"ROLE OF CLINICO HAEMATOLOGICAL PROFILE IN DIAGNOSIS OF DENGUE - ONE YEAR HOSPITAL BASED OBSERVATIONAL STUDY"

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LIST OF ABBREVIATIONS USED

/Cumm	-	Per cubic millimeter
°C	-	Degree centigrade
AD	-	Anno Domini
ADE	-	Antibody-dependent enhancement
AIIMS	-	All India Institute of Medical Sciences
ALP	-	Alkaline phosphatase
ALT	-	Alanine transaminase
AMAF	-	American African
AST	-	Aspartate amino transferase
C	-	Core protein
CBC	-	Complete blood count
CI	-	Confidence interval
DCs	-	Dendritic cells
DEN 1	-	Dengue Type 1
DEN2	-	Dengue Type 2
DEN3	-	Dengue Type 3
DENV	-	Dengue virus
DF	-	Dengue fever
DHF	-	Dengue hemorrhagicfever
DIC	-	Disseminated intravascular coagulation
DSS	-	Dengue shock syndrome
DV	-	Dengue virus
E	-	Envelope protein
e.g.	-	For example
ELISA	-	Enzyme-linked immunosorbent assay

etc.	-	Etcetera
gm%	-	Gram percentage
Hb	-	Haemoglobin
hrs	-	Hours
i.e,	-	Thatis,
IFN	-	Interferon
IgG	-	Immunoglobulin G
IgM	-	Immunoglobulin M
IL	-	Interleukin
IU/L	-	International units per liter
kb	-	kilo byte
L	-	Liter
LFT	-	Liver function tests
M	-	Membrane associated protein
MIP	-	Macrophage inflammatory protein
MPV	-	Mean platelet volume
mAb	-	Monoclonal antibody
meq/L	-	Milli equivalent per liter
mg/dL	-	Milligram per deciliter
mmHg	-	Millimeters of mercury
mm^3	-	Cubic millimeter
mmol/L	-	Millimole perliter
n	-	Total number
NVBDCP	-	National Vector Borne Disease Control Programme
Nm	-	Nanometer
NS	-	Non-structural protein
p	-	Probability

PAHO	-	Pan American Health Organization
PCV	-	Packed cell volume
PCR	-	Polymerase chain reaction
RBC	-	Red blood cell
RDTs	-	Rapid Diagnostic Tests
RT-PCR	-	Reverse transcriptase polymerase chain reaction
RNA	-	Ribonucleic acid
r	-	Correlation coefficient
SD	-	Standard deviation
SEA	-	Southeast Asia
SGOT	-	Serum glutamic oxaloacetic transaminase
SGPT	-	Serum glutamic pyruvic transaminase
Sr	-	Serum
Th	-	T helper cells
TLC	-	Total leucocyte count
TGF	-	Transforming growth factor
TNF	-	Tumor necrosis factor
US	-	United States
USA	-	United States of America
WBC	-	White blood cell
WHO	-	World Health Organization
WWII	-	World War II

ABSTRACT

Background and objectives

Dengue Fever (DF) is a self - limiting illness which is spread by the bite of Aedes aegypti mosquitoes. Arbovirus is the causative virus.[1] WHO estimates about 50-100 million dengue cases every year. Nearly 300,000 cases of dengue haemorrhagic fever (DHF) are reported with 24,000 deaths every year. Dengue diagnosis mainly depends on NS-1 antigen detection and IgM antibody detection.[2]

The aim of this study was to assess the haematological parameters along with clinical features in dengue patients to escalate the screening sensitivity by clinicians in severe cases and to recognize the laboratory markers that may assist in the early diagnosis and prognosis.

Methodology

This observational study of one year was conducted in the Department of Pathology, Jawaharlal Nehru Medical College and KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 120 dengue positive patients confirmed through NS1 antigen were studied from January 2018 to December 2018, correlating clinical, haematological and biochemical findings.

Results

Majority of the patients were males (66%). The most commonly affected age group was 14-50 years (70%). Out of 120 cases, 94 patients had DF and 26 had dengue haemorrhagic fever (DHF), none showed signs and symptoms of dengue shock syndrome (DSS).

NS1 was the inclusion criteria. IgM was positive in 77.50% patients. 20.8% patients showed both IgG and IgM positivity.

With regard to clinical features, fever was present in all the patients, followed by arthralgia, itching, severe myalgia, retro orbital pain, abdominal pain, bleeding manifestations and rash. The main haematological findings in all the patients were thrombocytopenia, leucopenia and raised haematocrit, along with raised liver enzymes.

Interpretation and Conclusion

It is important to correlate clinical examination with haematological and biochemical profile in dengue patients. Thrombocytopenia, raised haematocrit and raised liver enzymes are very important to monitor dengue cases for early and rapid diagnosis. This would reduce the morbidity and mortality of severe dengue cases.

Keywords

Dengue fever, Thrombocytopenia, Liver enzymes, Dengue Haemorrhagic fever, NS1 antigen, raised haematocrit.

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INTRODUCTION

Dengue is a mosquito borne disease caused by Arbovirus. In 1780, the first recognized epidemic of dengue occurred in the continents of North America, Asia and Africa concurrently. The first clinical dengue case was reported by Benjamin Rush in the year 1789 as a result of the study of the Philadelphia epidemic that took place in 1780 and he named it as “break-bone fever” because myalgia and arthralgia were the most common symptoms.[1]

With nearly 50 million cases of dengue every year and almost 2.5 billion people inhabiting in dengue primitive countries, without a doubt, it is the most fast spreading vector borne disease currently.[2]

This rampant rise in incidence has now grabbed the attention of public healthcare providers. Lack of vaccine or antiviral drugs has made this disease, which manifests in four serotypes, increasingly dangerous.[3]

The vast majority of dengue fever cases have been reported from America, Western Pacific regions and South-East Asia. Dengue in India was seen only in urban regions initially, however, it is now reported from the rural and peri-urban areas as well.[4]

DENGUE VIRUS (DV) is an enveloped, positively charged single stranded RNA virus belonging to the family of “Flaviviridae”. It consists of four serotypes; DV-I, DV-II, DV-III, and DV-IV. It is composed of three structural protein genes - an envelope glycoprotein (E), a membrane protein (M) and seven structural proteins that are non-stranded (NS). Aedes aegypti mosquito is the main transmitter of dengue

virus. All the four mentioned serotypes can cause diseases ranging from self limiting dengue fever (DF) which is mild in nature, to severe, potentially fatal dengue haemorrhagic fever or dengue shock syndrome (DHF/DSS).[1]

Dendritic cells and macrophages are the first to get infected and are recreated in regional lymph nodes, followed by 4 to 10 days incubation period during which the infection spreads through blood and lymphatic vessels.

Dengue fever has 3 stages:

1. Febrile stage
2. Critical stage
3. Recuperation stage

Febrile stage begins with high grade fever accompanied by pain around the retro orbital region, arthralgia and severe myalgia ("break-bone fever"), along with nausea as well as vomiting. Maculopapular rashes arequite commonly seen in youngsters towards the end of the febrile stage.[5]

In some cases, the disease escalates into a potentially fatal form hallmarked by haemorrhage, reduced platelet count, and blood plasma leakage resulting in Dengue shock syndrome.[3]

Early detection of dengue is essential for the subsequent management. Serological tests are widely used in general practice with dengue IgG and IgM being the two main types.The level of accuracy of these tests depends on the sample collection time. Usually IgG/IgM ELISA are helpful in confirming the clinical diagnosis in a short time span which is crucial in severe cases.[6] Other diagnostic

measures such as reverse transcription PCR (RT-PCR) and virus isolation are rather exorbitant and need vast amount of experience and expertise to execute.[7]

NS1 antigen detection is a fresh, up-to-the-minute test for the quick diagnosis of dengue fever. An immunosorbent assay which is enzyme linked is done along with NS1 glycoprotein monoclonal antibody (mAb) in human sera infected with dengue. Immunochromatographic strip kits along with other diagnostic kits have proved to be beneficial in rapid diagnosis of dengue.[8]

The NS1 antigen detected a high level of specificity and sensitivity towards this particular infection. The NS1 and IgM assay combination would further intensify the sensitivity of this test. However, early detection of dengue still remains an obstacle as these assays also have their own demerits.[7]

Till date numerous studies have analysed the clinical manifestations of dengue fever based on its diagnosis either by IgM with IgG or NS1 or using all the three tests. There is a wide variation in clinical profile based on the test used for the detection of dengue. Moreover, there is scanty data on correlation of clinical profile with different haematological and serological diagnostic parameters in dengue fever patients.

The aim of this study was to assess the clinical as well as haematological profile of dengue-affected patients so as to enhance the sensitivity of screening by the health professionals in severe cases and to discover laboratory markers that may specify the evolution and prognosis.

OBJECTIVES

The objective of this study was

1. To study and correlate the role of clinical and haematological profile in the diagnosis of Dengue.
2. To know the relationship of the relevant haematological parameters and clinical manifestations during the course of the disease.

