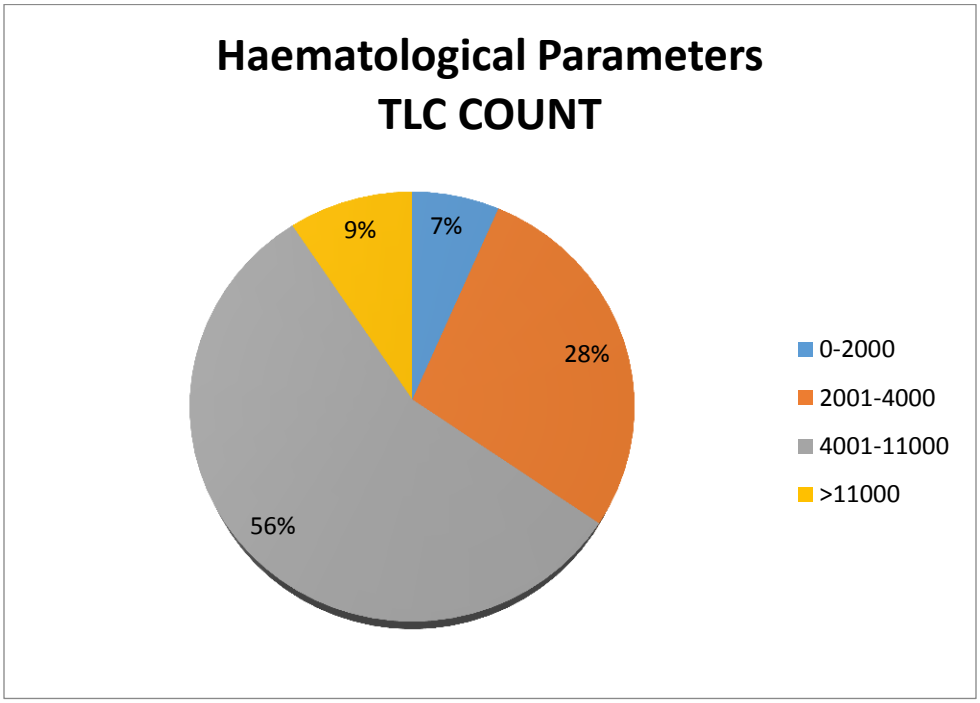


Haematological Parameters – Total Leucocyte Count

Table No – 16 Total Leucocyte Count(Cells/mm^3) in study population

TLC (cells/mm^3)	FREQUENCY	DISTRIBUTION
0-2,000	7	6.4
2,001- 4,000	30	28.1
4,001 – 11,000	60	56.2
>11,000	10	9.3

Graph No – 8 Total Leucocyte Count (Cells/mm^3) in study population



Haematological Parameters – Platelet count

Table No – 17 Platelet count (cells/mm^3) in study population

PLATELET COUNT	FREQUENCY	PERCENTAGE
0-10,000	5	4.7
10,001-50,000	41	38.3
50,001-1,00,000	29	27.1
1,00,000-1,50,000	13	12.1
>1,50,000	19	17.8

Graph No – 9 Platelet count (cells/mm^3) in study population

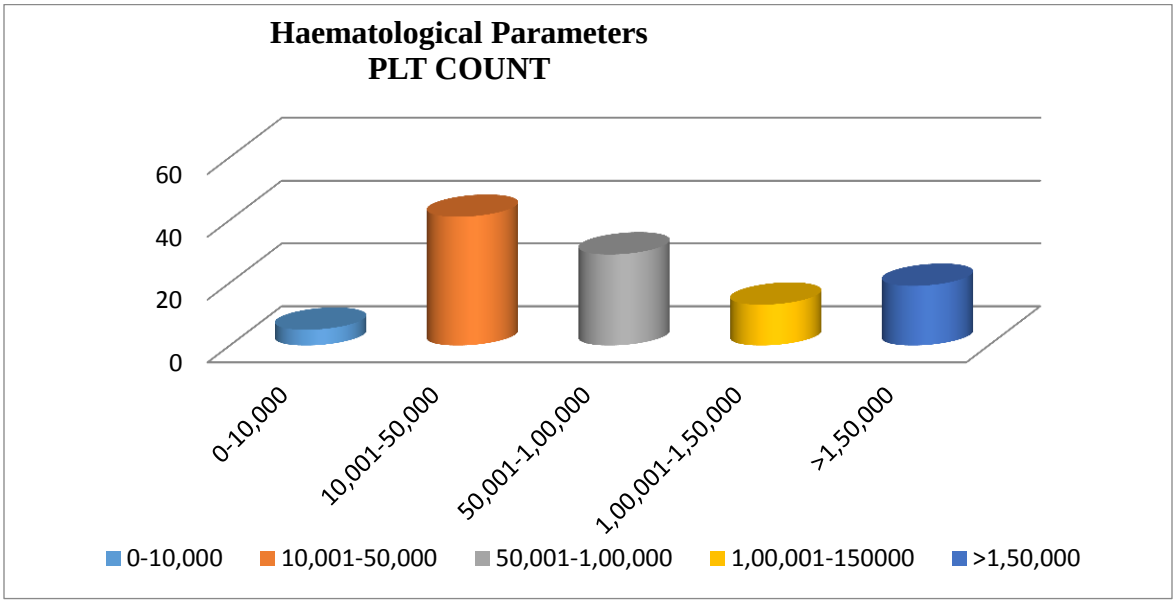


Table No 18 - Showing Association between Myalgia, Hb%, PCV and Platelet count among dengue patients

		Myalgia		Total (n=107)	
		Absent (n=29)	Present(n=78)		
Hb%	**<15**	19	57	76	X^2=0.587,df=1,p=0.444
	>15	10	21	31	
PCV	**< 45**	17	55	72	X^2=1.358,df=1, p=0.244
	>45	12	23	35	
Platelet count	**<50000**	15	34	49	X^2=0.564,df=1, p=0.453
	>50000	14	44	58	

In the study it was observed that there is no significant association between Myalgia and Hb%, PCV and Platelet Count i.e. p >0.05.

Table No 19 - Showing Association between Headache, Hb%, PCV and Platelet count among Dengue Patients

		Headache		Total (n=107)	
		Absent (n=57)	Present (n=50)		
Hb%	**<15**	41	35	76	X^2=0.048,df=1,p=0.826
	>15	16	15	31	
PCV	**< 45**	38	34	72	X^2=0.022,df=1, p=0.883
	>45	19	16	35	
Platelet count	**<50000**	30	19	49	X^2=2.297,df=1, p=0.130
	>50000	27	31	58	

In the study it was observed that there is no significant association between Headache and Hb%, PCV and Platelet Count i.e. p >0.05.

Table No 20 - Showing Association between Petechiae, Hb%, PCV and Platelet count among dengue patients

		Petechiae		Total (n=107)	
		Absent (n=95)	Present (n=12)		
Hb%	**<15**	69	7	76	X^2=1.058,df=1,p=0.304
	>15	26	5	31	
PCV	**< 45**	65	7	72	X^2=0.493,df=1, p=0.483
	>45	30	5	35	
Platelet count	**<50000**	42	7	49	X^2=0.856,df=1, p=0.355
	>50000	53	5	58	

In the study it was observed that there is no significant association between Petechiae and Hb%, PCV and Platelet Count i.e. $p > 0.05$.

Table No 21 - Showing Association between Sub-conjunctival haemorrhage, Hb%, PCV and Platelet count among dengue patients

		Sub-conjunctival Haemorrhage		Total (n=107)	
		Absent (n=101)	Present (n=6)		
Hb%	**<15**	71	5	76	X^2=0.468,df=1,p=0.494
	>15	30	1	31	
PCV	**< 45**	68	4	72	X^2=0.001,df=1, p=0.973
	>45	33	2	35	
Platelet count	**<50000**	46	3	49	X^2=0.045,df=1, p=0.831
	>50000	55	3	58	

In the study it was observed that there is no significant association between sub conjunctival haemorrhage and Hb%, PCV and Platelet Count i.e. $p > 0.05$.

Table No 22 showing association between Hb% and PCV among Dengue patients

		PCV		Total	
		<45	**>45**		
Hb	**<15**	72	4	76	X^2=89.8, df=1, p=0.00001
	>15	0	31	31	
Total		72	35	107	

In the study it was observed that there was highly significant association between Hb% and PCV among dengue patients i.e when PCV was raised (>45) Hb was >15gm% among 88.57% of patients.

Table No 23 showing association between Hb% and Platelet count among Dengue patients

		PLT		Total	
		<50000	**>50000**		
Hb	**<15**	30	46	76	X^2=4.222, df=1, p=0.04
	>15	19	12	31	
Total		49	58	107	

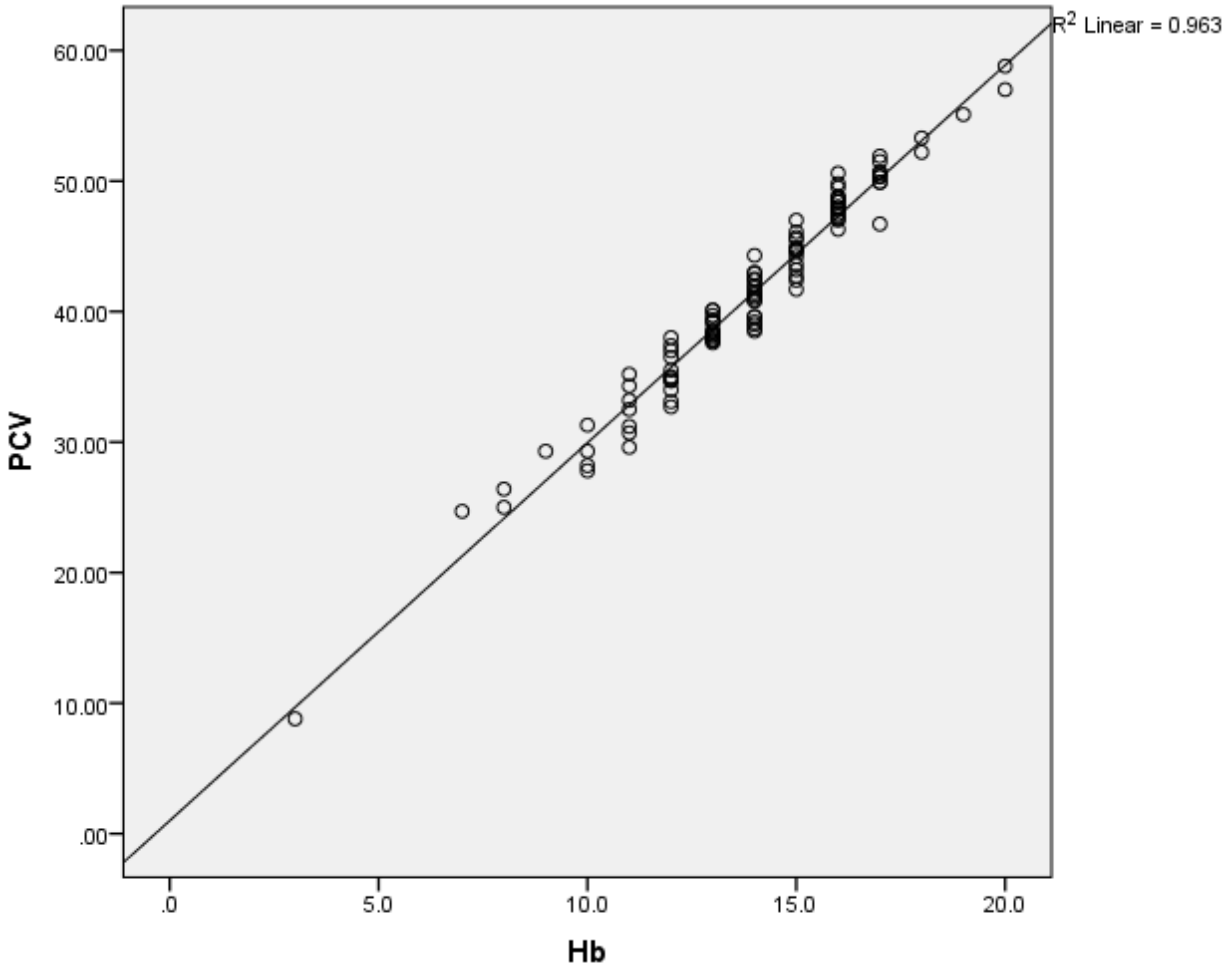
In the study it was observed that there was significant association between Hb% and Platelet count among dengue patients i.e. among 31 patients with Hb% >15, platelet count was <50000 in 61.29%.