REVIEW OF LITERATURE

Historical perspectives

The word “Dengue” is derived from“Ka-dinga pepo”, a Swahili phrase, which means "cramp-like seizure". In a 992 Chinese Medical Encyclopedia, dengue fever was mentioned as "water poison" because of its association to flying insects.[1]

In the 19th century, the Flavivirus and Alphavirus exanthems were reported commutable as dengue fever, implying that this disease was not of much clinical relevance. The recognition of DHF/DSS was only after these viruses were acclimatized to laboratory animals in the year 1940s with types 1 and 2 viruses and 1950s with types 3 and 4. [9]

A major outbreak took place in 1780, Philadelphia, outbreaks than became frequent in the USA during the beginning of the 20th century finally resolving the causative agent of viral infection and its spread by mosquitoes.[10,11]

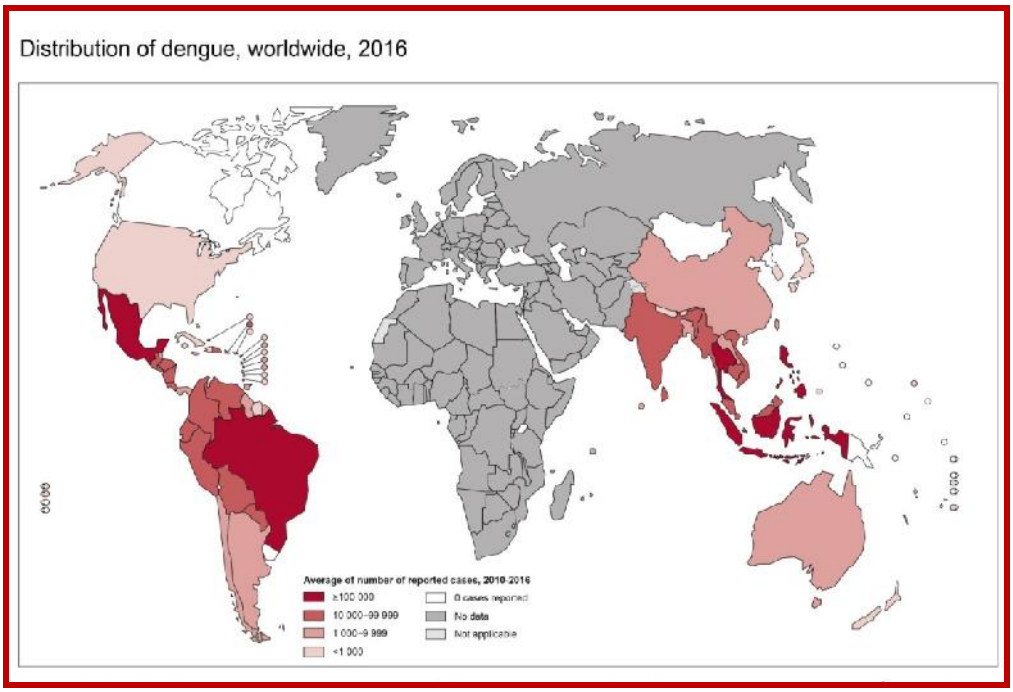
The primary mosquito vector, Aedes aegypti, is considered to be either an Asian or African origin. However, by the 1800’s it was spread all over thetropical urban coastal cities[12] by using vessels shipping for expansion commercially, transporting breeding sites for the vector, allowing transfer of the dengue virus. During World War II (WWII), the disease spread due to utilization of modern transportation by the troops between countries. This made dengue epidemics more extensive. By the end of the war, the virus spread to most of the Southeast Asia (SEA), with unfolding of severe dengue forms.[10,13,14]

In South East Asia, the first case of Dengue haemorrhagic fever was noted in Manila in the year 1953-54, since then outbreaks have been reported throughout Southeast Asia.[15]

Current dengue fever situation

Global

Figure 1 - Dengue cases reported in 2016, geographically distributed according to the World Health Organization (WHO).[15]



Almost 3.6 billion people are residing in subtropical and tropical regions, where transmission of dengue viruses are common. Global estimates differ, but approximately 50-200 million individuals are infected with dengue virus everyday, along with 500,000 cases of dengue with complications and more than 20,000 deaths related to dengue occurring every year.[14]

In the recent years the dengue incidence has increased. A current study has projected around 390 million cases of dengue yearly and among these 96 million show clinical manifestations.[16] Another study estimated that 128 countries with 3900 million people are at dengue virus risk.[17]

However, the actual number of dengue cases globally is uncertain which has led to the start of many campaigns in order to record all the cases and these have shown increased cases in the recent years, with more incidence of several other dengue virus serotypes in different countries and its effect on the health of the human beings as well as the global economy.[18]

The spreading of the virus to new areas led to increase in new cases. In the year 2012, in the Islands of Madeira in Portugal dengue epidemic took place infecting more than 2000 individuals.[18]

Florida along with Yunnan province of China reported dengue cases in the year 2013. After several years cases in Asia and Singapore were reported. Increase in dengue cases was seen in Vanuatu, Fiji, People's Republic of China and Malaysia affecting the Pacific Island countries in the year 2014, after over a 10 years lapse.[18]

In Delhi, India, the year 2015 reported its worst outbreak with above 15,000 dengue positive cases. Hawaii and USA also reported 181 dengue cases in the year 2015 with a continuation in 2016.[15]

Large outbreaks of the virus were recorded worldwide in the year 2016. The Western Pacific Region and the American region reported more 3,75,000 and 2.38 million respectively, among which 1,76,411 cases were reported by the Philippines and 1,00,028 cases by Malaysia.[15]

The year 2017 showed significant depletion in dengue cases. In 2016, United States reported reduction from 21,77,171 cases to 5,84,263 cases in a year, representing 73% depletion in dengue positive cases.[15]

In 2018, the South East Asian countries reported dengue from India, Bangladesh, Myanmar, Malaysia, Philippines, Pakistan and Yemen with a significant cutback in the dengue infected cases.[15]

An estimate of around 500,000 people suffering from dengue are hospitalised each year with approximately 2.5% mortality. Between the year 2010 and 2016, there was 28% decline in case fatality globally, with improved case management.[15]

WHO –South- East Asia region (SEA)

Dengue is confirmed to be a concern worldwide, 75% of the world population affected by dengue reside in Asia-Pacific regions, among these 1.3 billion live in areas known to be endemic to Dengue and are considered to be one of the main cause for hospitalization and even death.[19]

It is evident from the statistics collected by WHO, that overall spread of dengue has occurred in SEA in the past 10 years and severe dengue with complications is most prevalent in these regions. [10,20]

Epidemics of dengue fever in India

The incidence of dengue in India is very complex and has been changing over the past 60 years in terms of commonly affected strains, locations and the seriousness of it. In India, in the year 1946, the index case of the disease was reported.[21,22]

In 1963-64, the East Coast of India reported an outbreak of dengue which then spread towards north reaching Delhi and Kanpur in 1967 and 1968 respectively.[23]

This epidemic also spread to South India and slowly involved entire country with widespread outbreaks of all the dengue virus serotypes.[1,23]

In 1997, in Delhi, DV-1 was isolated. A phylogenetic analysis was conducted by the Molecular Evolutionary Genetics Analysis programme, that suggested the DV-2 isolates of Delhi 1996 came from genotype IV and the isolate from 1967 was similar to the isolate of 1957 from India of DV- 2. This was categorized by genotype V. This suggests that the DV-2 isolates of genotype V have been restored by genotype IV.[24,25] DV- 3 has been isolated in the year 1983 in Calcutta and in 1985 in Rajasthan along with Gwalior and Tamil Nadu in the year 2003 and 2010 respectively.[26,27] Pune and Andhra Pradesh reported the emergence of DV-4 which also showed increased severity of disease.[28]

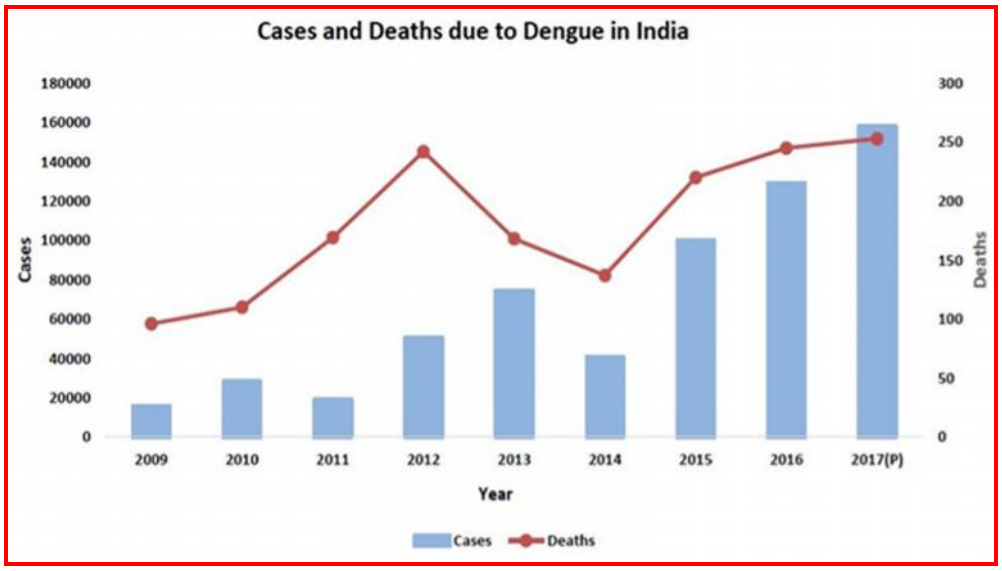
Currently, the dengue outbreaks history in India has been evaluated and more up to date systematic data are now accessible due to the National Vector-Borne Disease Control Programme (NVBDCP). The National Institute of Virology has reported 5 worst affected states by dengue virus in the year 2017 : Karnataka, Kerala, Tamil Nadu, West Bengal and Delhi.[29,30]

Figure 2 - Distribution of dengue infected cases among 5 worst affected Indian states in the year 2014-2017[29,30]

DENGUE CASES AND DEATHS: 5 WORST AFFECTED STATES IN 2017

	2014		2015		2016		2017	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
Kerala	2575	11	4075	25	7439	13	18,727	35
Karnataka	3358	2	5077	9	6083	8	13,016	5
Tamil Nadu	2804	3	4535	12	2531	5	11,552	18*
West Bengal	3934	4	8516	14	22,865	45	5389	13
Delhi	995	3	15,867	60	4431	10	4545	1

Figure 3 - Total dengue cases plotted against percentage mortality in India, 2009–17[29]



Dengue fever in Karnataka

Until mid-1990s, dengue was reported only from Karnataka, Tamil Nadu and Andhra Pradesh. In 2007, Davangere (41.2%), Shimoga (23%) and Udupi (7.5%) districts reported highest dengue cases.[31,32] As per the NVBDCP 2017, Karnataka reported 17,265 dengue fever cases including 5 deaths.[29]

Etiology

Vertebrate viruses like Arbovirus (Arthropod borne - viruses) are biologically transmitted by hematophagous vector. These belong to various families such as Rhabdoviridae, Bunyaviridae, Reoviridae, Arenaviridae and Togaviridae.

Dengue virus is a RNA virus which is single stranded, a nucleocapsid surrounds it and the covering is of lipid envelope. The virion is around 50nm in diameter[19] and is made up of three protein genes encoding: C - core protein or

nucleocapsid , M- membrane protein, E – envelope protein and 7 protein genes that are non - structural.[1,33]

Dengue virus was first isolated and detected during WWII. Bancroft was the first to discover the vector of dengue virus - Aedes aegypti mosquito, in the year 1906.[34]

In the year 1943 the dengue virus was isolated in Japan by inoculating patients serum into suckling mice. The same procedure was done in India in the year 1944 from serum samples of US soldiers.[35,36]

The dengue virus constitutes of 4 serotypes namely; DENV-I, DENV-II, DENV-III and DENV-IV, all four serotypes causing similar illness. DENV2 and DENV3 infections are more severe and are associated with fatal haemorrhagic disease.[34] In the year 1956, in Vellore DV-1 was isolated. The American African genotype (AMAF) consists of all the Indian isolates of DV -1, further distributed into India I, II and III. [37]

The DV-2 American genotype circulating predominantly in India, during 1971 was substituted by the genotype of Cosmopolitan.[38,39]

Over a time span of more than 50 years, the isolation of DV-2 strains took place in India. During 2003 in Delhi, once again the emergence of DV -3 took place. Circulating DV-4 strains are also seen occasionally.[40,41]

Transmission and vector

Aedes aegypti is the principle vector of dengue virus, distributed widely in the subtropics and tropics.[42] The female is a day time, indoor biter, feeding on humans exclusively. It's sites for depositing her eggs are artificial containers.[43,44] A mosquito which is infected with virus can transfer the virus throughout its life after 4-7 days of its incubation period. Individuals infected with the virus, can impart infection after their first symptoms appear via Aedes mosquitoes and these infected people become the principle carriers.[45]

Aedes Aegypti favours cold climate: low-latitude of 10°C in the northern and southern hemispherical regions. [46,47]

Natural History

After 5 to 8 days of incubation, high fever begins with arthralgia and severe myalgia followed by development of rash after 3-4 days and a positive tourniquet test. Most patients completely recover, while some have complications like bleeding manifestations presenting as epistaxis, petechiae, malena, gum bleeding and hematemesis and these symptoms help in early identification of severe cases of dengue. Apart from these symptoms, for early detection of dengue infection tourniquet test is also used.[49]

Wintrobe technique is the standard tourniquet test, performed by increasing the pressure for five minutes in between systolic and diastolic and then deflating the pressure, wait for a minute then note the result. The test is interpreted as positive if ≥ 10 petechiae/mm^3 is present. Other technique is the Daisy technique which is used in

children. In this procedure a pressure of 80 mmHg is applied for 5 minutes and deflated, result is noted just like in the Wintrobe test.[50]

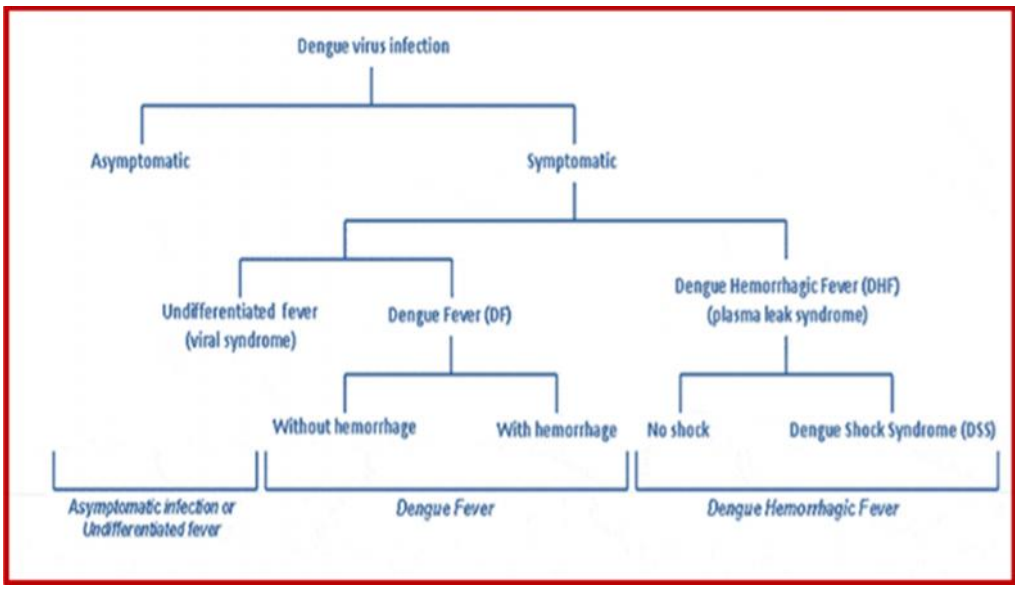
The other serious types of dengue, present with excessive bleeding also known as dengue haemorrhagic fever and shock which is also known as dengue shock syndrome. In the simple variant of dengue, the only sign is petechiae which are usually seen only after the tourniquet test.[49]

In cases of severe full blown infection, delay in administration of correct treatment can lead to high morbidity and mortality. Detecting and intensive monitoring of serious forms of disease is an important aspect in the management. The platelet levels depletes progressively in the transition of simple dengue infection to DSS.[49]

Clinical presentation

Dengue extends from mild asymptomatic disease to a complicated illness which may lead to death if it is not diagnosed early and treated properly. The dengue cases with symptoms are classified into dengue fever (DF), undifferentiated fever (UF), dengue haemorrhagic fever (also known as plasma leak syndrome). DHF along with shock leads to dengue shock syndrome.[50]

Figure 4 - Classification of dengue infection manifestations [51]



According to the WHO 2011,[50] patients with high grade fever along with 2 of the following symptoms or signs can be suspected for dengue :

- Rash
- Arthralgia/ bone pain
- Intense Myalgia
- Haematocrit rising 5–10%.
- Leucopenia (WBC ≤ 5,000 cells/mm3)
- Bleeding manifestations
- Retro-orbital pain

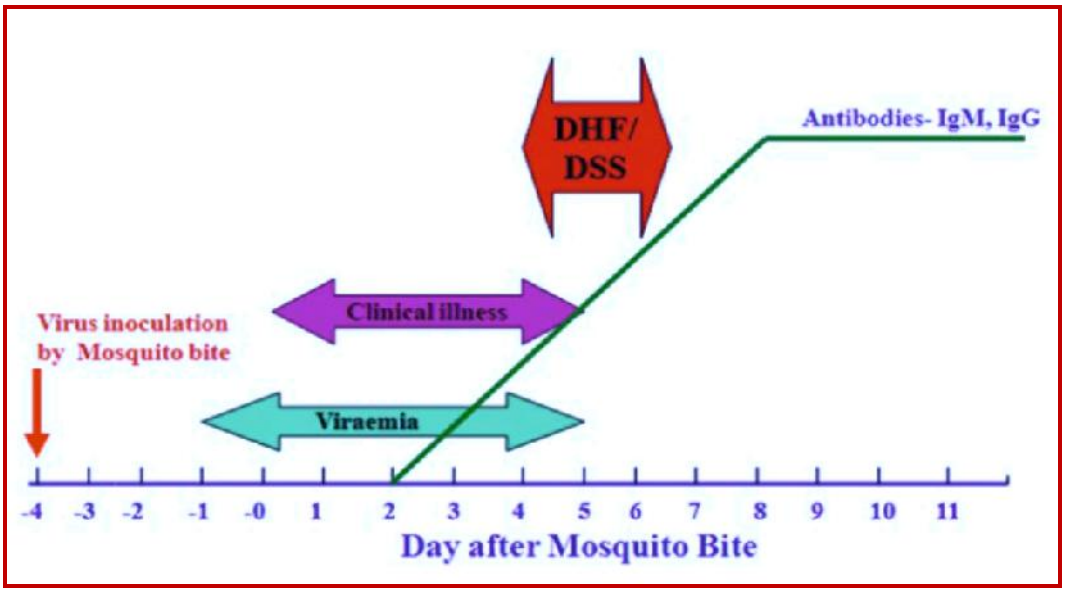
Clinical Diagnostic criteria of DHF (WHO) [52]

- Sustained high fever for 2 to 7 days
- Petechiae or epistaxis with tourniquet test positivity
- Thrombocytopenia (platelet levels of less than 100×10^9/L)
- Haemoconcentration – evidence of leakage of plasma (hematocrit value of ≥20%) ascites and pleural effusion.

Dengue Haemorrhagic fever (DHF) is further classified into 4 grades based on the severity:

- Grade I and II – Dengue Haemorrhagic fever
- Grade III and IV – Dengue shock syndrome [53]

Figure 5 - Events occurring during virus infection after the bite of an infected mosquito[53]



DF frequently occurs in adolescents and adults and presents in either mild form with fever as the only symptom or a more aggressive form. The aggressive form of presentation is defined by sudden high grade fever along with myalgia, arthralgia, rash and retro-orbital pain. All these symptoms occur mainly in the initial febrile period.[54,55]

Petechial rash flush the skin during the critical phase of the disease. This occurs mainly near the time of abatement and presents with capillary wall leakage which leads to haemorrhage.[54]

Severe form of dengue, i.e DHF is mainly found in children below 15 years of age, rarely it may happen in adults as well. It leads to sudden rise in vascular wall permeability which leads to plasma exudation which in turn leads to haemoconcentration along with high grade fever, thrombocytopenia and haemorrhage. All these events lead to a state of shock which is known as dengue shock syndrome (DSS). Mainly during the initial acute phase of the illness it is very hard to distinguish DHF from simple dengue fever and other illnesses of viral etiology eg, typhoid fever.[53,54]