Table No 24 - showing correlations between Hb% and other continuous variables among Dengue patients

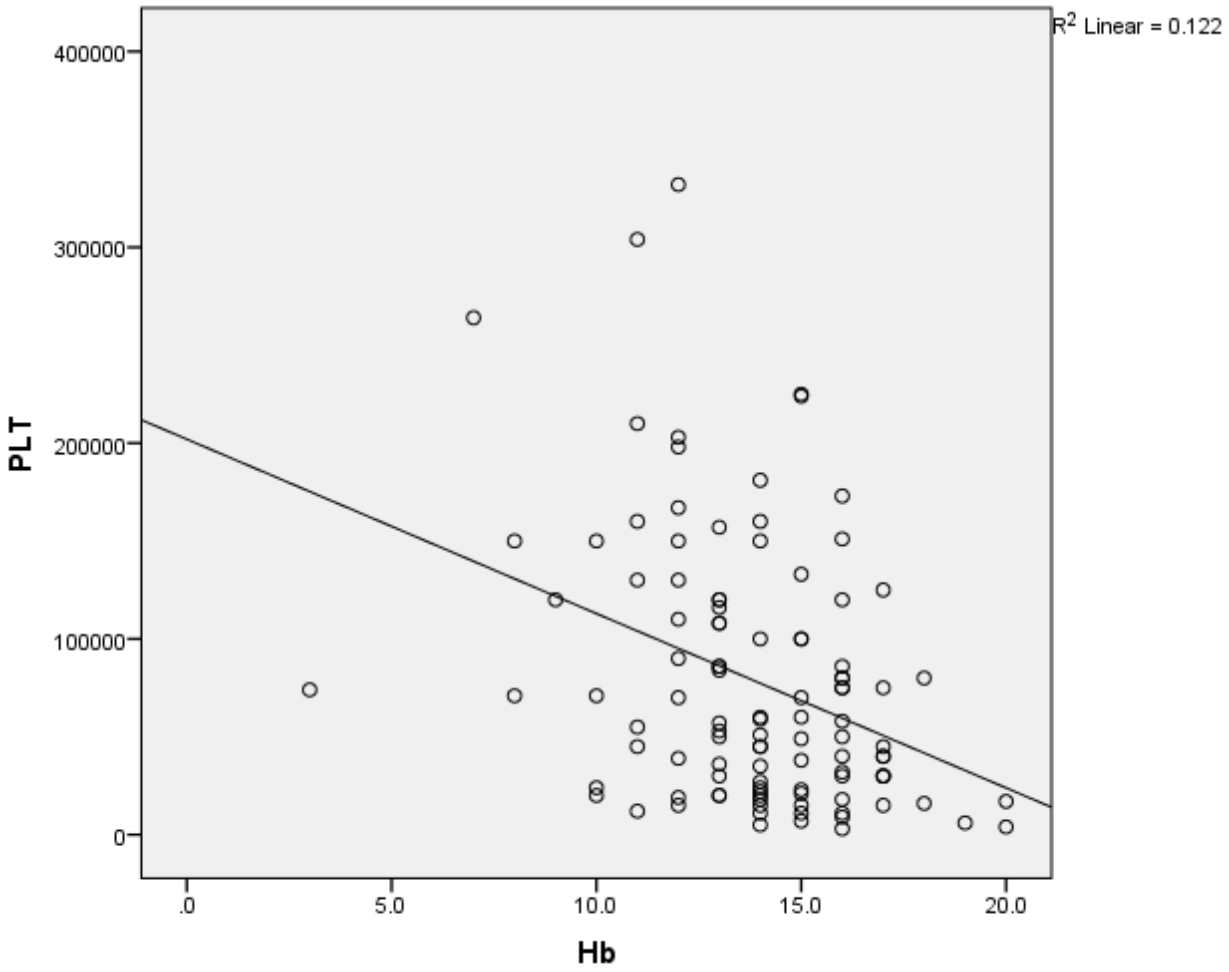
		PCV	TLC	PLT	TP	ALB
Hb	Pearson Correlation	0.981**	0.089	-0.349**	-0.204	-0.253
	Sig. (2-tailed) – p value	0.000	0.359	0.000	0.264	0.162
	N	107	107	107	32	32

**. Correlation is significant at the 0.01 level (2-tailed).

In the study it was observed that there is highly significant positive correlation between Hb and PCV i.e. as Hb increases there is significant increase in PCV. Similarly there was highly significant negative correlation between Hb and Platelet count i.e. as Hb increases there is decrease in platelet count. There was no significant correlation for other parameters with Hb%.



Graph No 10 - Scatter Plot showing Positive Correlation between Hb% and PCV



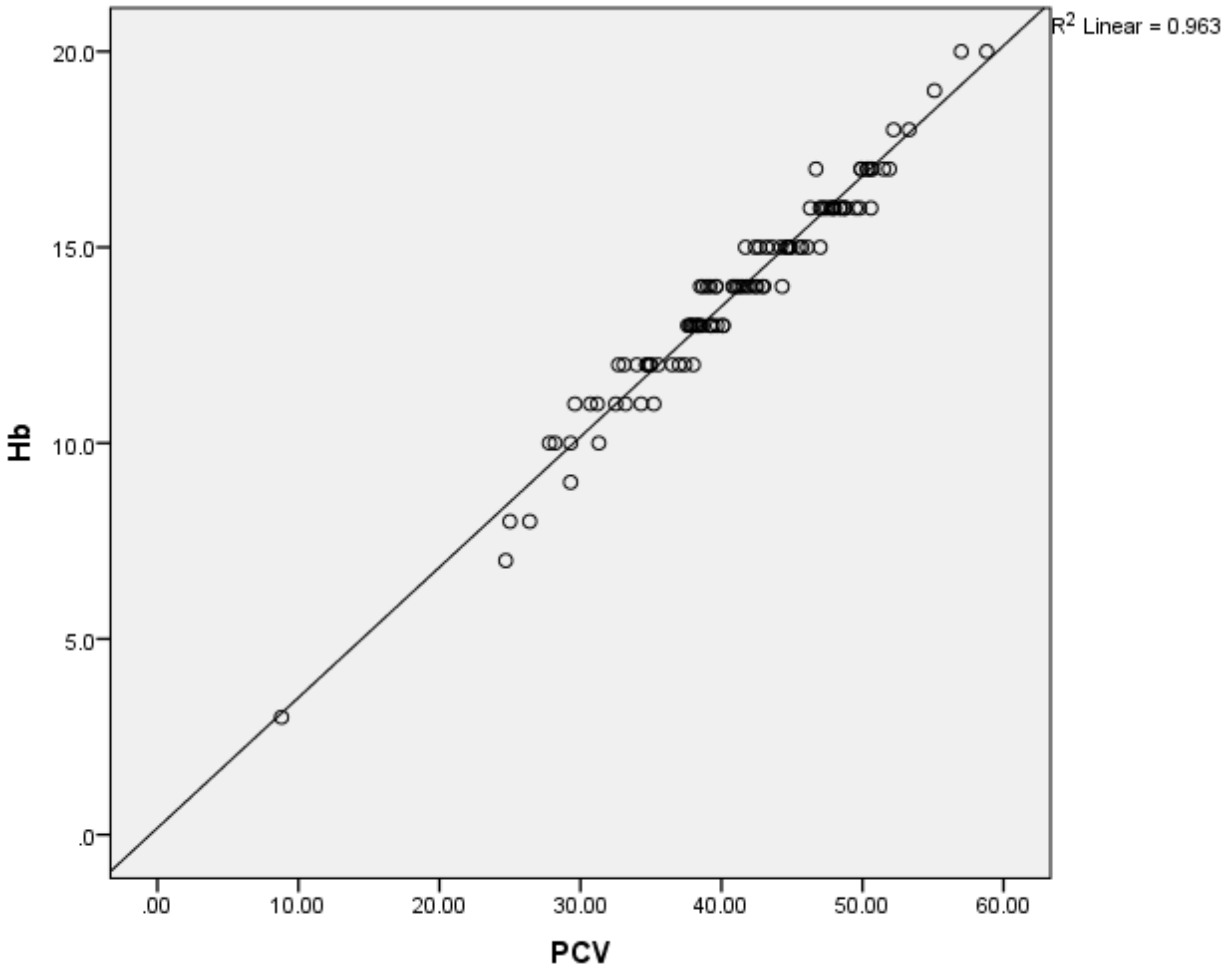
Graph No 11 - Scatter Plot showing negative correlation between Hb% and Platelet count

Table No 25 - showing correlations between PCV and other continuous variables among Dengue patients

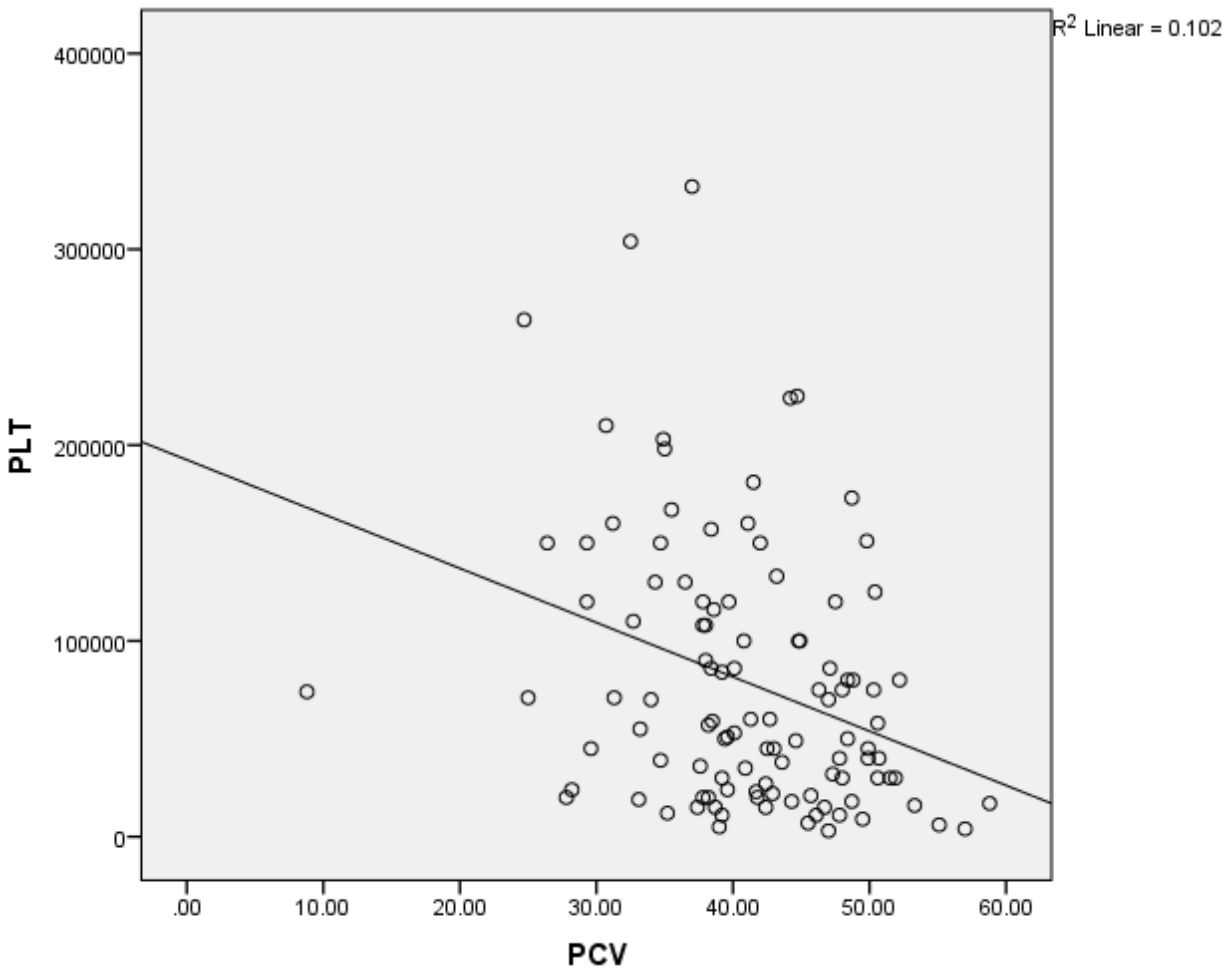
			Hb	TLC	PLT	TP	ALB
PCV		Pearson Correlation	0.981**	0.094	-0.320**	-0.189	-0.249
		Sig. (2-tailed)	0.000	0.335	0.001	0.299	0.170
		N	107	107	107	32	32

**. Correlation is significant at the 0.01 level (2-tailed).

In the study it was observed that there is highly significant positive correlation between PCV and Hb i.e. as PCV increases there is significant increase in Hb%. Similarly there was highly significant negative correlation between PCV and Platelet count i.e. as PCV increases there is decrease in platelet count. There was no significant correlation for other parameters with PCV.