Dengue fever

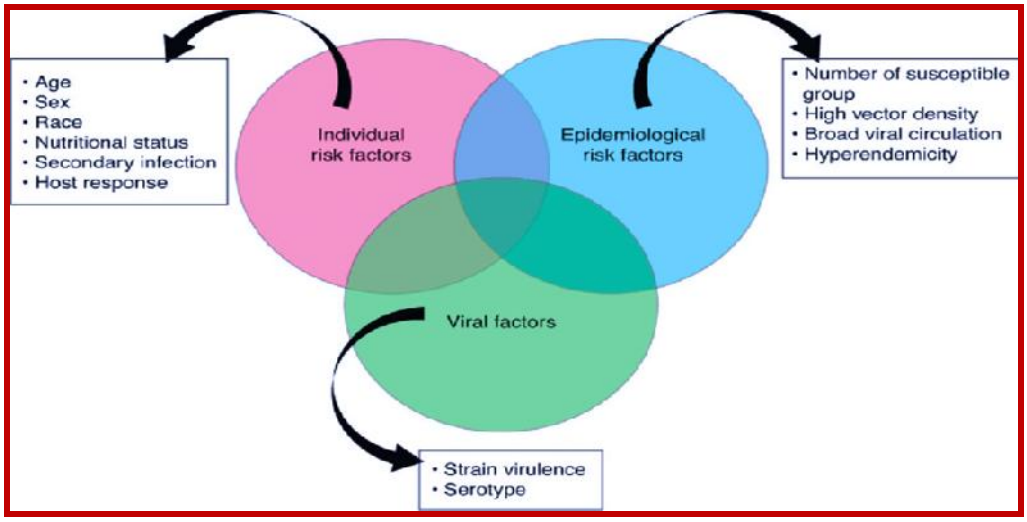
High grade fever of sudden onset usually is the initial presenting symptom which lasts for 2-7 days accompanied by arthralgia, myalgia, pain in abdomen, retro-orbital ache, along with vomiting and loose stools. Skin manifestations occur in the form of rashes which mainly includes the face, limbs & the trunk along with other symptoms like mild epistaxis, bleeding from gums, menorrhagia and petechiae. Many individuals also show a positive tourniquet test.[56]

Dengue haemorrhagic fever

It presents with fever accompanied by hepatomegaly and haemorrhagic manifestations.[56,57]

Risk factors for DHF include three types – individual, epidemiological and viral

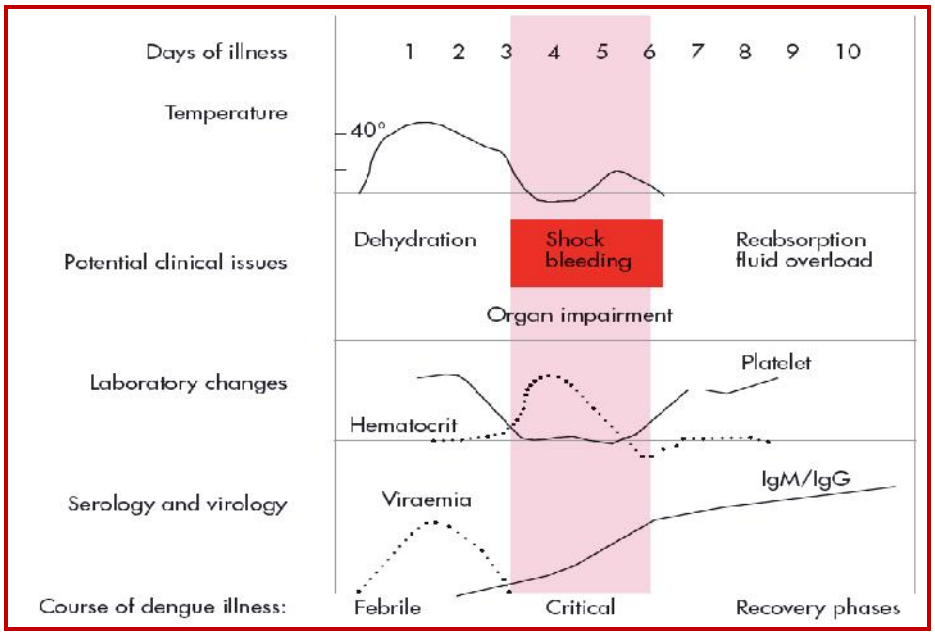
Figure- 6 Risk factors for dengue haemorrhagic fever[2]



DHF is further classified into 3 stages :[57]

1. Febrile stage
2. Critical stage
3. Recovery stage

Figure – 7: Course of DHF[57]



The first stage of febrile begins with onset of high fever with chills and rigor along with the appearance of rashes and bleeding disorders. After 2-7 days, fever starts falling. However the patient still remains ill, inspite of normal temperature.[57] In severe cases there is leakage of plasma, hepatomegaly, pleural effusion, shock with cyanosis, ascites, pericardial effusion, melena, gastrointestinal bleeding followed by epistaxis. Haemorrhagic manifestations along with circulatory failure is the warning sign in DHF. The haematological findings arer educed platelet levels, ≤100,000/mm^3 as sign of vascular leakage.[57,58]

Dengue shock syndrome (DSS)

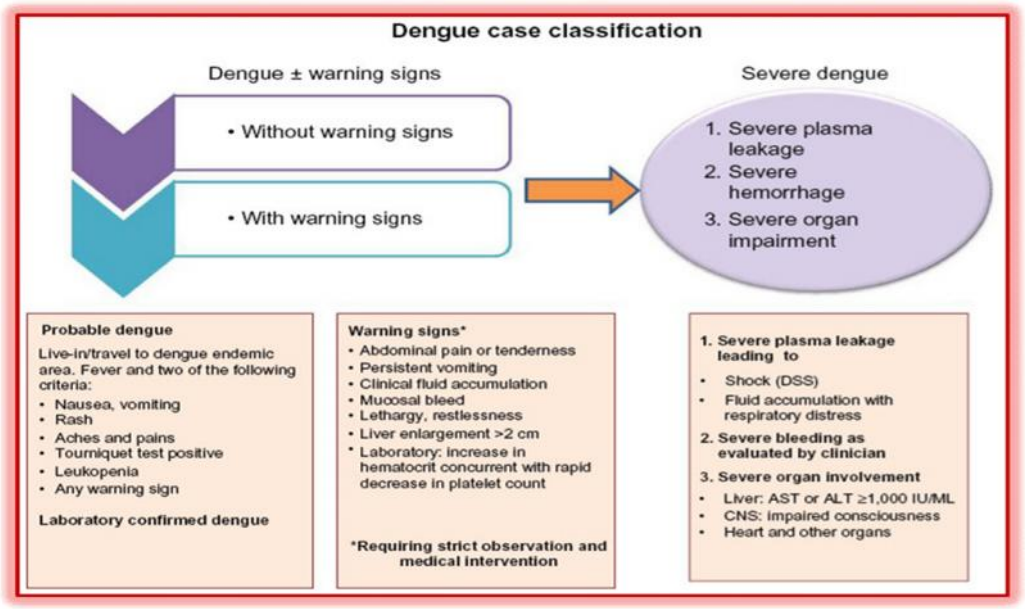
Dengue shock syndrome is associated with a narrow pulse pressure <20 mmHg, weak rapid pulse, cyanosis, restlessness along with cold clammy skin. Death occurs in patients because of worsening shock, disseminated intravascular coagulation and multi-organ dysfunction.[57,59]

Earlier dengue was categorised into three types:

1. Dengue Fever
2. Dengue Haemorrhagic Fever - characterized by increased vascular permeability
3. Dengue Shock Syndrome – that may lead to shock and death.[60,61]

The revised clinical classification of dengue classifies into two: Dengue with/ without warning signs and Severe dengue.[60,61]

Figure 8 - Dengue classification according to severity[60]



According to WHO for disease control and prevention, community oriented education campaigns should be organised with the aim of reducing breeding sites for the vector. This can contribute immensely in reducing the prevalence of dengue.[62,63]

A study in Thailand, Benthem et al, asserted that people who are well aware of dengue and its consequences are more cautious as compared to the population of people who are still in the dark. It also stated that in areas where clean – up campaigns are promoted, particularly during monsoon, there is a considerable reduction in the cases of DHF.[64]

According to the study by Nijhawan DM et al, out of 200 dengue positive patients, maximum were from lower middle class of socio economic status according to Kuppuswamy classification. None from the upper class suffered from dengue fever further proving the importance of knowledge on dengue.[62]

Preventive measures such as mosquito bed nets, repellent creams/ sprays, window and door screens and air-conditioning and protecting oneself by wearing long sleeves for additional protection has proved to be vital in dengue prevention.[65]

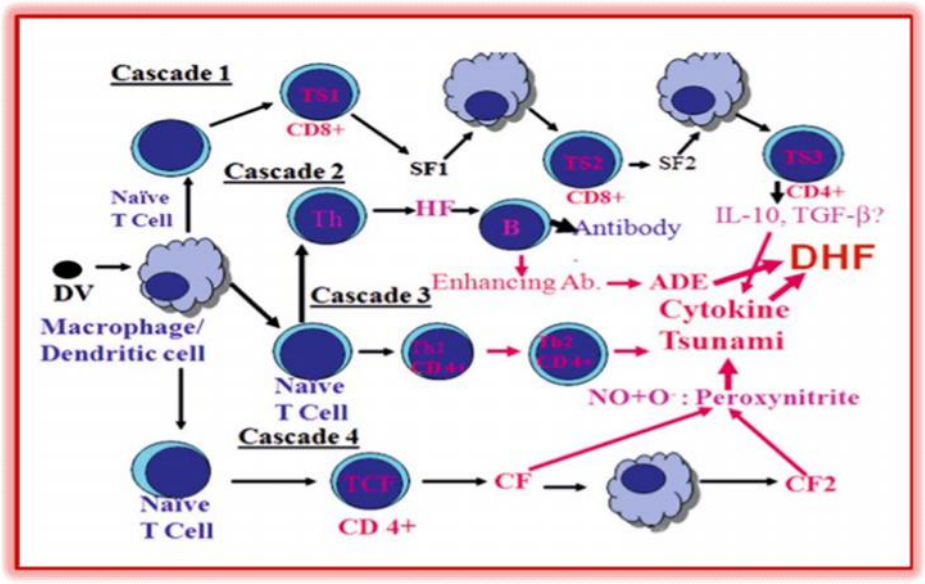
Pathogenesis

The most active areas of research in dengue is the pathogenesis of DHF. Antibody-dependent enhancement, T cell response and shift from Th-1 to Th-2 response are the mechanisms considered to cause DHF.[1] The outcome of dengue infections is mainly dependent on the cell and tissue tropics.[66]