Graph No 12 - Scatter Plot showing Positive Correlation between PCV and Hb%



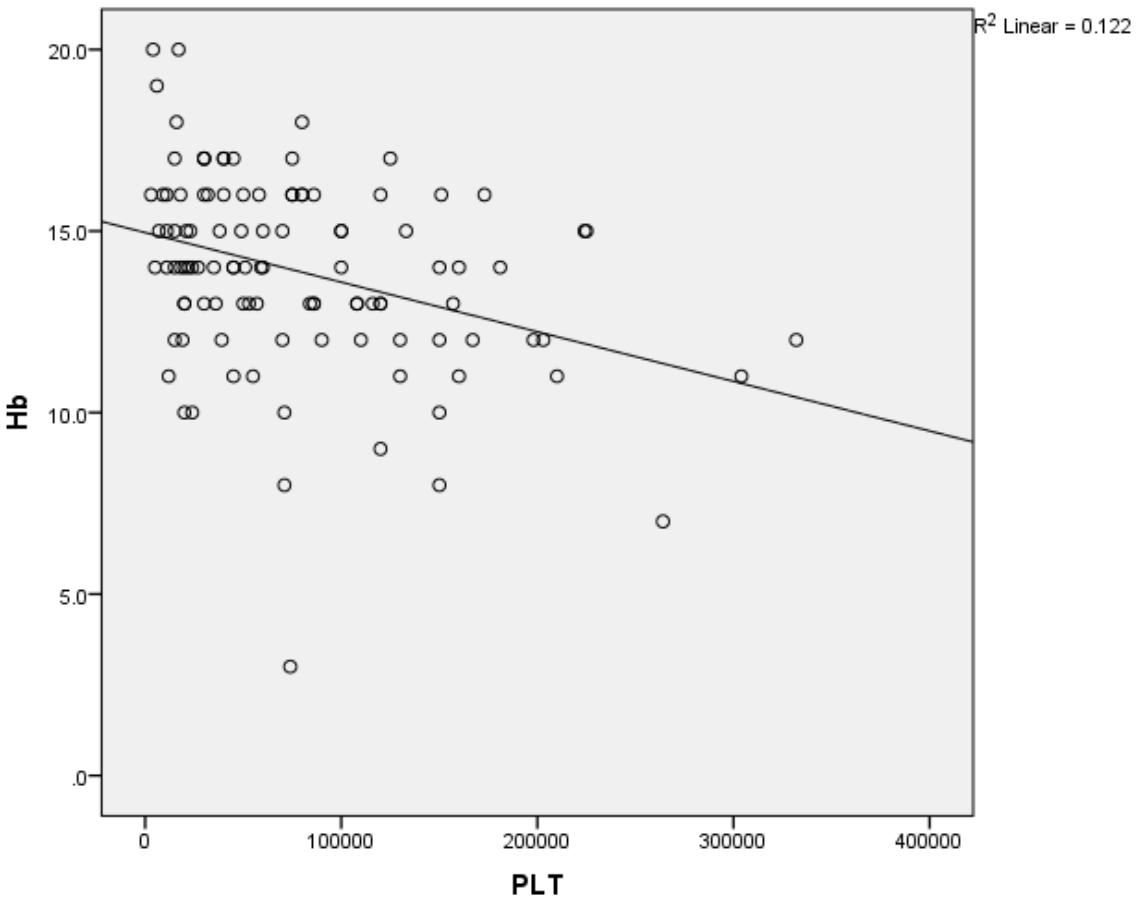
Graph No - 13 Scatter Plot showing Negative Correlation between PCV and Platelet count

Table No 26 - showing correlations between Platelet count and other continuous variables among Dengue patients

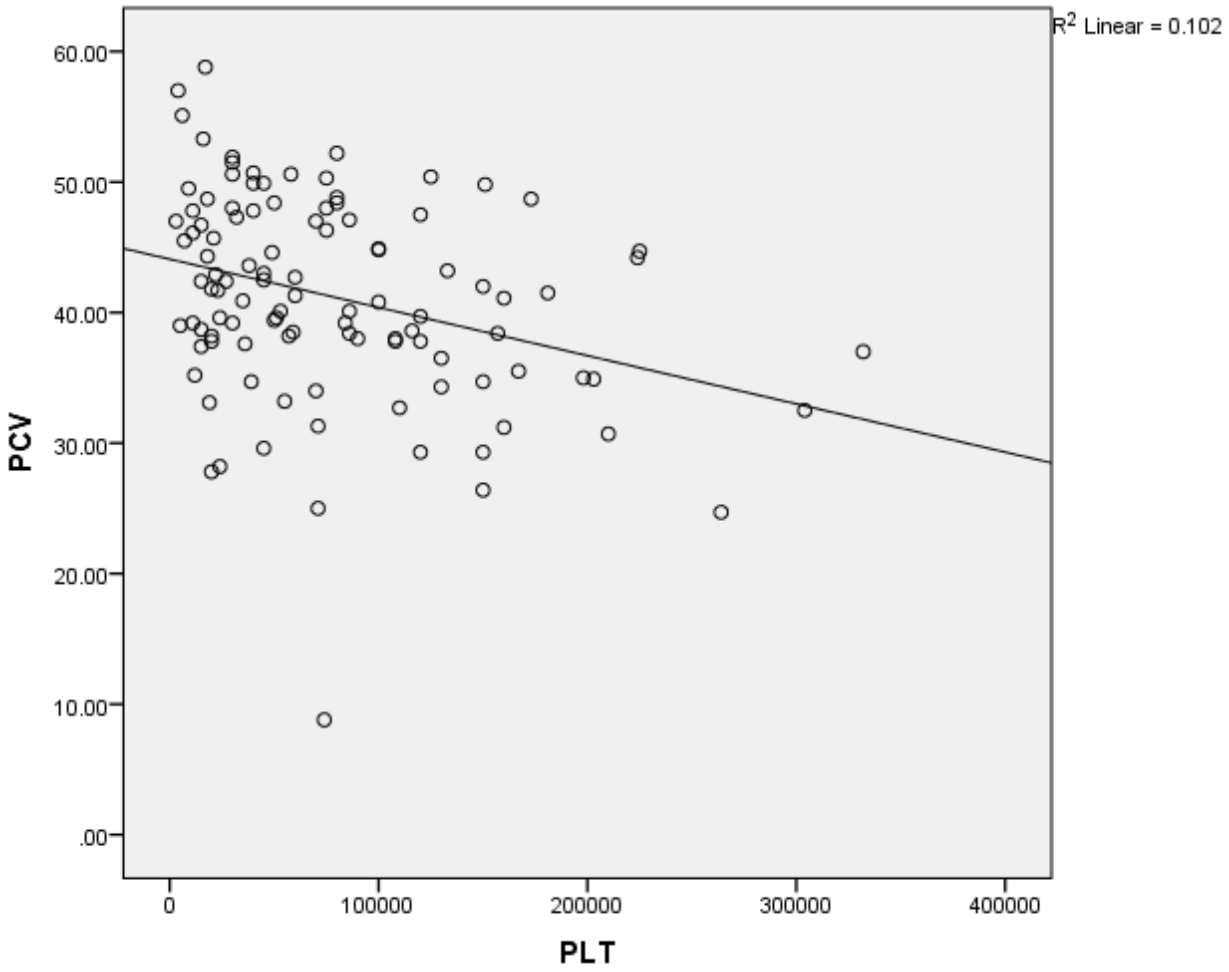
		Hb	PCV	TLC	TP	ALB
PLT	Pearson Correlation	-0.349**	-0.320**	-0.101	0.160	0.315
	Sig. (2-tailed)	0.000	0.001	0.300	0.382	0.079
	N	107	107	107	32	32

**. Correlation is significant at the 0.01 level (2-tailed).

In the study it was observed that there is highly significant negative correlation between Platelet count and Hb% and PCV i.e. as Platelet count increase there is decrease in Hb% and PCV. There is no significant correlation between Platelet and other parameters.



Graph No 14 -Scatter Plot showing Negative correlation between Platelet count and Hb%



Graph No 15 - Scatter Plot showing Negative correlation between Platelet count and PCV

Table No 27 - showing correlations between Total Leucocyte count and other continuous variables among Dengue patients

		Hb	PCV	PLT	TP	ALB
Total Leucocyte count	Pearson Correlation	0.089	0.094	-0.101	0.012	-0.040
	Sig. (2-tailed)	0.359	0.335	0.300	0.947	0.827
	N	107	107	107	32	32

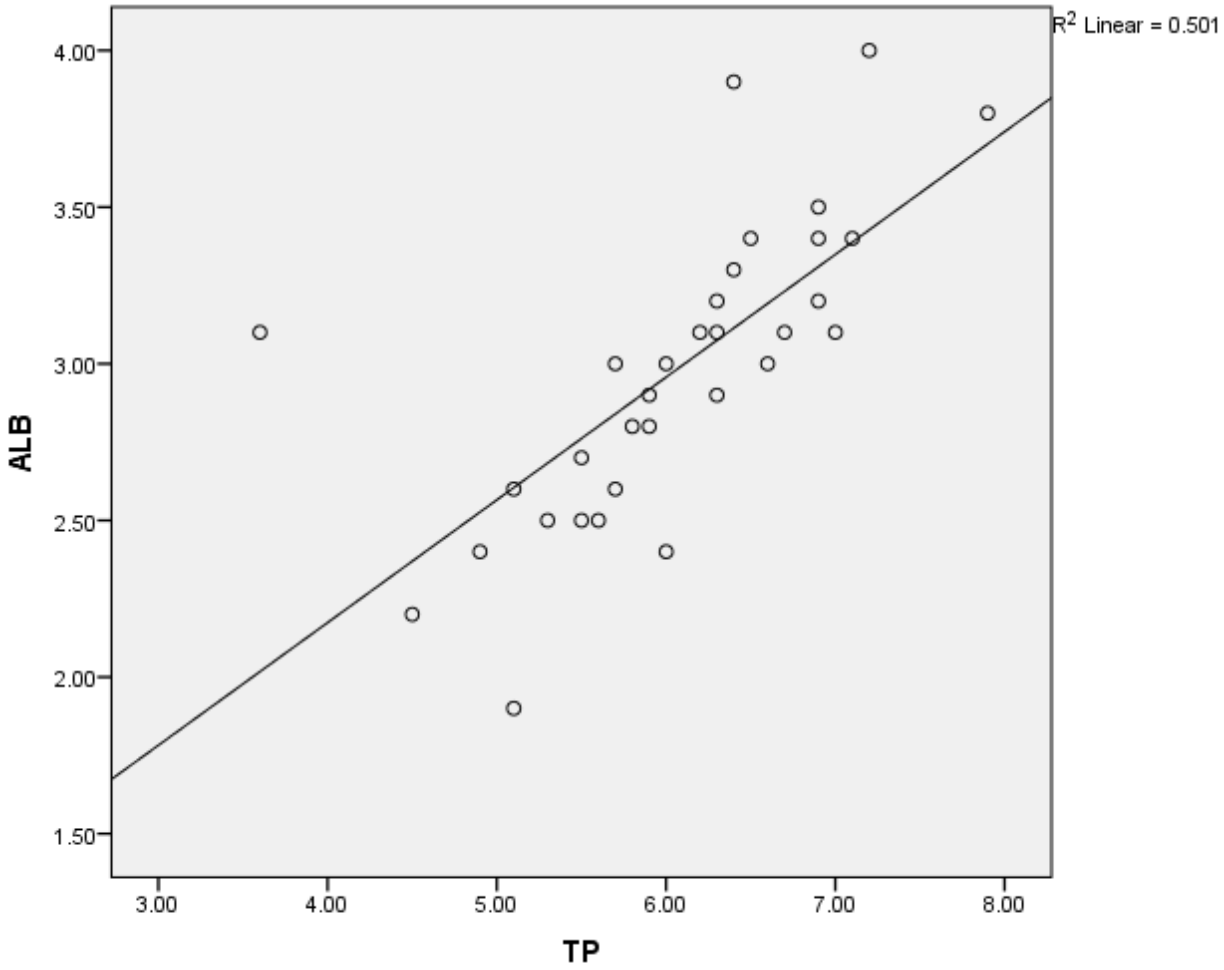
In the study it was observed that there is no significant correlation between TLC and other parameters.

Table No 28 - showing correlations between Total Protein and other continuous variables among Dengue patients

		Hb	PCV	TLC	PLT	ALB
Total protein	Pearson Correlation	-0.204	-0.189	0.012	0.160	0.708**
	Sig. (2-tailed)	0.264	0.299	0.947	0.382	0.000
	N	32	32	32	32	32

**. Correlation is significant at the 0.01 level (2-tailed).

In the study it was observed that there is highly significant correlation between Total protein and Albumin i.e. as Total protein increase there is increase in Albumin. There is no significant correlation between Total protein and other parameters.



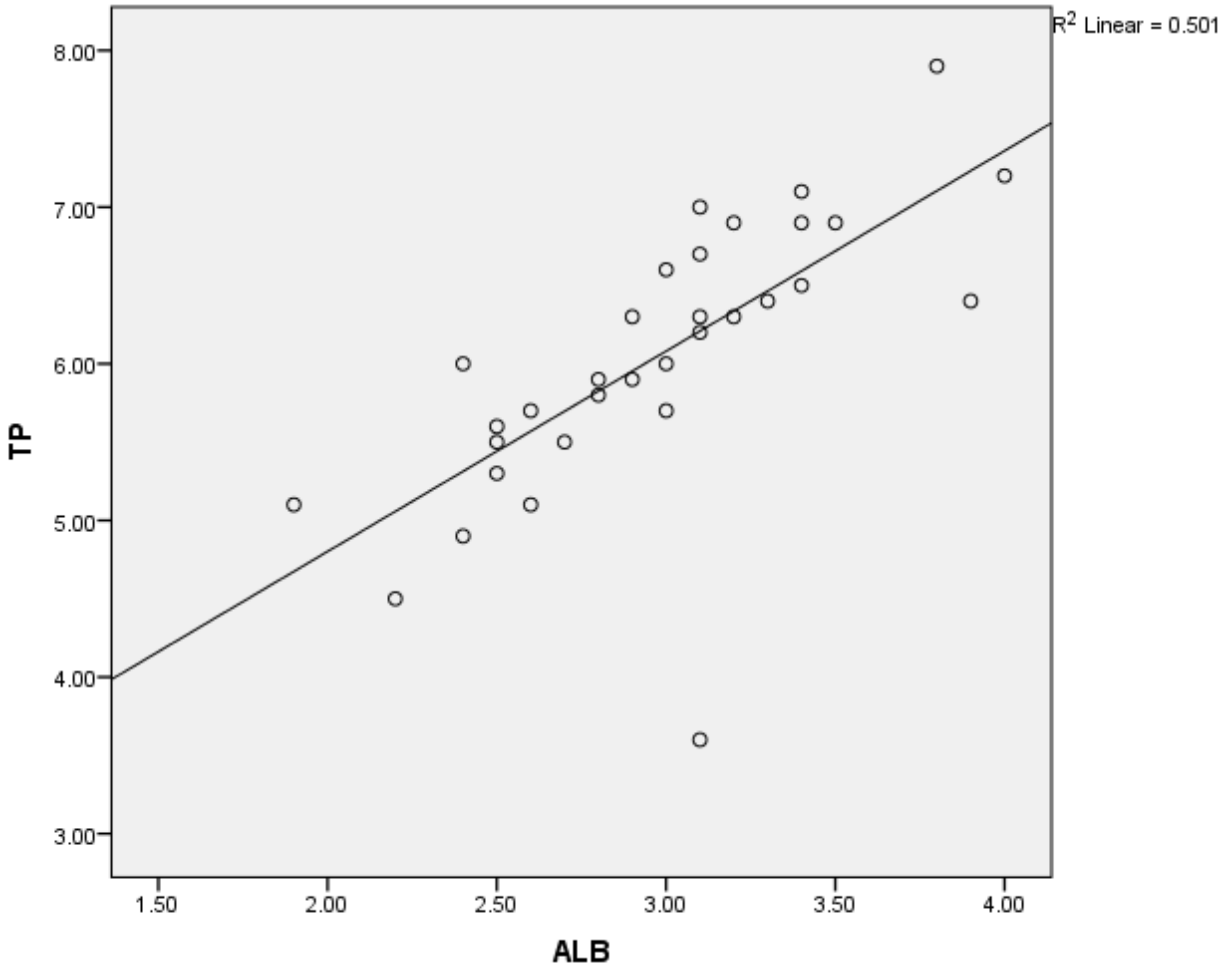
Graph No 16 -Scatter Plot showing Positive correlation between Total Protein and Albumin

Table No 29 - showing correlations between Albumin and other continuous variables among Dengue patients

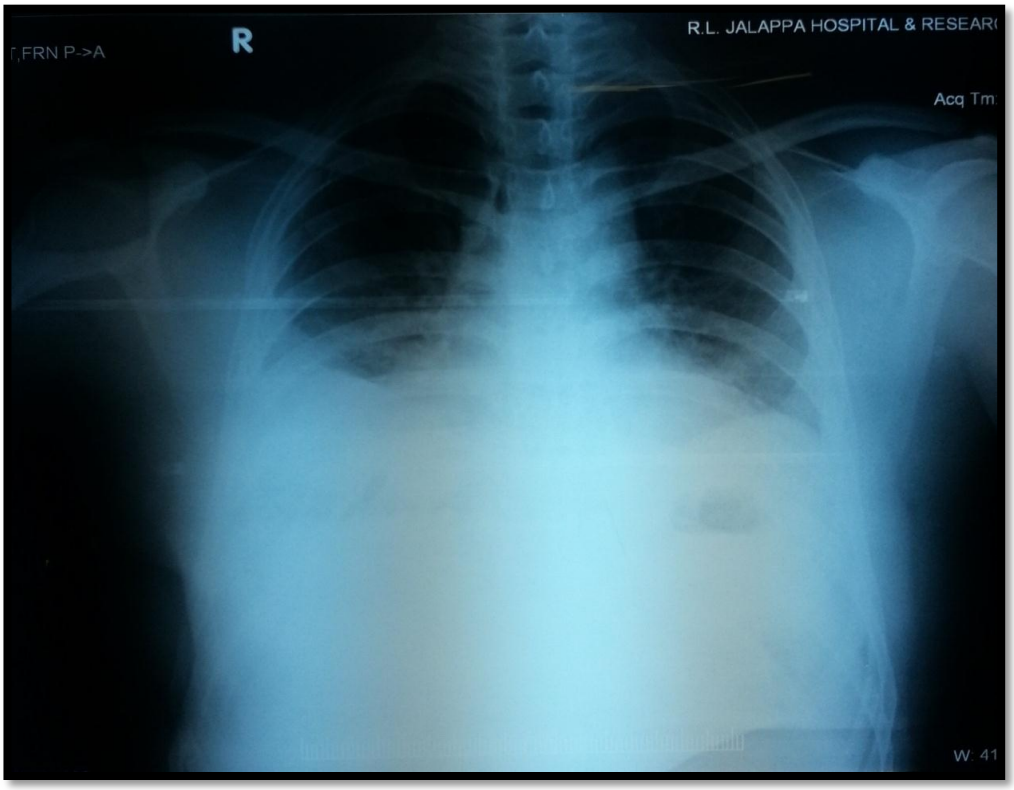
		Hb	PCV	TLC	PLT	TP
Albumin	Pearson Correlation	-0.253	-0.249	-0.040	0.315	0.708**
	Sig. (2-tailed)	0.162	0.170	0.827	0.079	0.000
	N	32	32	32	32	32

**. Correlation is significant at the 0.01 level (2-tailed).

In the study it was observed that there is highly significant correlation between Albumin and Total protein i.e. as Albumin increase there is increase in Total protein. There is no significant correlation between Albumin and other variables.

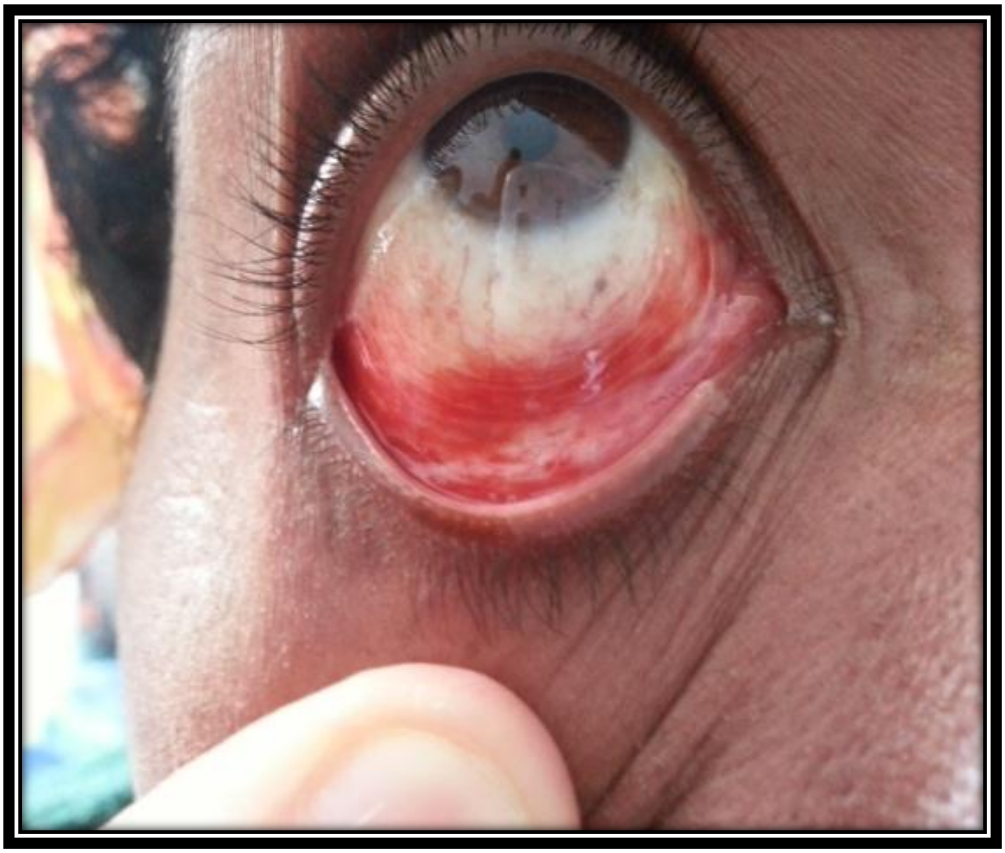


Graph No 17 - Scatter Plot showing Positive Correlation between Albumin and Total Protein

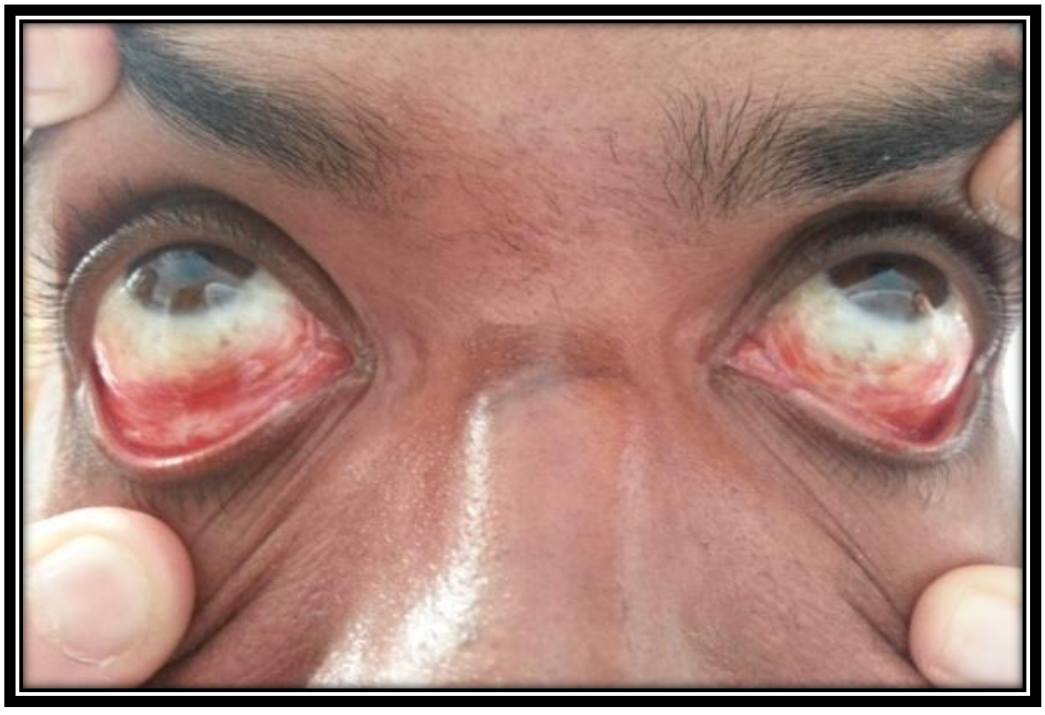


BILATERAL PLEURAL EFFUSION

RIGHT SIDED PLEURAL EFFUSION



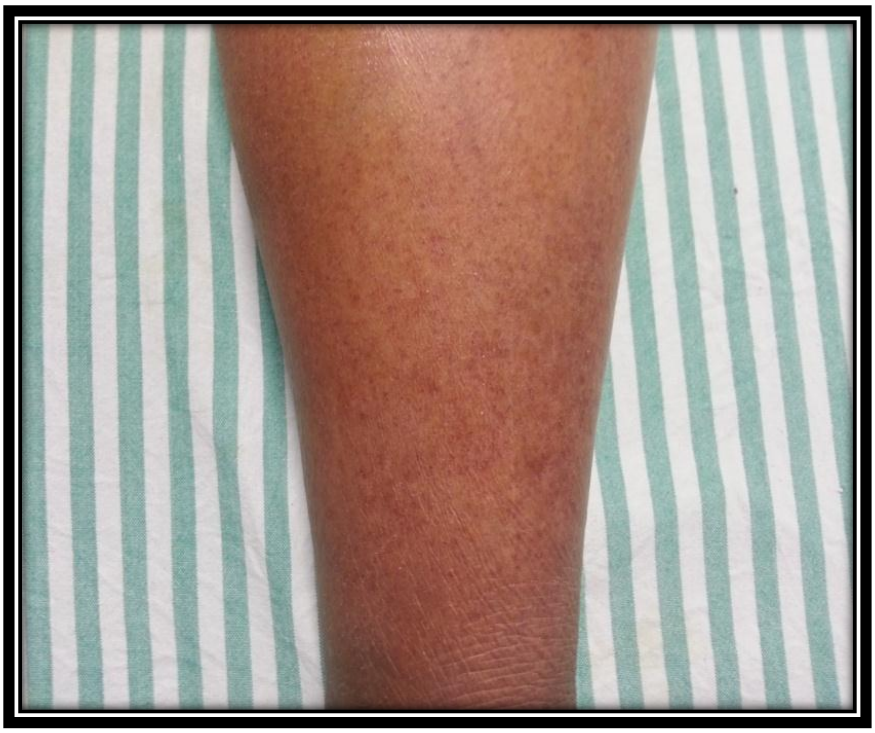
CONJUNCTIVAL SUFFUSION



CONJUNCTIVAL SUFFUSION

PETECHIAE OVER LOWER PALPEBRAL CONJUNCTIVA

PETECHIAE OVER LOWER PALPEBRAL CONJUNCTIVA



PETECHIAL RASH

PETECHIAE OVER SOFT PALATE

DISCUSSION

DISCUSSION

Dengue fever is the most common arthropod-borne self-limiting viral disease with clinical spectrum ranging from asymptomatic infection to life threatening shock. The presenting features in Dengue Fever are not very much different from any other viral illness. Common presenting features in dengue are myalgia, arthralgia & headache. Other Features observed are conjunctival suffusion, retro orbital pain & pain abdomen.