Thrombocytopenia, altered numbering and functioning of leucocytes, increased permeability of vessel wall without damaging the capillary endothelium, altered haemostasis along with liver damage are the essential features of DHF. There is extensive plasma leakage associated with haemorrhage in patients with grades III and IV of DHF resulting in DSS.[53]

There are different hypothesis proposed to explain the pathogenesis of dengue, among them 3 are the benchmark. The role of enhancing antibodies is the first by Halstead in 1970. A shift from mild Th1 response to severe dengue Th2 response proposed by Chaturvedi et al in 1999a, this resulted in a “Cytokine Storm” because of the disturbed cytokine cascade leading to many pathological lesions. Presence of memory T-cells cross reacting and inducing the generation of a number of cytokines by Mongkolsapaya et al in 2003-2006, is the third hypothesis. Ultimately targeting the endothelial cells resulting in pathological lesions and severe dengue.[53]

Figure 9 - Immunopathogenesis of DHF proposed by U C Chaturvedi and colleagues by inducing four cascades of T cells [53]



In DHF/DSS patient's, both the cytokines inflammatory (IFN-γ) and anti-inflammatory cytokines (IL-10) are present concurrently.[67] Dengue patients present with leucopenia during the acute infection, with reduction in the absolute number of monocytes and neutrophils.[68]Dengue virus causes the activation of neutrophils and release of chemokines like Interleukin-8 (IL-8), MIP-1β, MIP-1α which majorly takes part in the pathogenesis of DHF/DSS.[67]

Dengue virus (DV) is known to cause damage to the liver secondary to hypoxia, direct effect of virus or immune mediated damage.[6] DV targets the hepatic cells along with the kupffer cells in the liver. Aside from the programmed cell death of the target cells, the free radicals precisely regulate the generation of pro-inflammatory cytokines like tumour necrosis factor (TNF)-alpha, Interleukin-8, Interleukin-1 (IL-1) and H_2O_2 in macrophage. Oxidative stress develops from the beginning of dengue infection.[1]

There is a shift of the response from Th1-dominant to a Th2 biased response which results in worsening of the dengue disease. There is increase in the vascular permeability due to mass effect of cytokine, histamine release, products of the complement pathway and free radicals.[1]

The exact mechanism of pathogenesis of dengue disease still remains unexplained.

Diagnosis

In the diagnosis of any disease, management is the most crucial step. In case of diagnosis of dengue, it is very important to recognize the nature of the disease. The duration of this disease is limited to 1 week as it is a mosquito borne viral illness. Therefore, dengue has to be investigated as one of the differential diagnosis of acute febrile illness.[7]

Complete history of the patient must be taken. Valuable information which can lead to dengue suspicion are: travelling history to dengue endemic regions, history of febrile disease since a week without relief by acetaminophen along with history of bleeding complications.[7] In areas which are endemic, tourniquet test is the most widely used physical examination tool for screening.[7] About 4/5th of dengue patients can be readily detected by using tourniquet test.[69] Often false positives have to be ruled out in cases of other tropical haemorrhagic fevers.[70] A study by Cao et al[71] determined that "A positive test is to be kept under close observation or referred early to hospital however, a negative test does not exclude dengue infection".

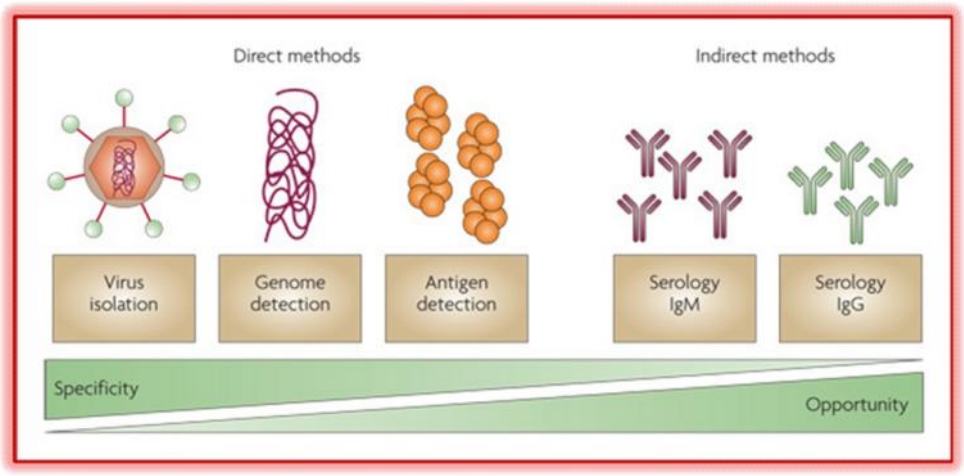
The most definitive sign for dengue diagnosis can be from simple lab investigations by doing a complete blood count. Severe bleeding episodes can be detected by haematocrit and platelet count. The 2 main laboratory investigations for dengue are IgM and IgG. The precision of these tests are often dependent on the sample collection time. IgM is elevated during 4 to 6 days of illness whereas IgG is delayed and is raised during 5 to 10 days of the disease. IgG/IgM ELISA are suitable to confirm the clinical diagnosis as serious dengue cases require treatment at the earliest. Initial diagnostic approach, including molecular test like RT-PCR and virus isolation are affluent and need expert hands to perform.[7]

NS1 antigen detection is a recent test for early diagnosis of this disease. NS1 glycoprotein is detected by ELISA using a glycoprotein monoclonal antibody (mAb) specific for NS1 in human sera of dengue infected patients. Many diagnostic kits like the immunochromatographic strip kit can aid in timely diagnosis and even decrease the turn over time.[8,72]

Laboratory tests

The best window for diagnosis of dengue is approximately from fever onset to a few days post-infection. But not all cases can be diagnosed during this time period, therefore a model diagnostic test should be used which is sensitive at any stage of this infection.[73]

Figure 10 - Comparison between direct and indirect laboratory methods for diagnosis of dengue virus[74]



Recent laboratory tests for diagnosis of dengue

NS1- assays for dengue

A simple method for the diagnosis of dengue in the acute stage is the detection of viral antigens in the bloodstream. New developments in rapid immunochromographic assays and ELISA that target NS1 have shown that raised concentrations of this antigen can be picked up to 9 days after the advent of illness. During the acute phase, NS1 has been proved as a diagnostic tool by many studies. A recently developed mAb based NS1 antigen ELISA shows better specificity.[74]

IgM- assays for dengue

Assays based on IgM detection of dengue-specific IgM is a useful diagnostic tool. In approximately 50% of patients its detection is done between 3-5 days after beginning of fever. It has a sensitivity of 90% and specificity of 98%. Dengue-specific IgM manifests earlier than dengue- IgG.[74,75]

The sensitivity as well as specificity of IgM-based assays are based on antigen quality used and can also differ among products available commercially. For the observation of the virus ELISA-based assays have become invaluable.[76]

IgG- assays for dengue

Assays based on Dengue-specific IgG are vital indicators for the patients affected with dengue previously and current infections.[76]

In recent years, the most important development in dengue is the emergence of specific detection of dengue NS1 antigen. Dengue RDTs (Rapid Diagnostic Tests) which detects NS1 antigen engage several anti-NS1 monoclonal antibodies specific to a particular serotype to arrest and make the NS1 antigen detectable in blood, plasma, or serum. ELISA format was the first commercial used assay for dengue NS1 antigen detection and it demonstrated excellent specificity and sensitivity in the early phase of infection which declined with the viraemia levels. [77,78]

NS1- antigen is detected in the serum only during the beginning of infection. Dengue IgM antibodies are present from day 2 to 5 following infection, and the cummulative results of dengue NS1 antigen and IgM antibody detection, can give precise diagnosis during this.[78]

Other Laboratory Tests

The following laboratory tests are essentially performed :

- Complete blood count
- Liver function tests
- Renal function test

In dengue fever the characteristic findings are thrombocytopenia, leucopenia, raised haematocrit and increase in liver enzymes. Liver enzymes start to increase during the initial stage and peak during the 2nd week.[79] The platelet counts < 100 x 10^9/L are seen in dengue fever and occur before shock. To enable early diagnosis of DHF the platelet levels should be monitored every day.[80]

The most common electrolyte imbalance is hyponatremia mostly found in patients having DHF/DSS.[81,82]

Due to climatic changes, prevalence and incidence of dengue infection is increasing all over the world. The diagnosis of this infection plays a pivotal role in clinical management of dengue cases and thereby determining their success. Newer tools for diagnosis should be continuously developed, consistent with the ever expanding nature of the disease.

METHODOLOGY

The present study was done from January 2018 – December 2018 in Jawaharlal Nehru Medical College and KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

Study design and duration

One year hospital based observational study.

Study period

January 2018 – December 2018

Place

The present study was done in the Department of Pathology in Jawaharlal Nehru Medical College and KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi

Source of Data

All dengue positive patients admitted in KLES Dr.Prabhakar Kore Hospital and Medical research centre, Belagavi.

Sample size

120 dengue positive cases.

Sampling procedure

All dengue positive (NS1 positive) patients admitted in KLES Dr.Prabhakar Kore Hospital and Medical research centre from January 2018 – December 2018.

Selection criteria

Inclusion Criteria:

Any male or female patient diagnosed as having dengue fever and confirmed in laboratory with N1 Positivity.

Exclusion Criteria:

1. Patients having other co-infection like malaria, typhoid or infective hepatitis interfering with interpretation of laboratory diagnosis.
2. Immunocompromised patients.
3. Patients who are not willing.

Ethical clearance

Obtained from the Institutional Ethical Committee, J N Medical College, Belagavi.

Method of collection of data

Informed consent was taken by all dengue positive patients. Detailed clinical history was taken along with complete haematological and serological investigations.

The blood count was performed on fully automated haematology analyser.The peripheral smears were stained with Wrights stain (Annexure IV).

The biochemical investigations for liver and renal involvement was performed on automated biochemistry analyser.

Investigations

The data regarding the following investigations of the selected patients from case records done for diagnosis and management of dengue fever was documented in predesigned proforma.