A feature unique to dengue which differentiates it from other viral illnesses is its ability to cause plasma leakage. It determines the severity of infection in dengue & its clinical categorization into dengue fever, dengue Haemorrhagic fever & dengue shock syndrome. Haemoconcentration and thrombocytopenia are the distinctive features of dengue hemorrhagic fever. Plasma leakage complicates the clinical picture in dengue and causes fluid accumulation in body cavities, leading to the development of bilateral pleural effusion (right being the dominant side) and ascites. This in turn reduces the effective circulating volume leading to the development of shock referred to as dengue shock syndrome. The duration over which the patient progresses into complicated stage depends on factors such as viral load & the duration of febrile phase.

The spectrum in dengue at present seems to have transformed from a picture causing severe debilitating myalgia & arthralgia, conventionally referred to as Break bone fever to a more systemic involvement. Clinical features such as pain abdomen, secondary to acalculous cholecystitis mimicking an acute abdomen are not uncommon at present.

The complications in dengue in contrary to other illnesses start after the end of febrile phase. At this stage patients develop haemorrhagic manifestations namely petechiae, sub conjunctival hemorrhages, malaena & bleeding PV.

In the present study there were 67 males and 40 females constituting 62.6% and 37.4% of the study population respectively. Higher prevalence of dengue infection was noted among males than females which is congruent with other Indian studies (Gupta et al.,2005; Ukey et al., 2010; Kumar et al., 2010).[63]

In the present study out of 107 patients, 93 patients were of the age group between 18 – 45 years, 55 (51.4%) between the age group of 18 – 30 years & 38 (35.6%) were between 31-45 years of age. This correlates with study done by Garg et al in which the above mentioned age groups had the maximum burden among adult population.[63] However, in the study done by Garg et al, majority of the population belonged to pediatric age group as it had no age based exclusion criteria.

Majority of the patients i.e., 65 out of 107 (60.8%) in our study presented with complaints of fever of 4-7 days duration. 34 of 107 (31.8%) of the study population gave history of fever of 1-3 days. Similar results of all patients (100%) presenting with history of fever were noted in study done by Ratageri et al.[64] Second most common symptom noted in our study was myalgia, seen in 78 0f 107 (72.9%), the next common being headache seen in 50 of 107 people accounting for 46.7% of the study group. However, the second & third common complaints in the study of Ratageri et al were vomiting (82%) & pain abdomen (61%). Present study bears a correlation between with a study done by Shukla et al in which 83% patients had myalgia.[65]

The commonest haemorrhagic manifestation noted in the study group was petechiae, seen in 10 of 107 patients (11.2%) and the next common being subconjunctival haemorrhage seen in 6 patients (5.6%) of the study group.

All the patients in the study group underwent complete blood counts at admission. The mean PCV in the study group is 41.2%. Analysis revealed that 35 of 107 (32.71%) patients had haematocrit> 45%, 72 of 107 (67.28%) patients had haematocrit < 45%.

Total leucocyte count was < 4,000 cells/ mm^3 in 37 patients (34.5%) of the study population. The mean total leucocyte count of the study population was 7193 cells/mm^3

The mean platelet count in the study population was 78,336 cells /mm^3 at the time of admission. 93 0f 107 patients had platelet count less than 1,50,000 cells/mm^3 accounting for 82.2% of the study group. This has very close resemblance to study done by Ratageri et al in which thrombocytopenia was seen in 82 % of the study group. [64]

Liver function tests were done on 32 out of 107 patients. Analysis of it revealed mean serum bilirubin level of 1.17gm/dL. Mean SGOT values in study population were 170 U/L which is about four times the normal value & the mean SGPT values were 93U/L. This has significant correlation with study done by Shukla et al in which higher SGOT levels were found than SGPT levels.[65]

In our study there were 8 patients who had pleural effusion accounting for about 7.5% of the study group, predominantly on the right side. This is comparatively less than that observed by Shukla et al in which 15 % had pleural effusion.[65]

Ultrasonography was performed on 22 patients amongst the study group. Out of 9 patients detected to have ascites, 5 patients had moderate ascites and 4 patients had minimal ascites which contribute to about 40% on whom ultrasonography was performed. This is significantly less than the study done by Shukla et al in whom ultrasonography was done on all cases which revealed evidence of ascites in 70% of the cases.[65]

From the analysis of the data it was observed that there was no significant statistical association/ correlation with clinical spectrum and lab investigations.

However there is a very significant positive statistical association between haemoglobin and haematocrit with a ‘p’ value of <0.01, which means that with increase in haemoglobin, haematocrit increases and with decrease in haemoglobin, haematocrit decreases. Also there is a significant negative association with haemoglobin & platelets with a ‘p’ value of <0.05. It means that with increase in haemoglobin, platelets decrease indicating the development of

haemoconcentration and with decrease in platelet count the haemoglobin improves indicating recovery.

There is also significant positive association between total protein & albumin and viceversa.

CONCLUSION

CONCLUSION

The following conclusions can be drawn from the study:

- The clinical spectrum in patients of dengue are similar to any viral illness.
- The Determining factor in patients with dengue fever is the development of plasma leakage.
- The onset of complications & duration of recovery are determined by the signs & extent of Plasma leakage – development of ascites & pleural effusion.
- Development of complications in dengue are commonly seen at the end of febrile phase.
- A patient with dengue should be clinically monitored based on the extent of hydration, general wellbeing & by daily regular monitoring of blood counts.
- It is of utmost importance to assess for the development of haemorrhagic manifestations daily.
- Adequate hydration should be the corner stone in the management of dengue & haematocrit should be used as a tool in assessing the extent of plasma leakage & management.

SUMMARY

SUMMARY

- The Study done was a prospective study between the months of April 2013 & August 2013 at R. L. Jalappa Hospital attached to Sri Devaraj Urs Medical College, Kolar.
- The study was conducted on 107 patients admitted to the hospital. It included 67 male & 40 female patients.
- Majority of the subjects belonged to the age group of 18- 35 years contributing to 55% of study group.
- Majority of the subjects tested positive for IgM by serological methods comprising 62.6% of the study group.
- The common presenting symptoms to the hospital included fever, seen in all the cases. Other common complaints were headache, myalgia, arthralgia & pain abdomen.
- Most common haemorrhagic manifestation noted was petechiae seen in 11.2% of the study population.
- Pleural effusion was seen in 8 patients constituting 7.5% of study population.
- Ascites was seen in 9 patients constituting 8.4% of study population.
- Most common haematological abnormality noted was thrombocytopenia, seen in 82.2% of the study population. Mean platelet count in the population was 78,336 cells/mm^3.
- Significant proportion of the patients had leucopenia which was noted in 34.5% of the study population.
- Mean PCV in the study group was 41.2 %. Study group constituted 32.7% patients who had PCV > 45%.
- Analysis of LFT revealed about four fold rise in SGOT values & about 2 fold rise in SGPT values in comparison with the normal population.
- There was no significant positive (or) negative statistical correlation between symptoms & Lab parameters.
- There was a significant positive statistical correlation noted between Hb & PCV with ‘p’ value less than 0.01

- There was a significant negative statistical correlation between Hb & platelet count with p value of 0.04
- There was a significant positive correlation between Total protein & Albumin.

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ANNEXURE

AT THE TIME OF ADMISSION

Duration of fever :

Any febrile illness in the past :

Headache : + / -
Retro-orbital pain : + / -
Myalgia : + / -
Arthralgia : + / -
Rash : + / -
Hepatomegaly : + / -
Conjunctival suffusion : + / -

EXAMINATION:

PR: RR:

BP: Temp:

Pallor :
Icterus :
Cyanosis :
Clubbing :
Lymphadenopathy :

CVS:

RS:

PA:

CNS:

HAEMORRHAGIC MANIFESTATIONS

Sub-conjunctival hemorrhages	:	+ / -
Haematuria	:	+ / -
Epistaxis	:	+ / -
Gum bleeding	:	+ / -
Haematemesis	:	+ / -
Malaena	:	+ / -
Positive tourniquet test	:	+ / -
Petechiae/Petechial rash	:	+ / -
Easy bruising & bleeding at Venepuncture site	:	+ / -

SIGNS OF PLASMA LEAKAGE

1. Hematocrit :
2. Presence of pleural effusion
    a. Clinical findings :

    b. Radiological

        X-ray findings :

        Ultrasonography :

3. Presence of ascites in USG :

WARNING SIGNS

1. Abdominal pain	:	+ / -
2. Persistent vomiting	:	+ / -
3. Lethargy/restlessness (or) Irritability	:	+ / -
4. Oliguria	:	+ / -
5. Refusal of oral intake	:	+ / -

LAB INVESTIGATIONS

1. Confirmatory method :
   NS 1 Ag
   IgM (or) Ig G Antibodies

2. Complete blood count

   Hb :
   TLC :
   DLC
   N -
   L -
   E -
   B -
   ESR :
   Hematocrit :
   Platelet count :

3. Coagulation profile

   PT :
   aPTT :

4. Liver function test
   Total protein :
   Serum albumin :
   AST :
   ALT :
   AST/ALT :

PREDICTORS OF COMPLICATIONS

1. Hematocrit & its response to correction with I V fluids :

2. Thrombocytopenia

3. Leucopenia
   N -
   L -
   N / L -

4. Hepatomegaly :

5. Urine output :

6. Hypoproteinemia/ Hypoalbuminemia :

Sl. No.	Age	Sex	Hospital No.	NS1 Ag /IgM/IgG	Lepto	Rapid card/PS for MP	Duration	Head ache	Ret-ort Pain	Myalgia	Arthralgia	Rash	Hepatome galy	Conjunctival Suffusion	Pain Abdomen	Vomiting	Convulsion	CVS	RS
1	26	M	811194	IgM+ve	Neg	Neg	7Days	0	0	1	0	0	0	0	0	0	0	HR-55/Min	NAD
2	35	M	814626	IgM+ve	Neg	Neg	5Days	1	0	1	0	0	1	0	1	0	0	HR-50/Min	NAD
3	18	M	806619	IgM+ve	Neg	Neg	2Days	0	0	0	0	0	1	0	0	0	0	NAD	NAD
4	48	M	810444	NS1Ag+ve	Neg	Neg	10Days	0	0	0	0	1	0	0	0	1	0	NAD	LTUL-Consolidation BS over Rt Apical areas
5	24	F	810410	IgM+ve	Neg	Neg	3Days	0	0	1	0	0	0	0	0	0	0	NAD	NAD
6	28	M	815311	IgM+ve	Neg	Neg	3Days	0	0	1	0	0	0	0	0	0	0	NAD	NAD
7	50	M	815028	IgM+ve	Neg	Neg	6Days	1	1	1	1	0	0	0	0	0	0	HR - 58/Min	NAD
8	35	M	811455	IgM+ve	Neg	Neg	4Days	0	0	1	1	0	0	0	0	1	0	NAD	NAD
9	22	F	814482	NS1Ag+ve	Neg	Neg	1Day	0	0	1	0	0	0	0	0	0	0	NAD	NAD
10	30	M	814205	NS1 Ag+ve & IgM+ve	Neg	Neg	2Days	1	0	0	1	1	0	0	0	0	0	NAD	Absent BS over Rt InfraScapular areas
11	26	M	814547	NS1 Ag+ve & IgM+ve	Neg	Neg	5Days	1	1	1	1	0	0	0	0	0	0	NAD	NAD
12	18	M	814619	NS1 Ag+ve & IgM+ve	Neg	Neg	4Days	0	0	0	0	0	1	0	0	0	0	NAD	NAD
13	38	F	810482	IgM+ve	Neg	Neg	5Days	0	0	1	0	0	0	0	1	0	0	NAD	Decreased intensity of BS over Rt Basal areas
14	26	F	810511	IgM+ve	Neg	Neg	5Days	0	0	0	0	0	0	0	1	1	0	NAD	Decreased intensity ofBS over Rt Basal areas
15	50	M	807390	IgM+ve	Neg	Neg	7Days	0	0	1	0	0	0	0	0	0	0	NAD	B/L Basal crepts
16	60	F	807121	IgM+ve	Neg	Neg	7Days	0	0	0	0	0	1	0	0	0	0	NAD	NAD
17	45	M	807109	IgM+ve	Neg	Neg	7Days	0	0	0	0	0	0	0	1	0	0	NAD	Rt Basal crepts
18	28	M	807082	IgM+ve	Neg	Neg	3Days	0	0	0	0	0	1	0	0	0	0	NAD	NAD
19	34	M	814565	NS1Ag+ve	Neg	Neg	3Days	1	1	1	1	1	0	1	0	0	0	NAD	NAD
20	25	F	814561	IgG+ve	Neg	Neg	5Days	0	0	1	0	0	0	0	0	1	0	NAD	NAD
21	33	F	814629	IgM+ve	Neg	Neg	4Days	1	0	1	1	0	0	0	0	0	0	HR-52/Min	NAD
22	22	M	814647	IgM+ve	Neg	Neg	4Days	1	0	1	1	1	0	1	0	0	0	NAD	NAD
23	23	F	814988	NS1Ag+ve	Neg	Neg	3Days	0	0	1	1	0	0	0	0	0	0	NAD	Decreased intensity of breath sounds over right basal area
24	32	M	811214	IgM+ve	Neg	Neg	3Days	0	0	1	1	1	1	1	1	0	0	NAD	NAD
25	18	F	815085	NS1Ag+ve	Neg	Neg	5Days	0	0	1	1	1	0	0	0	0	0	NAD	NAD
26	19	M	806606	IgM+ve	Neg	Neg	4Days	1	0	0	0	0	0	1	0	1	0	NAD	NAD
27	35	M	801709	IgM+ve	Neg	Neg	7Days	0	0	0	0	0	0	0	0	1	0	NAD	NAD
28	61	F	799887	IgM+ve	Neg	Neg	4Days	0	0	1	0	0	1	0	0	0	0	NAD	NAD
29	32	M	799290	IgM+ve	Neg	Neg	4Days	1	0	1	0	0	1	0	1	0	0	NAD	NAD
30	18	F	797763	IgM+ve	Neg	Neg	15Days	0	0	0	0	0	1	0	0	1	0	NAD	NAD
31	23	M	808340	IgM+ve	Neg	Neg	1Days	1	0	0	0	0	0	0	1	1	0	NAD	NAD
32	35	F	808536	IgM+ve	Neg	Neg	4Days	0	0	1	0	0	0	0	0	1	0	NAD	NAD
33	22	M	808257	IgM+ve	Neg	Neg	15Days	0	0	1	0	0	0	0	0	0	0	NAD	NAD
34	19	M	766881	IgM+ve	Neg	Neg	4Days	0	0	1	0	0	0	0	0	0	0	NAD	NAD
35	40	F	784371	IgM+ve	Neg	Neg	4Days	1	0	0	0	0	0	0	1	0	0	NAD	B/L crepts (+) Pleural Rub
36	18	F	816427	IgM+ve	Neg	Neg	4Days	1	0	1	1	0	0	0	0	0	0	NAD	NAD
37	20	M	816462	NS1Ag+ve	Neg	Neg	10Days	1	0	1	0	0	0	0	0	0	0	NAD	NAD
38	29	M	816461	IgM+ve	Neg	Neg	7Days	0	0	1	1	1	1	1	1	0	0	HR-48/min	NAD
39	32	M	816854	IgM&IgG+ve	Neg	Neg	7Days	1	0	0	0	1	1	1	0	0	1	HR-48/min	NAD
40	20	M	812801	NS1Ag+ve	Neg	Neg	4Days	1	0	1	1	1	1	1	0	0	0	NAD	NAD
41	35	M	812845	NS1Ag+ve	Neg	Neg	2Days	1	1	1	0	1	0	1	0	0	0	HR-50/min	NAD
42	31	M	812525	NS1Ag+ve	Neg	Neg	4Days	0	1	1	1	0	0	0	0	0	0	NAD	NAD
43	40	F	811882	IgM+ve	Neg	Neg	1Day	1	0	1	0	0	0	0	0	1	0	NAD	NAD
44	50	F	808852	IgM&IgG+ve	Neg	Neg	1Day	1	0	1	1	0	0	0	0	0	0	NAD	Decreased intensity of BS over Rt Basalareas
45	24	F	815314	IgM+ve	Neg	Neg	6Days	1	0	1	1	0	0	1	0	0	0	NAD	NAD
46	60	F	816288	IgM+ve	Neg	Neg	7 Days	0	0	1	1	0	0	0	0	0	0	NAD	NAD
47	22	F	812877	NS1Ag+ve	Neg	Neg	1Day	0	0	0	0	0	0	0	0	1	0	NAD	NAD
48	54	F	809029	NS1Ag+ve	Neg	Neg	5Days	0	0	1	1	0	1	0	1	0	0	NAD	Decreased intensity of BS over Rt Basalareas
49	60	M	809242	IgM+ve	Neg	Neg	3Days	0	0	1	1	0	0	0	0	0	0	NAD	NAD
50	33	M	813895	NS1Ag+ve	Neg	Neg	1Day	1	0	1	1	1	0	0	0	0	0	NAD	NAD
51	48	M	815374	IgM+ve	Neg	Neg	4Days	1	0	1	1	0	0	0	0	0	0	NAD	NAD
52	24	M	816140	IgM+ve	Neg	Neg	3Days	0	0	1	1	0	0	0	0	0	0	NAD	NAD
53	40	F	816087	IgM+ve	Neg	Neg	1Day	1	0	1	1	0	0	0	1	0	0	NAD	NAD
54	25	F	815375	IgM+ve	Neg	Neg	3Days	1	0	1	1	0	0	0	1	0	0	NAD	NAD
55	30	M	818471	NS1Ag+ve	Neg	Neg	3Days	1	0	1	1	0	0	0	0	0	0	NAD	NAD
56	38	M	814484	IgM&IgG+ve	Neg	Neg	2Days	1	0	1	1	0	1	0	0	0	0	NAD	NAD
57	34	M	815306	IgM+ve	Neg	Neg	3Days	0	0	1	1	1	0	0	0	0	0	NAD	NAD
58	25	F	815717	IgM+ve	Neg	Neg	3days	1	1	1	1	1	0	1	0	0	0	NAD	NAD
59	25	M	815264	IgM+ve	Neg	Neg	4Days	1	0	0	0	0	0	1	0	0	0	NAD	NAD
60	26	M	814199	IgM+ve	Neg	Neg	7Days	0	0	1	0	0	0	0	0	0	0	NAD	NAD
61	30	M	816148	NS1Ag+ve	Neg	Neg	3Days	0	0	1	0	0	0	0	0	0	0	NAD	NAD
62	28	M	818764	IgM+ve	Neg	Neg	7Days	1	0	1	0	0	1	0	0	0	0	NAD	NAD
63	38	F	817822	NS1Ag+ve	Neg	Neg	3Days	1	0	1	0	0	0	0	0	0	0	NAD	NAD
64	40	M	813869	IgM+ve	Neg	Neg	6Months	0	0	0	0	0	0	0	0	0	0	NAD	Rs-reduced BS over interscapular & infrascapular areas. Absent BS over Lt Mammary areas Tubular bronchial BS over (Rt) infraclavicular areas infraclavicular flattening present
65	36	M	813912	NS1Ag+ve	Neg	Neg	2Days	0	0	0	0	0	0	0	0	0	0	NAD	NAD
66	25	M	816151	IgM+ve	Neg	Neg	5Days	1	0	1	0	0	0	0	0	0	0	NAD	NAD
67	48	F	815766	IgM+ve	Neg	Neg	7Days	0	0	0	0	0	0	0	0	0	0	Elevated JVP	B/L Rhonchi & crepts
68	20	F	816162	IgM+ve	Neg	Neg	4Days	0	0	1	0	1	0	0	0	0	0	NAD	NAD
69	38	M	817521	IgM+ve	Neg	Neg	4Days	1	0	1	0	0	0	1	0	0	0	NAD	NAD
70	22	F	817795	NS1Ag+ve	Neg	Neg	4Days	0	0	1	0	0	0	0	0	0	0	NAD	NAD
71	18	M	817191	NS1Ag+ve	Neg	Neg	7Days	0	0	0	0	0	0	0	0	0	0	NAD	NAD
72	55	F	817208	IgM+ve	Neg	Neg	7Days	1	0	1	0	0	1	1	1	0	0	Hr-48/min	NAD
73	23	M	817509	NS1Ag+ve	Neg	Neg	4Days	1	0	1	0	0	0	0	1	0	0	NAD	NAD
74	18	F	808577	NS1Ag+ve	Neg	Neg	7Days	0	0	1	0	0	0	0	0	0	0	NAD	NAD
75	25	M	770352	IgM&IgG+ve	Neg	Neg	5Days	1	0	0	0	0	0	0	0	0	0	NAD	NAD
76	45	M	817122	IgM+ve	Neg	Neg	15Days	1	0	1	1	0	1	0	0	0	0	NAD	NAD
77	40	M	807987		Neg	Neg	5Days	1	0	1	0	0	1	0	1	0	0	NAD	NAD
78	22	M	807404	IgM+ve	Neg	Neg	5Days	0	0	0	0	0	0	0	0	0	0	NAD	NAD
79	40	M	807395	IgM+ve	Neg	Neg	2Days	0	0	1	0	0	0	0	0	0	0	NAD	NAD
80	40	F	809001	IgM+ve	Neg	Neg	3Days	0	0	0	0	0	0	0	1	0	0	JVP - Elevated,myocarditis	NAD
81	32	M	807743	IgM+ve	Neg	Neg	6Days	1	0	1	1	0	0	0	0	0	0	NAD	NAD
82	38	M	821793	IgM+ve	Neg	Neg	4Days	1	0	1	0	0	0	0	0	0	0	NAD	NAD
83	55	F	81786	IgM+ve	Neg	Neg	5Days	1	0	1	0	0	0	0	0	1	0	NAD	NAD