- Dengue serology
- Complete blood count
- D-dimer
- Total bilirubin
- SGOT and SGPT
- Alkaline phosphatase
- Serum urea
- Serum creatinine
- Serum sodium
- Serum potassium
- Serum chloride

Clinical profile

The patients were evaluated for clinical features based on symptoms of fever, arthralgia, myalgia, bleeding disorders, abdominal and retro orbital pain, itching and rash.

Haematological profile

Based on the case sheet the haematological profile was assessed and abnormalities like anaemia, leucopenia, raised haematocrit and thrombocytopenia

were looked for based on haemoglobin levels, total count, haematocrit levels and platelet count.

Liver profile

The liver profile was assessed by evaluating bilirubin, SGOT and SGPT, alkaline phosphatase levels.

Renal profile

The assessment of renal profile was based on serum urea and serum creatinine levels.

Serum electrolytes

The electrolyte imbalance was determined by assessing serum sodium, serum potassium and serum chloride.

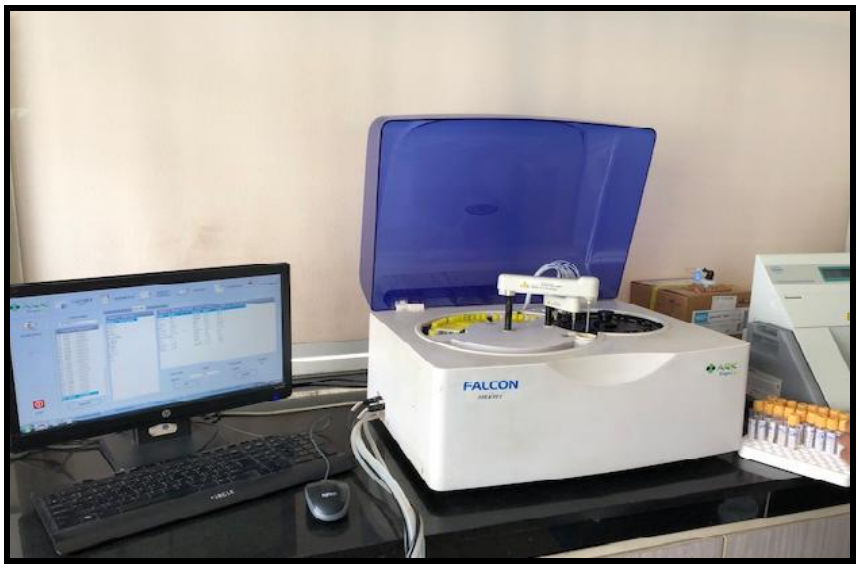
Statistical analysis

The data achieved was coded and entered into Microsoft Excel. Association between variables was determined using “chi-square test” or “Fisher’s exact test” and “Spearman’s correlation coefficient”. The continuous data was expressed as mean ± standard deviation (SD). A probability value i.e, ‘p’ value of equal to or less than 0.05 was considered as significant statistically.

Photograph 1 : Equipments used for routine haematological investigations

Photograph 2 : Sysmex Haematology Analyzer XN- 350

Photograph 3 : Tulip Fully Automatic 5-Part Haematology Analyzer, Councell – 23 V2



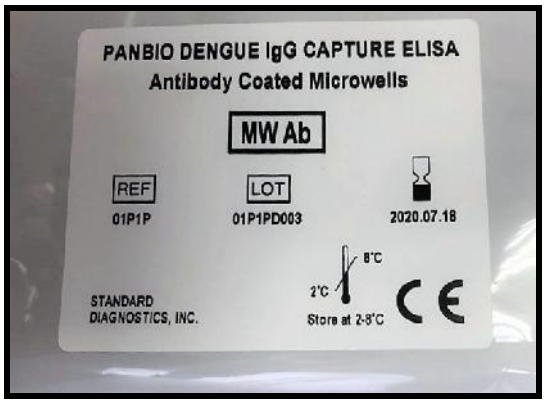
Photograph 4 :Falcon mini- Fully Automated Random Access Chemistry Analyzer used for the estimation of LFT and RFT

Photograph 5 : 9180 Electrolyte Analyzer used for estimation of serum electrolytes

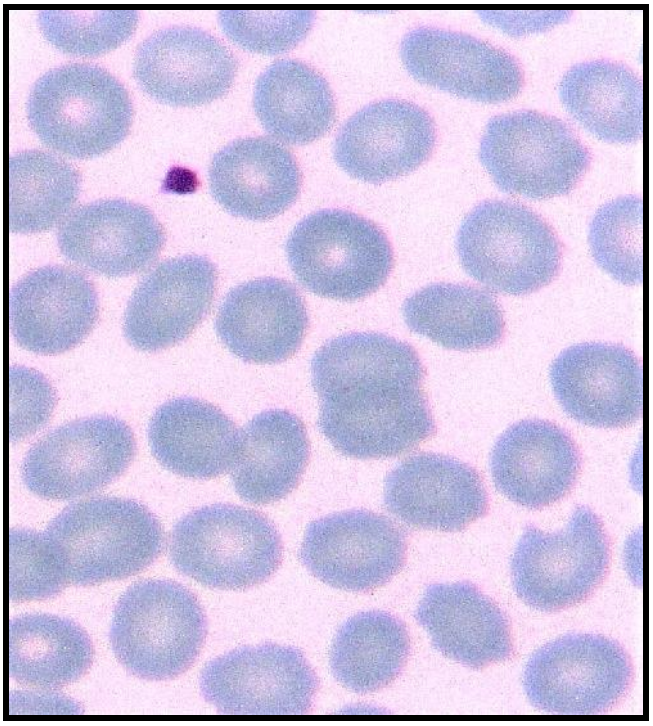
Photogarph 6: Instrumentation Laboratory's ACL Top 300/500 used for estimation of D Dimer levels

Photograph 7 :Meriscreen dengue card test- Dengue Ab (IgG/IgM) + NS1 Ag Combo

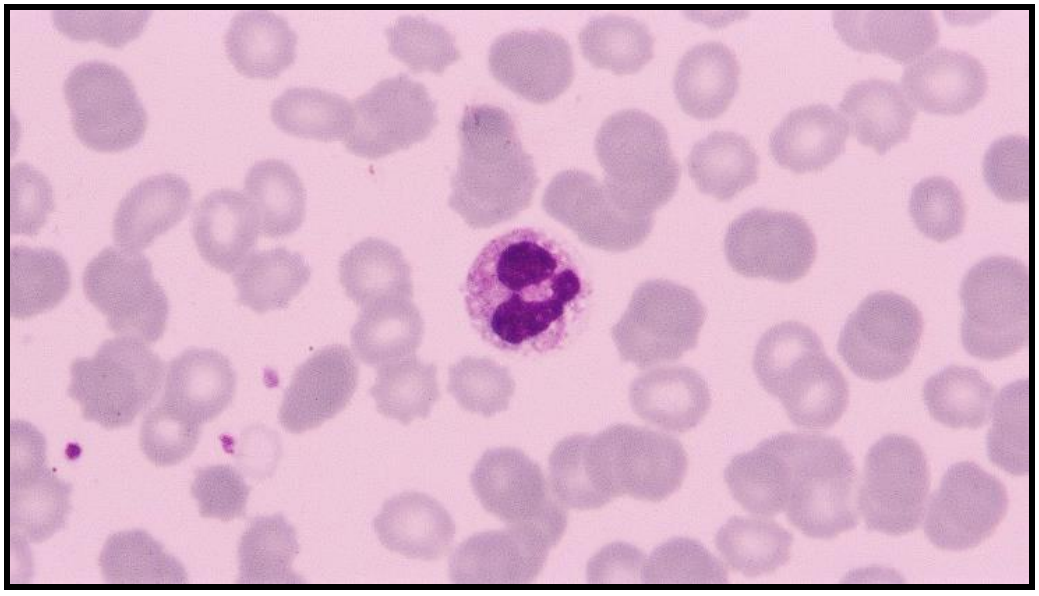
Photograph 8 :Dengue specific IgM ELISA kit



Photograph 9 :Dengue specific IgG ELISA kit



Photograph 10 : Wright's stain photomicrograph showing Normocytic Normochromic anaemia with thrombocytopenia and leucopenia (100x)



Photograph 11 : Wright's stain photomicrograph showing Normocytic normochromic anaemia with thrombocytopenia (100x)

RESULTS

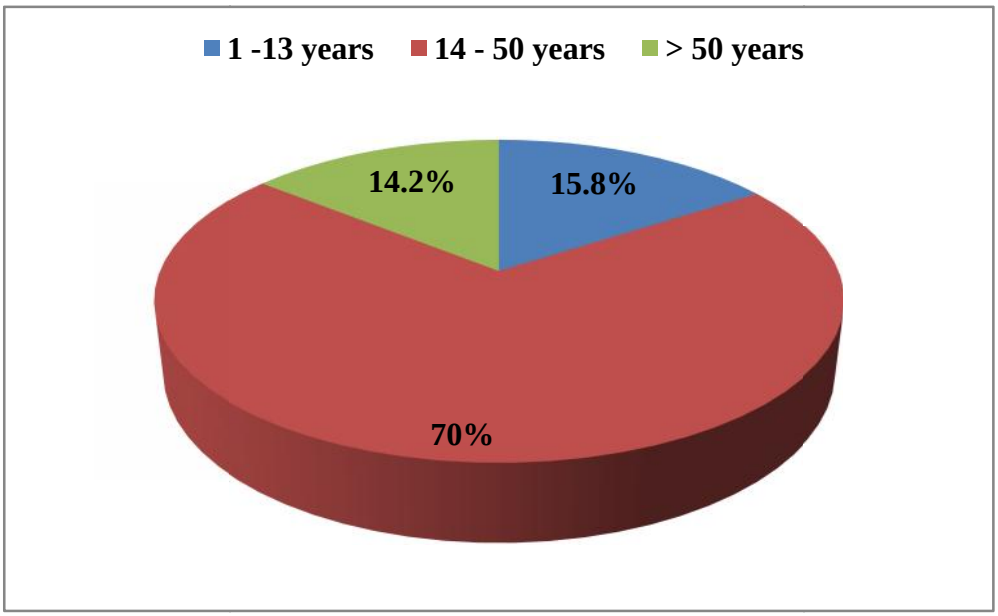
The present study is an observational study of one year, conducted in the Department of Pathology, JNMC and KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 120 dengue fever patients from January 2018 – December 2018 were studied. Out of the 120 dengue positive patients, 94 were diagnosed as DF and 26 of the patients were diagnosed with DHF.