Sl. No.	PA	CNS	Sub-con	Haem	EPI	Gum b	Hemate Mesis	Malena	Petechiae	Bleeding PV	PLT's Transfused	Hb	TLC	TLC N	L	E	M	B	PCV	PLT	PBS
1	Epigastric tenderness	NAD	0	0	0	0	0	0	0	0		16.2	6500						47.1	86000	Normocytic Normochromic picture with Thrombocytopenia
2	Mild hepatomegaly	NAD	0	0	0	0	0	0	0	0		7.3	6400	62	30	08			24.7	264000	Dimorphic Anemia
3	Hepatomegaly(+)	NAD	0	0	0	0	0	0	0	0		13.9	2400	58	40	02			40.9	35000	Normocytic Normochromic picture with Leucopenia and Thrombocytopenia
4	Tenderness(+) Hepatomegaly & Splenomegaly	NAD	1	0	0	0	0	0	1	0	2Units	16.4	13900	46	15	3	26	10	49.5	9000	Normocytic Normochromic Picture with Leukocytosis & severe Thrombocytopenia
5	Splenomegaly	NAD	0	0	0	0	0	0	0	1		12.2	2700	78	19	03			36.5	130000	Nomocytic Normochromic Picture With Leucopenia & Thrombocytosis
6	Mild Splenomegaly	NAD	0	0	0	0	0	0	0	0		14.0	2000	43	50		7		41.1	160000	Normocytic Normochromic picture with Leucopenia & Thrombocytopenia
7	NAD	NAD	0	0	0	0	0	0	0	0		16.7	6900	33	57	6	4		50.6	30000	Normocytic Normochromic picture with Thrombocytopenia
8	Mild Splenomegaly	NAD	0	0	0	0	0	0	0	0		19.9	7300	74	19	01	4	02	58.8	17000	Normocytic Normochromic picture with Thrombocytopenia
9	NAD	NAD	0	0	0	0	0	0	0	0		12.7	3200	79	18	03			38.4	157000	Normocytic Normochromic picture with Thrombocytoena & Polycythemia
10	Minimal tenderness (+) over Rt hypochondriac region	NAD	0	0	0	0	0	0	0	0	3Units	19	6700	67	30	03			55.1	6000	Normocytic Normochromic picture with Leucopenia & Polycythemia
11	NAD	NAD	0	0	0	1	0	0	1	0	6Units	12.7	1500	58	40	02			37.8	120000	Thrombocytopenia
12	Hepatomegaly(+)	NAD	0	0	0	0	0	0	0	0		16.2	3600						47.3	32000	Normocytic Normochromic picture with Thrombocytopenia
13	Hepatomegaly,Splenomegaly&Tenderness over Rt hypochondriac region	NAD	0	0	0	0	0	0	0	1	2Units	14.0	8400	54	33		7	06	40.8	100000	Normocytic Normochromic picture with Leucopenia with Shift to left
14	Tenderness(+)over Rt hypochondriac region	NAD	0	0	0	0	0	0	0	1	6Units	12.5	7100	30	56		10	04	37.4	15000	Normocytic Normochromic picture with Neutropenia & Thrombocytopenia
15	NAD	NAD	0	0	0	0	0	0	0	0		14.6	2000	61	30	04	5		44.8	100000	Normocytic Normochromic picture with Leucopenia & Thrombocytopenia
16	NAD	NAD	0	0	0	0	0	0	0	0		12.1	7900	40	50	02	8		37.0	332000	Normocytic /Macrocytic Pioture
17	Hepatomegaly(+) Shifting dullness Splenomegaly	NAD	1	0	1	0	0	0	0	0	3 Units	11.7	15400	35	55	04	2	04	34.0	70000	Normocytic Normochromic picture with Leucocytosis & Thrombocytopenia
18	NAD	NAD	0	0	0	0	0	0	0	0		15.1	3800	48	40	10	2		44.9	100000	Normocytic Normochromic picture with Leucopenia & Thrombocytopenia
19	NAD	NAD	0	0	0	0	0	0	0	0		13.3	4600						39.2	84000	Normocytic Normochromic Blood picture with Thrombocytopenia
20	NAD	NAD	0	0	0	0	0	0	0	0		11.5	2200						34.7	39000	Normocytic Normochromic Blood picture with Thrombocytopenia
21	NAD	NAD	0	0	0	0	0	0	0	1	4 Units	14.5	2800					08	42.9	22000	Normocytic Normochromic picture with Leucopenia & Thrombocytopenia
22	NAD	NAD	0	0	0	0	0	0	0	0		16.7	5600	61	25		6	02	49.9	45000	Normocytic Normochromic picture with Thrombocytopenia
23	Abdomen Distended, Shifting dullness(+)	NAD	0	0	0	0	0	0	0	1	8Units	17	7300	76	20		2		49.9	40000	Normocytic Normochromic picture with Thrombocytopenia
24	Hepatomegaly(+)	NAD	0	0	0	0	0	0	1	0	11Units	16.0	6400						47.0	3000	Normocytic Normochromic Blood picture with severe Thrombocytopenia
25	NAD	NAD	0	0	0	0	0	0	0	0	3Units	10.6	4500	87	12	01			32.5	304000	Normocytic Normochromic picture with Thrombocytopenia
26	NAD	NAD	0	0	0	0	0	0	0	0		16.1	4700	54	43	03			48.4	50000	Normocytic Normochromic Picture with Thrombocytopenia
27	NAD	NAD	0	0	1	0	0	0	0	0		11.8	5500	69	30	01			34.7	2.36L	Normocytic Normochromic Picture
28	Hepatomegaly(+)	NAD	0	0	0	0	0	0	0	0		9.5	11300	75	23	02			29.3	5.95L	Normocytic Normochromic Picture with Leukocytosis & Thrombocytosis
29	Hepatomegaly(+) Shifting Dullness(+)	NAD	0	0	0	0	0	0	1	0		15.9	9500	31	58	11			47.8	11000	Normocytic Normochromic Picture with Reactive Lymhocytosis & Relative Eosinophilia
30	Hepatomegaly(+)	NAD	0	0	0	0	0	0	0	0		3.1	3800	18	62	02	6	08	8.8	74000	Dimorphic Anemia with Leucopenia & Thrombocytopenia
31	Soft, Diffuse Tenderness(+)	NAD	0	0	0	0	0	0	1	0		15.9	5700	40			10	5	48.0	75000	Normocytic Normochromic picture with Thrombocytopenia
32	NAD	NAD	0	0	0	0	0	0	0	0		12.9	6400	60	45	02	7	04	37.8	20000	Normocytic Normochromic Picture
33	NAD	NAD	0	0	0	0	0	0	0	0		13.9	7800	53	42	05			41.8	20000	Normocytic Normochromic Blood picture with Thrombocytopenia
34	NAD	NAD	0	0	0	0	0	0	1	0		13.9	6700	52	40	08			39.0	1.76L	Normocytic Normochromic picture with Eosinophilia
35	NAD	NAD	0	0	0	0	0	0	0	0		10.9	4700	60	40				29.6	45000	Microcytic hypochromic anemia with Thrombocytopenia
36	NAD	NAD	0	0	0	0	0	0	0	0		10.7	9800	61	40		2	02	30.7	210000	Normocytic Normochromic Anemia
37	NAD	NAD	0	0	0	0	0	0	0	0		13.9	4100	76	35	02	2		39.6	51000	Normocytic Normochromic picture with Thrombocytopenia
38	Hepatomegaly(+)	NAD	0	0	0	0	0	0	0	0		14.9	4600						41.7	23000	Normocytic normochromic picture with thrombocytopenia
39	Hepatomegaly(+)	NAD	0	0	0	0	0	0	0	0		13.4	4900	68	20		3	02	38.2	20000	Normocytic Normochromic picture with Thrombocytopenia
40	Splenomegaly	NAD	0	1	0	0	0	0	0	0		16.3	5900	76			3		47.5	120000	Normocytic Normochromic picture with Neutrophilia and Thrombocytopenia
41	Hepatomegaly(+) Shifting Dullness(+)	NAD	0	0	0	0	0	0	0	0		14.2	4000	85	27				42.0	150000	Normocytic Normochromic picture with Thrombocytopenia
42	Hepatomegaly(+)	NAD	0	0	0	0	0	0	0	0		15.9	5700	40	21		10	03	46.3	75000	Normocytic Normochromic picture with Leucopenia
43	Hepatomegaly(+)	NAD	0	0	0	0	0	0	1	0		13.9	1500		15				41.3	60000	Normocytic Normochromic picture with Leucopenia and Thrombocytopenia
44	NAD	NAD	0	0	0	0	0	0	0	0		13	6700	40	45	10			38.4	86000	Normocytic Normochromic picture with Thromocytopenia
45	NAD	NAD	0	0	0	0	0	0	0	0		13.5	3200						39.2	11000	Normocytic normochromic picture with leucopenia & Thrombocytopenia
46	NAD	NAD	0	0	0	0	0	0	0	0		12.1	5700	70	50		3		34.9	203000	Normocytic Normochromic picture
47	NAD	NAD	0	0	0	0	0	0	0	0		11.5	7700	88		02			35.0	198000	Normocytic Normochromic picture with Neutrophilia
48	NAD	NAD	0	0	0	0	0	0	1	0		16.5	5700	50	27	06	8		48.0	30000	Normocytic Normochromic picture
49	NAD	NAD	0	0	0	0	0	0	0	0		8.4	3000	53	10		3		25.0	71000	Normocytic Normochromic picture with Leucopenia
50	NAD	NAD	0	0	0	0	0	0	0	0		16.4	2700		36				48.4	80000	Normocytic normochromic picture with Leucopenia & Thromocytopenia
51	NAD	NAD	0	0	0	1	1	1	1	0		15	3900		44				44.2	224000	Normocytic normochromic picture with mild leucopenia
52	NAD	NAD	0	0	0	0	0	0	0	0		10	1900						27.8	20000	Pancytopenia
53	Severe Tenderness in Epigastric region	NAD	0	0	0	0	0	0	1	0		14	15700	65	30	3	2		39.6	24000	Normocytic Normochromic picture with Reactive Lymphocytosis and Thrombocytopenia
54	NAD	NAD	0	0	0	0	0	0	0	0		11.1	2900	58	40	2			33.2	55000	Normocytic Normochromic picture with Leucopenia, Relative Neutropenia, Hypersegmented Neutrophils & Thrombocytopenia
55	NAD	NAD	0	0	0	0	0	0	1	0		15.1	11000	69	25	6			42.4	15000	Normocytic Normochromic picture with Thrombocytopenia
56	Hepatomegaly	NAD	0	0	0	0	0	0	0	0		19.5	5200	58	35		5	2	57.0	4000	Normocytic Normochromic picture with Thrombocytopenia
57	NAD	NAD	0	0	0	0	0	0	0	0		17.7	23000	40	50		4	6	52.2	80000	Normocytic/Macrocytic, Normochromic with Leucopenia and Thrombocytopenia
58	Soft, uterus not Palpable	NAD	0	0	0	0	0	0	0	0		8.1	4300	64	30	4			26.4	150000	Normocytic normochromic anemia
59	NAD	NAD	0	0	0	0	0	0	1	0		13.7	2000						38.5	59000	Leucopenia & Thrombocytopenia
60	NAD	NAD	0	0	0	0	0	0	0	0		15.3	10600	52	45	03			45.7	21000	Reactive Lymphocytosis & Thrombocytopenia
61	Diffuse Tenderness(+)	NAD	1	0	1	0	1	0	0	0		15.4	4500						43.6	38000	Thrombocytopenia
62	Hepatomegaly(+)	NAD	1	0	0	0	0	0	0	0		12.6	7500						37.8	108000	Normocytic Normochromic picture with Thrombocytopenia
63	NAD	NAD	0	0	0	0	0	0	0	0		10.8	6100	82	18				31.2	160000	Normocytic Normochromic Anemia
64	NAD	NAD	0	0	0	0	0	0	0	0		14.2	6000	70	30				42.4	27000	Normocytic Normochromic Blood picture with Thrombocytopenia
65	Splenomegaly Castell's point dullness. Miniminal Distension(+)	NAD	0	0	0	0	0	0	0	0		17.1	5700	55	42	3			51.5	30000	Normocytic Normochromic Picture with Thrombocytopenia
66	NAD	NAD	0	0	0	0	0	0	0	0		14.5	6100	66	30	2	2		41.5	181000	Normal study
67	NAD	NAD	0	0	0	0	0	0	0	0		10.4	12200	60	35	5			31.3	71000	Normocytic Normochromic Anemia with Leukocytosis & Thrombocytopenia
68	NAD	NAD	0	0	0	0	0	0	0	0		12.7	3600	42	48	03	5	2	38.6	116000	Normocytic Normochromic picture with Leucopenia & Thrombocytopenia
69	NAD	NAD	0	0	0	0	0	0	0	0		15.2	5800	52	42		6		42.7	60000	Normocytic Normochromic picture with Thrombocytopenia
70	NAD	NAD	0	1	0	0	0	1	0	0		11.5	2200	63	34	02	1		33.1	19000	Normocytic Normochromic picture with Leucopenia & Thrombocytopenia
71	NAD	NAD	0	0	1	1	0	1	0	0		10	3200	64	32	02	2		28.2	24000	Normocytic Normochromic Anemia with Leucopenia & Thrombocytopenia
72	Hepatomegaly(+)	NAD	0	0	0	0	0	0	0	0		13.3	11200	58	38		4		37.6	36000	Normocytic Normochromic picture
73	Hepatosplenomegaly(+)	NAD	0	0	0	0	0	1	0	0		16.7	3000	40	57	03			46.7	15000	Normocytic Normochromic picture with Leucopenia Thrombocytopenia
74	NAD	NAD	0	0	0	0	0	0	0	0		13	77000	57	34		7	2	39.2	30000	Normocytic Normochromic picture with Thrombocytopenia
75	NAD	NAD	0	0	0	0	0	0	0	0		16.5	6700	43	50	05	2		49.8	151000	Normocytic Normochromic picture
76	Hepatomegaly	NAD	0	0	0	0	0	0	0	0		12.1	6300	76	19	02	3		35.5	167000	Normocytic Normochromic picture
77	Hepatosplenomegaly	NAD	0	0	0	0	0	0	0	0		14.9	10900	33	35	03	5		46.1	11000	Normocytic Normochromic picture with Thrombocytopenia
78	NAD	NAD	0	0	0	0	0	0	0	0		16.5	2600						48.7	18000	Normocytic Normochromic picture with Leucopenia
79	NAD	NAD	0	0	0	0	0	0	0	0		14.9	2700	72	23		3	02	44.6	49000	Normocytic Normochromic picture with Leucopenia Thrombocytopenia
80	Epigastric tenderness	NAD	0	0	0	0	0	0	0	0		13.4	7900						40.1	53000	Thrombocytopenia
81	NAD	NAD	0	0	0	0	0	0	0	0		16.5	6600	72	25		2	01	48.7	173000	Normocytic Normochromic picture
82	NAD	NAD	0	0	0	0	0	0	0	0		17.7	5400	46	44		6	4	53.3	16000	Normocytic Normochromic picture with Thrombocytopenia
83	NAD	NAD	0	0	0	0	0	0	0	0		12.3	2400	50	37	2	4	5	38	90000	Normocytic Normochromic picture Leucopenia and Thrombocytopenia