The data obtained was analysed and the observations are interpreted below.

TABLE – 1: Age wise distribution of Dengue patients

AGE GROUPS	NUMBER OF PATIENTS	PERCENTAGE
1 – 13 years	19	15.8%
14 – 50 years	84	70%
>50 years	17	14.2%
Total	120	100%

GRAPH– 1 : Age wise distribution of Dengue patients

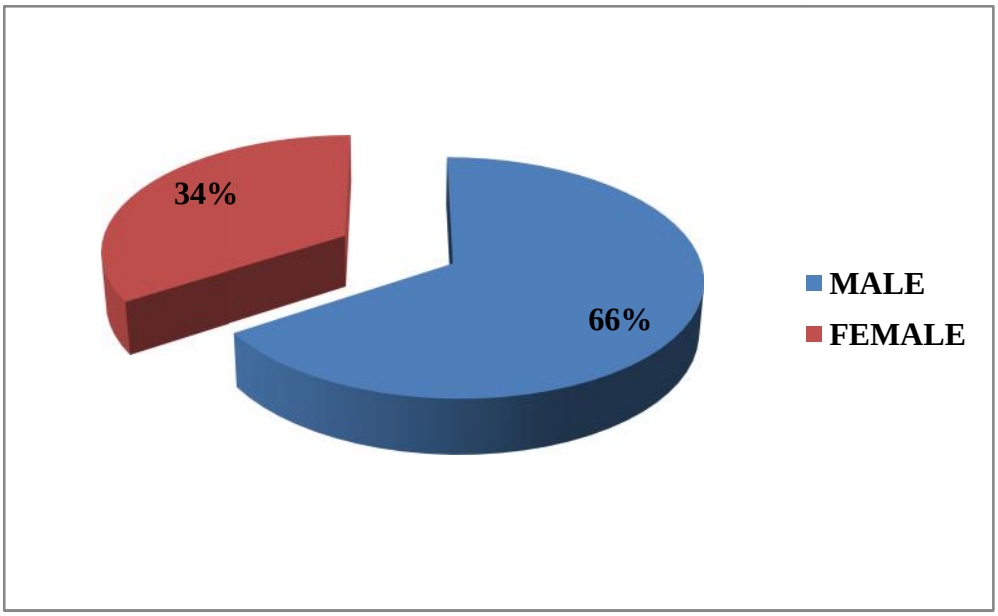


The common age group in this study was 14-50 years (70%). (Table-1, Graph-1).

TABLE – 2 : Distribution of patients according to sex

SEX	NUMBER OF PATIENTS	PERCENTAGE
Male	79	66%
Female	41	34%
Total	120	100%

GRAPH– 2 : Distribution of patients according to sex

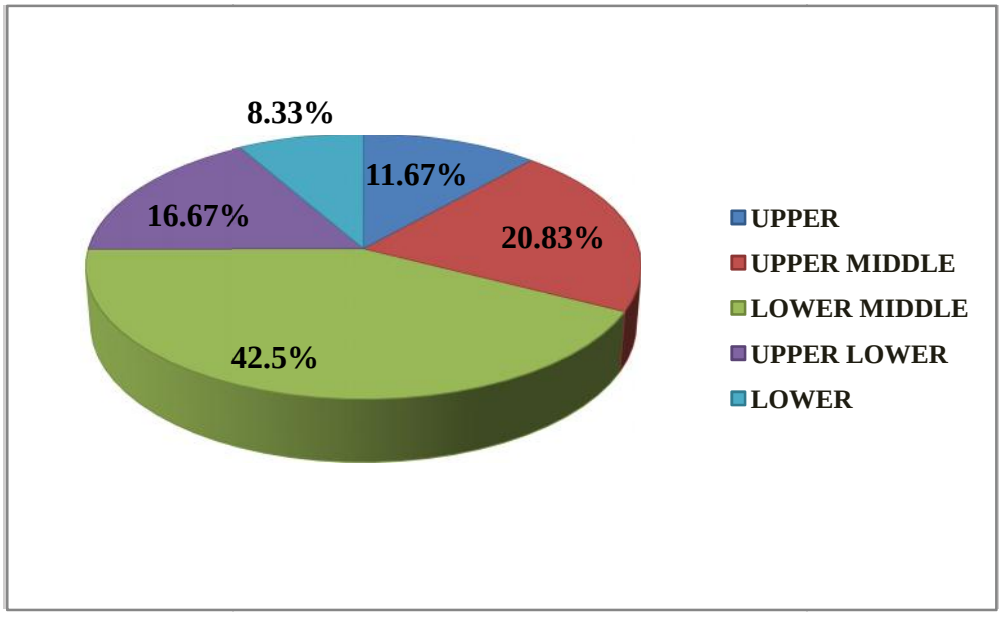


The present study showed majority males (66%) and 34% females, with a male to female ratio of 1.9:1 (Table-2, Graph-2).

TABLE – 3 : Distribution according to socio economical status

SOCIO-ECONOMIC STATUS	NUMBER OF PATIENTS	PERCENTAGE
Upper	14	11.67%
Upper Middle	25	20.83%
Lower Middle	51	42.5%
Upper Lower	20	16.67%
Lower	10	8.33%
Total	120	100%

GRAPH – 3 : Distribution according to socio economical status

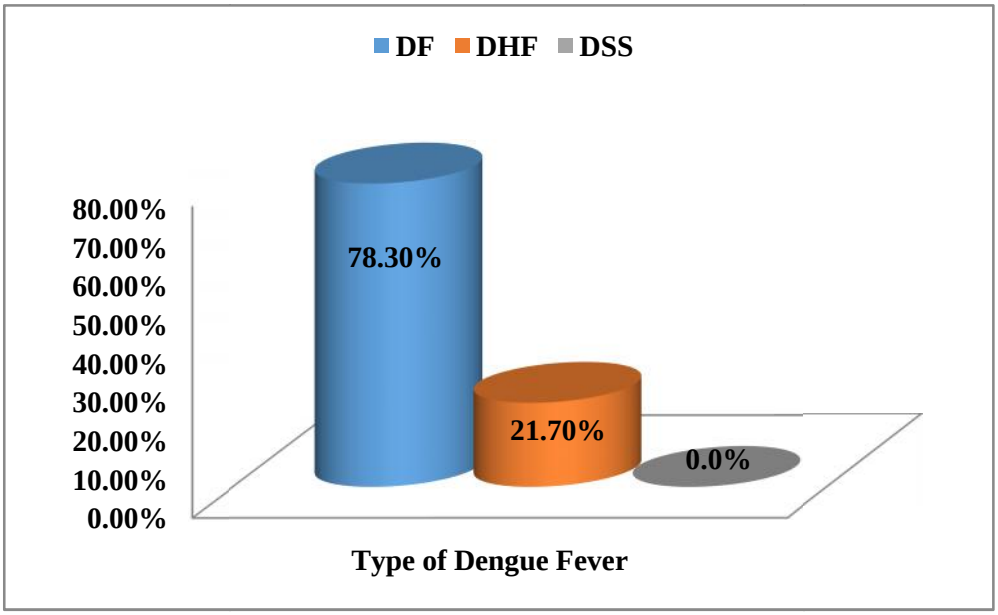


In this study, maximum patients (42.5%) were from the lower middle socio economical status. (Table-3, Graph-3)

TABLE - 4 : Distribution according to the clinical manifestation of Dengue Fever

TYPE OF FEVER	NUMBER OF PATIENTS	PERCENTAGE
Dengue Fever	94	78.3%
Dengue Haemorrhagic Fever	26	21.7%
Dengue Shock Syndrome	0	0.0%
Total	120	100%

GRAPH – 4 : Distribution according to the clinical manifestations of Dengue Fever

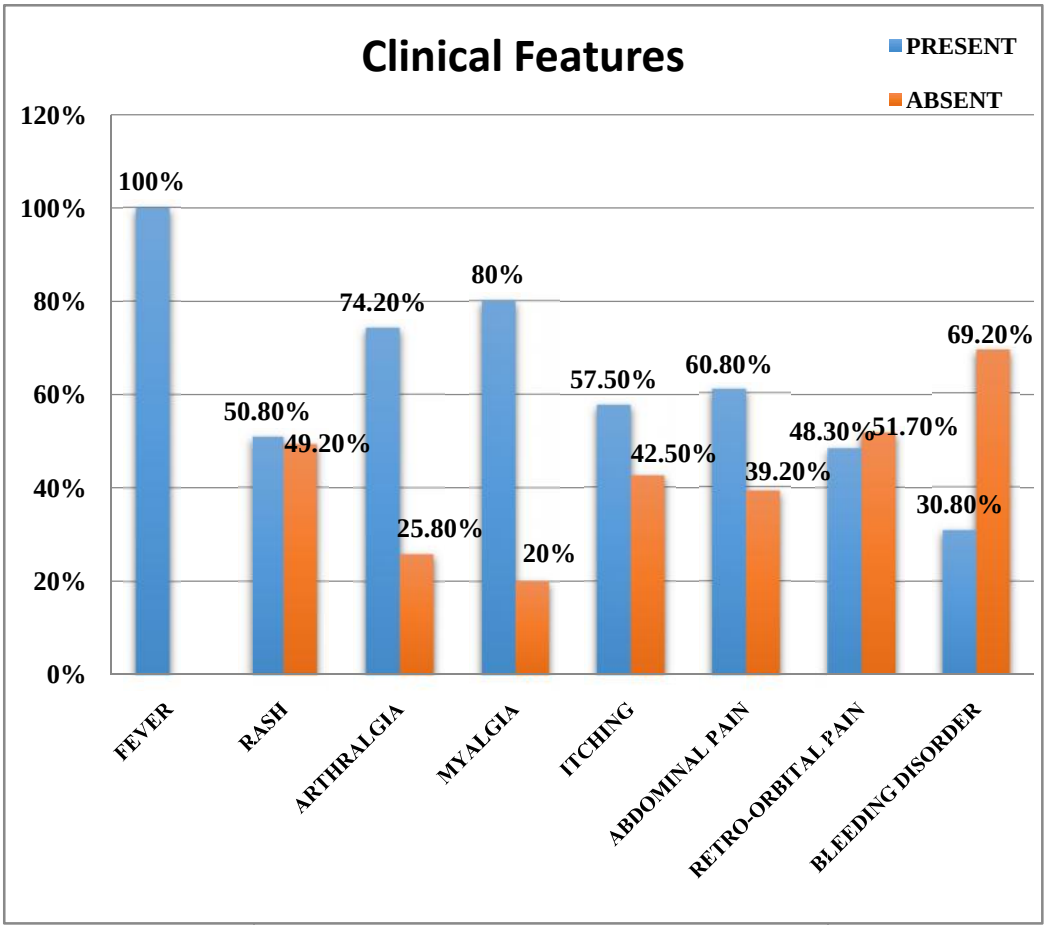


In this study, 94 cases showed clinical profile of DF, and 26 presented with manifestations of DHF. None showed signs and symptoms of DSS. (Table-4, Graph - 4)