Sl. No.	PLATELET COUNTS D1	D2	D3	D4	D5	D6	D7	LFT STB	DB	SGOT	SGPT	ALP	GGT	TP	ALB	GLB	A/G	PT Test	PT Ctrl	Ratio	INR	PTT Test	PTT Ctrl	USG	CXR
1	86000																								
2	264000	130000			144000			0.52	0.08	33	40	78	58	5.7	3.0	2.7	1.1								
3	35000		20000	60000			150000																		
4	9000							0.7	0.2	1570	470	147	193	6.0	2.4	3.6	0.7							Nothing significant	
5	130000	60000																							
6	160000																								
7	30000	75000	58000					0.9	0.2	65	73	318	141	7.0	3.1	3.9	0.8	13.7	13.5	1.01	1.02	26.8	33.8		
8	17000		50000			255000																			
9	157000	150000	100000		24000	30000																			
10	6000							0.44	0.23	151	115	89	229	5.1	2.6	2.5	1.0								Rt sided Pleural Effusion
11	120000		120000	195000																					
12	32000	20000	30000		75000		115000																		
13	100000	10000	12000	30000	1.5L	1.5L	2L																	Moderate ascites, pod collection, Minimal Rt sided Pleural effusion	Rt sided Pleural Effusion
14	15000		102000					0.65	0.2	267	125	99	294	5.5	2.7	2.8	1.0	12.1	13.0	0.93	0.91	54.3	33.8		Right sided pleural effusion.
15	100000																								
16	332000																	11.4	13.0	0.87	0.85	30.1	33.8	Hepatomegaly crepts(+) Fattychanges Splenomegaly & Ascites	
17	70000	30000			19000		D10-10200	2.1	2.0	425	178	376	611	5.5	2.5	3.8	0.8	13.3	14.0	1.02	1.02	30.0	33.8		
18	100000	50000																							
19	84000		45000	74000	150000			4.3	2.6	108	82	165	451	6.5	3.4	3.1	1.1	14.6	13.5	1.16	1.21	37.0	33.8	Nothing significant	
20	39000		63000	80000																				Mild Splenomegaly, Rt minimal Pleural Effusion mildly thickened GB wall	
21	22000	20000	40000					0.63	0.51	122	110	184	500	5.8	2.8	3.0	0.9	14.6	13.5	1.16	1.14	25.8	33.8	Hepatomegaly fattychanges	
22	45000	52000			102000			0.5	0.3	395	219	75	109	6.3	3.1	3.2	0.9	16.9	13.5	1.25	1.35	28.4	33.8		
23	40000		90000	67000	94000																			Moderate Ascites B/L pleural effusion	
24	3000	30000			165000																			Hepatomegaly & splenomegaly Moderate Ascites	
25	204000	1.5L	36000	31000	60000	75000	160000	0.34	0.18	72	33	66	50	6.0	3.0	3.0	1.0	12.5	13.0	0.96	0.95	45.2	33.8		
26																									
27	2.36L	1.60L	81000		20D2L													14.7	14	1.09	1.12	30.2	33.8		
28																								Hepatomegaly with Fatty changes	
29	11000	20000	60000	80000				2.1	1.4	174	45	112	364	4.9	2.4	2.6	0.9							Mild splenomegaly Moderate Ascites B/L pleural Effusion	
30	74000	140000						3.2	0.3	91	45	26	10	6.4	3.9	2.5	1.5								
31																									
32	20000		18000		1.5L																				
33	20000	40000	70000	61000	1.5L																				
34	176000			215000																					
35	45000	130000				173000		0.56	0.10	94	190	222	130	5.7	2.6	3.1	0.8								
36																									
37	51000	38000																							
38	23000	43000			103000																				
39								8.6	7.0	111	81	145		5.1	1.9	3.3	0.6	18.2	13.5	1.35	1.49	39.1	33.8		
40	120000		15000	11000	45000			0.39	0.12	108	46	88	126	4.5	2.2	2.2	1	18.6	13.8	1.38	1.54	42.6	33.8		
41	150000	63000	30000	25000	40000	150000		0.5	0.3	96	43	110	116	5.3	2.5	2.8	0.9	17.3	13.8	1.28	1.39	32.6	33.8		
42	75000	58000	150000					2.1	0.6	164	32	48	111	6.7	3.1	3.6	0.9	15.4	13.8	1.14	1.19	29.3	33.8		
43	60000			40000			187000											14.2	13.0	1.09	1.10	29.4	33.8		
44	86000							0.3	0.1	30	28	6	18	7.1	3.4	3.6	0.9	12.1	13.5	0.93	0.91	31.8	33.8		Right sided pleural effusion
45	11000	80000	60000					0.35	0.18	71	58	125	74	5.9	2.8	3.1	0.9								
46	203000		230000	160000				0.2	0.16	92	74	99	70	6.9	3.5	3.4	1.0	15.6	13.5	1.16	1.21	28.9	33.8		
47	198000	156000						0.43	0.2	76	43	59	33	6.9	3.4	3.5	1.0								Right sided pleural effusion
48	30000		21000	31000			96000																		
49	71000																								
50	80000		140000					1.0	0.2	116	147	88	82	7.2	4	3.2	1.2	12.6	13.8	0.93	0.91	30.3	33.8		
51	224000																								
52	20000		60000	76000														12.6	13.5	0.96	0.96	41.3	33.8		
53	24000	29000	64000		162000																				Normal
54	55000		45000		45000			0.3	0.17	115	57	43	159	6.3	2.9	3.4	0.8	12.1	13.5	0.93	0.91	40.1	33.8		Normal
55	15000	10000	25000	20000	65000	20000	19000																		
56	4000	11000	40000	70000				1.0	0.14	139	69	118	5.7	5.9	2.9	3.0	1.0	13.4	13.8	0.99	0.99	37.4	33.8		
57	80000							0.7	0.4	30	28	77	17	3.6	3.1	3.3	0.9	15.2	13.5	1.13	1.17	31.7	33.8		
58	150000																							Early IUG Corresponding to [illegible]	
59	59000		29000	80000	90000													13.7	13.5	1.01	1.02	37.9	33.8		
60	21000	60000																							
61	38000	23000	7000	10000	20000	62000	120000																		
62	108000																							Mild splenomegaly	
63	160000	130000																							
64	27000						220000																		
65	30000							1.7	0.7	162	109	182	317	6.9	3.2	3.6	0.9							Hepatosplenomegaly Mild Rt sided effusion. Moderate ascites	
66	181000																	14.5	13.5	1.07	1.1	28.2	33.8		
67	71000	75000			151000			0.36	0.21	129	57	117	77	6.6	3	3.6	0.8								
68	116000	112000						0.37	0.29	78	68	87	76	7.9	3.8	4.1	0.9	13.7	13.5	1.01	1.02	28.8	32.8		
69	60000																								
70	19000	30000	40000		125000		270000											26.7	13.5	1.98	2.49			Mild ascites	
71	24000	97000	150000															16.5	13.5	1.22	1.31	38.1	33.8		
72	36000	45000	30000	60000	90000	121000	202000																		
73	15000	15000																							
74	30000	180000																							
75																									
76	167000				193000	160000		1.1	0.3	95	71	142	130	6.2	3.1	3.1	1.0								
77	11000	45000			228000			0.5	0.2	119	122	133	118	5.6	2.5	2.8	1.0							Hepatosplenomegaly(+) Minimal Ascites	
78	18000	20000	60000																						
79	40000	119000																							
80	53000																								
81																									
82	16000	15000	45000	55000																					
83	90000																								

84	28	F	822143	IgM+ve	Neg	Neg	4Days	1	0	1	1	0	0	1	0	1	0	NAD	NAD	NAD	NAD	0	0	0	0	0	0	0	0		9	2400	58	36	2	4		29.3	120000	Microcytic/Normocytic Hypochromic anemia with Leucopenia and Thrombocytopenia	120000	150000																							
85	30	M	822454	IgM+ve	Neg	Neg	7Days	0	0	1	1	0	0	0	0	0	0	HR-52/min	NAD	NAD	NAD	0	0	0	0	0	0	0	0		16.5	5600						48.8	80000	Normocytic Normochromic picture with Thrombocytopenia	80000	93000	105000																						
86	46	M	820042	IgM+ve	Neg	Neg	10Days	0	0	1	0	0	0	1	0	0	0	NAD	NAD	Hepatosplenomegaly	NAD	1	1	0	0	0	0	0	0		14.7	11700						44.7	225000	Normocytic Normochromic picture with leukocytosis	225000	280000																						Hepatosplenomegaly(+)	
87	19	F	820010	IgM+ve	Neg	Neg	2Days	0	0	1	1	0	0	0	0	0	0	NAD	NAD	NAD	NAD	0	0	0	1	0	0	0	0		13.2	3700	68	30		2		40.1	86000	Normocytic Normochromic picture with Leucopenia Thrombocytopenia	86000																								No significant abnormality	
88	75	M	820298	NS1Ag+ve	Neg	Neg	7Days	1	0	1	1	0	0	0	0	1	0	NAD	NAD	NAD	NAD	0	0	0	0	0	0	0	0		14.3	4100	57	36	4	3		44.3	18000	Macrocytic/Normocytic Normochromic picture with Thrombocytopenia	18000	75000																							
89	21	F	820303	NS1Ag+ve	Neg	Neg	3Days	0	0	0	1	0	0	0	0	1	0	NAD	NAD	NAD	NAD	0	0	0	0	0	0	0	0		12.8	2600	69	27	2	2		39.4	50000	Normocytic Normochromic picture with Leucopenia	50000																								
90	28	M	820015	IgM&IgG+ve	Neg	Neg	5Days	0	0	1	0	1	1	1	1	0	0	NAD	NAD	Hepatomegaly	NAD	0	0	0	0	0	0	0	0		17.1	3400	30	63	3	4		50.7	40000	Normocytic Normochromic picture with Leucopenia and severe Thrombocytopenia	40000	35000	45000	100000	90000	140000	160000																	Hemangioma in right lobe of liver	
91	35	F	820979	IgM+ve	Neg	Neg	5Days	1	0	1	1	0	0	0	0	1	0	NAD	NAD	NAD	NAD	0	0	0	0	0	0	0	0		14.1	4900	49	43	4	4		43	45000	Normocytic Normochromic picture with Thrombocytopenia	45000																								
92	35	M	821460	NS1Ag+ve	Neg	Neg	2Days	0	0	0	1	0	0	0	1	1	0	NAD	NAD	NAD	NAD	1	0	0	0	0	1	0	0	14 units	15.3	2600	57	37	2	4		45.5	7000	Normocytic Normochromic picture with Leucopenia and severe Thrombocytopenia	7000	5000	8000	47000																					
93	35	M	820965	IgM+ve	Neg	Neg	3Days	1	0	0	0	0	0	0	0	0	0	NAD	NAD	NAD	NAD	0	0	0	0	0	0	0	0		16.7	5200	76	21	2	1		50.3	75000	Normocytic Normochromic picture with Thrombocytopenia	75000	60000	80000	81000																					
94	40	F	820975	IgM+ve	Neg	Neg	5Days	1	0	1	0	0	0	0	1	0	0	NAD	NAD	Severe Epigastric tenderness	NAD	0	0	0	0	0	0	0	0		13.8	1800	65	30	3	2		42.5	45000	Normocytic Normochromic picture with Leucopenia and Thrombocytopenia	45000	22000	30000																						
95	25	F	820989	NS1Ag+ve	Neg	Neg	7Days	0	0	1	1	0	0	0	0	1	0	NAD	B/L Basal crepts (+) Pleural Rub	NAD	NAD	0	1	0	0	0	0	0	0		15.9	14500	51	42	1	2		47.8	40000	Normocytic Normochromic picture with leukocytosis and Thrombocytopenia	60000	110000																							
96	29	M	821103	NS1Ag+ve	Neg	Neg	5Days	0	0	0	0	0	1	0	1	1	0	NAD	NAD	NAD	NAD	0	0	0	0	0	0	0	0		15.4	5700						47	70000	Normocytic Normochromic picture with Thrombocytopenia	70000	227000						0.3	0.04	93	47	45	26	6.3	3.2	3.1	1							No significant abnormality	
97	18	F	820980	NS1Ag+ve	Neg	Neg	2Days	1	0	0	0	0	0	0	0	1	0	NAD	NAD	NAD	NAD	0	0	0	0	0	0	0	0		11.4	3600	73	21	4	2		34.3	130000	Macrocytic Anemia With Mild Leucopenia and Mild Thrombocytepenia	130000	82000	25000	20000	40000																				
98	21	M	820112	NS1Ag+ve	Neg	Neg	5Days	0	0	1	0	0	0	0	0	1	0	NAD	NAD	NAD	NAD	0	0	0	0	0	0	0	0		16.4	4700	46	40	3	11		50.6	58000	Normocytic Normochromic picture with Thrombocytopenia	58000	90000	140000																						
99	35	M	820359	NS1Ag+ve	Neg	Neg	5Days	1	0	1	1	0	0	0	1	0	0	NAD	NAD	NAD	NAD	0	0	0	0	0	0	0	0		16.7	5000	65	27		5	3	50.4	125000	Normocytic Normochromic picture with Thrombocytopenia	125000			150000																					
100	35	M	820361	IgM+ve	Neg	Neg	3Days	0	0	0	0	0	0	0	1	0	0	NAD	Decreased intensity of BS Over Right Basal areas	Shifting Dullness present Diffuse Tenderness Present	NAD	0	0	0	0	0	0	0	0	4 units	17.2	3100						51.9	30000	Normocytic/Macrocytic, blood picture with Mild Leucopenia and Thrombocytepenia	30000	25000		35000	80000													16.9	13.5	1.25	1.35	29.2	33.8	Hepatomegaly with fatty changes,GB wall thickening,Bilateral pleural effusion,moderate ascites	Right sided pleural effusion
101	18	M	820459	IgM&IgG+ve	Neg	Neg	4Days	1	0	1	0	0	0	0	1	0	0	NAD	NAD	NAD	NAD	0	0	0	0	0	0	0	0		13.1	6800	32	57	7	2	2	39.7	120000	Normocytic Normochromic picture with Thrombocytopenia with reactive Lymphocytes	120000	138000						0.3	0.1	48	69	87	20	6.4	3.3	3.1	1.1								
102	38	M	817141	IgM+ve	Neg	Neg	10Days	1	0	1	1	0	1	1	0	0	0	NAD	NAD	Hepatomegaly	NAD	0	0	0	0	0	0	0	0		15.2	4900	60	37	3			43.2	133000	Normocytic Normochromic picture with Thrombocytopenia	133000	256000	45000		130000																				
103	26	F	818806	NS1Ag+ve	Neg	Neg	5Days	1	0	1	0	0	0	0	0	1	0	NAD	NAD	NAD	NAD	0	0	0	0	0	0	0	0		13.2	5400	56	31		9	4	38.2	57000	Normocytic Normochromic picture with Thrombocytopenia	57000	60000																							
104	28	M	818764	IgM+ve	Neg	Neg	7Days	1	0	1	1	0	1	0	0	0	0	NAD	NAD	Hepatomegaly	NAD	0	0	0	0	0	0	0	0		12.6	7500	75	17	2	6		38	108000	Normocytic Normochromic picture with Thrombocytopenia	108000	130000																							
105	24	M	817828	IgM+ve	Neg	Neg	4Days	0	0	1	1	0	0	0	0	1	0	NAD	NAD	NAD	NAD	0	0	0	0	0	0	0	0		12.2	2700	45	43	2	4	3	32.7	110000	Normocytic Normochromic picture with Leucopenia and Thrombocytopenia	110000	79000																						Hepatomegaly with fatty changes	
106	34	M	817796	IgM+ve	Neg	Neg	7Days	0	0	1	1	0	0	0	0	0	0	NAD	NAD	NAD	NAD	0	0	0	0	0	0	0	0		14	13400	56	39	1	2	2	38.7	15000	Normocytic Normochromic picture with Leukocytosis and severe Thrombocytopenia	15000	15000	20000	45000	110000	124000																			
107	25	F	817517	IgM+ve	Neg	Neg	6Days	0	0	1	0	0	0	0	0	0	0	NAD	Absent BS Over Right Basal areas	NAD	NAD	0	0	0	0	0	0	0	0	4 Units	10.9	13800	60	35	1	2	2	35.2	12000	Normocytic Normochromic picture with Leukocytosis and severe Thrombocytopenia	12000	37000	200000																					Right sided pleural effusion.Minimal Ascites	Right sided pleural effusion