TABLE – 5: Distribution of clinical features in dengue cases

1. FEVER	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	120	100%
Absent	0	0
Total	120	100%
2. RASH	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	61	50.8%
Absent	59	49.2%
Total	120	100%
3. ARTHRALGIA	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	89	74.2%
Absent	31	25.8%
Total	120	100%
3.MYALGIA	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	96	80%
Absent	24	20%
Total	120	100%
4. ITCHING	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	69	57.5%
Absent	51	42.5%
Total	120	100%
5. ABDOMINAL PAIN	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	73	60.8%
Absent	47	39.2%
Total	120	100%
6. RETRO-ORBITAL PAIN	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	58	48.3%
Absent	62	51.7%
Total	120	100%
7. BLEEDING DISORDERS	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	37	30.8%
Absent	83	69.2%
Total	120	100%

GRAPH – 5 :Distribution of clinical features in dengue cases



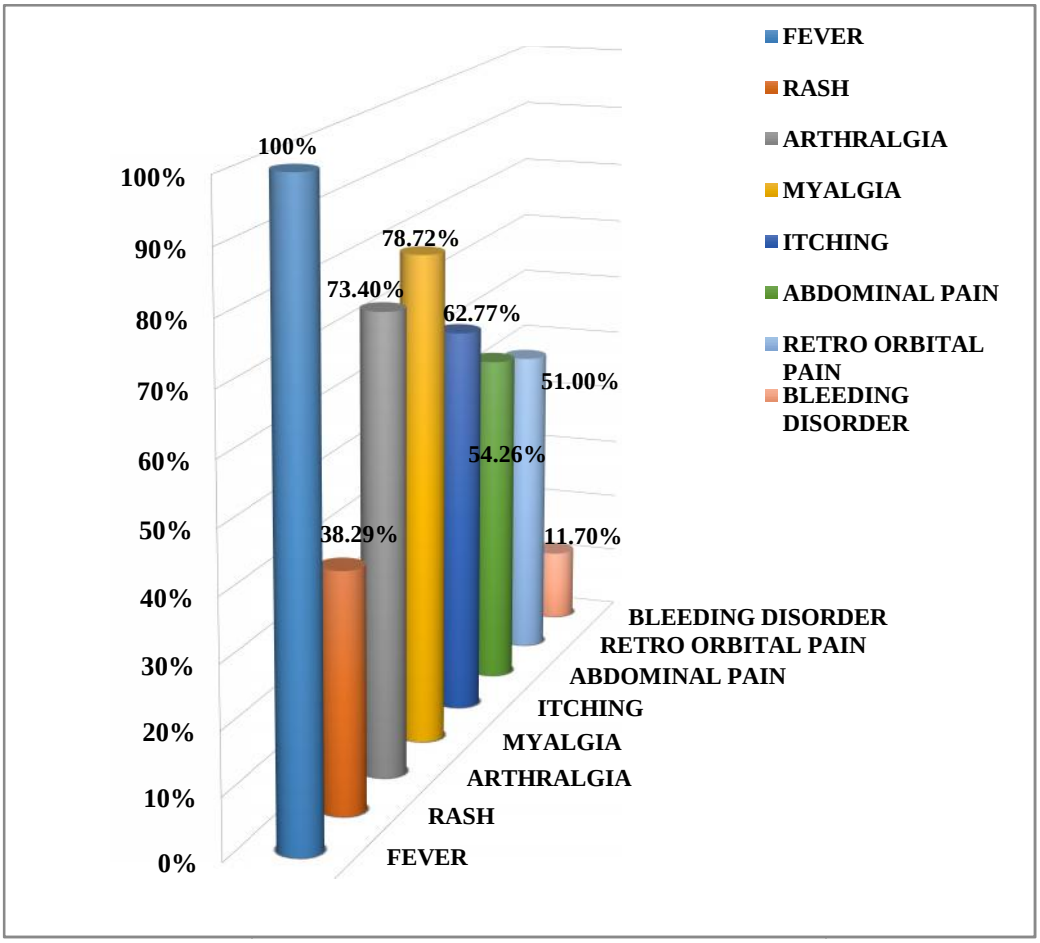
In the present study, all the patients had fever as their initial symptom along with myalgia in 80% and arthralgia in 74.2% of patients. Further, 60.80% of patients complained of abdominal pain, itching was present in 57.50% of patients along with rash in 50.80% of patients. Bleeding disorder was present in 37 (30.8%) patients out of the 120 patients. In this study 58 patients (48.30%) also complained of retro orbital pain. (Table-5, Graph-5)

TABLE – 6 : Distribution of clinical features in Dengue Fever

Total 94 cases showed DF manifestations.

1. FEVER	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	94	100%
Absent	0	0
Total	94	100%
2. RASH	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	36	38.29%
Absent	58	61.71%
Total	94	100%
3. ARTHRALGIA	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	69	73.40%
Absent	25	26.50%
Total	94	100%
3.MYALGIA	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	74	78.72%
Absent	20	21.28%
Total	94	100%
4. ITCHING	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	59	62.77%
Absent	35	37.23%
Total	94	100%
5. ABDOMINAL PAIN	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	51	54.26%
Absent	43	45.74%
Total	94	100%
6. RETRO-ORBITAL PAIN	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	48	51.0%
Absent	46	49.0%
Total	94	100%
7. BLEEDING DISORDERS	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	11	11.70%
Absent	83	88.30%
Total	94	100%

GRAPH – 6 : Distribution of clinical features in Dengue Fever



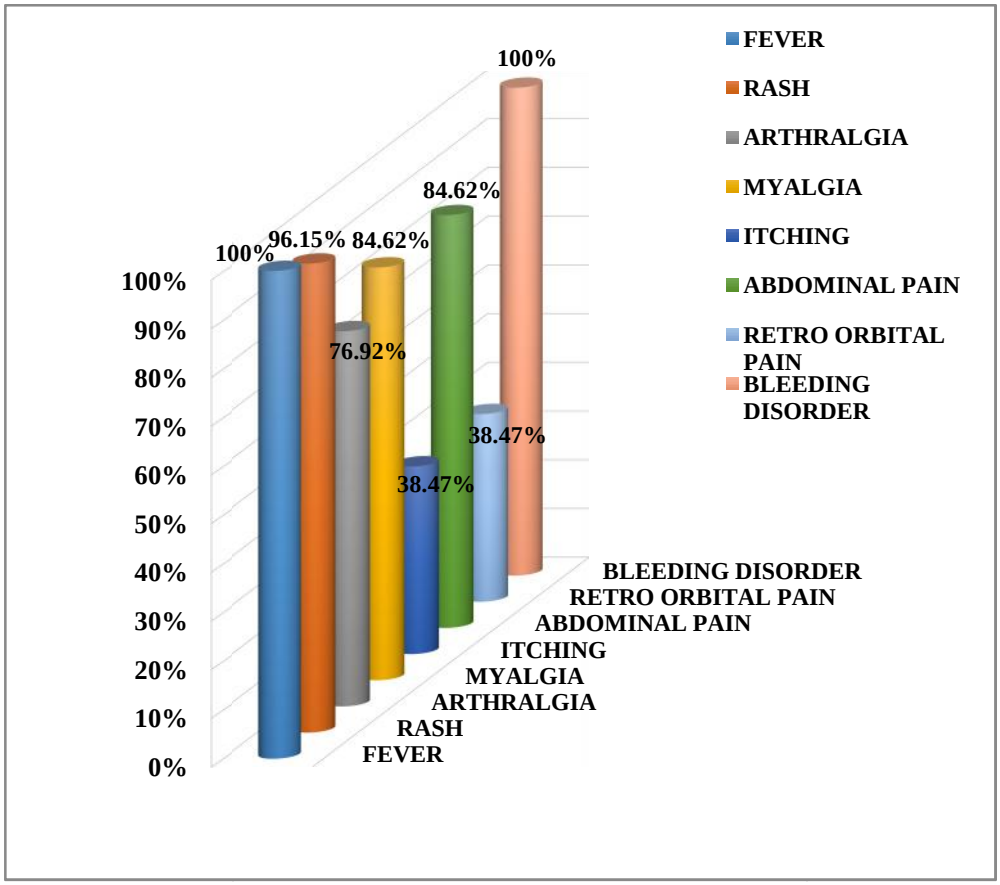
The present study showed all patients with fever (100%), followed by myalgia (78.72%), arthralgia (73.40%), itching in 62.77% and retro orbital pain in 51.0% of patients. Rash was seen in 38.29% and bleeding disorder in 11.70% of patients.(Table –6, Graph –6)

TABLE – 7 : Distribution of clinical features in Dengue Haemorrhagic Fever

A total of 26 patients out of 120 were diagnosed as Dengue Haemorrhagic Fever

1. FEVER	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	26	100%
Absent	0	0
Total	26	100%
2. RASH	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	25	96.15%
Absent	01	3.85%
Total	26	100%
3. ARTHRALGIA	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	20	76.92%
Absent	06	23.08%
Total	26	100%
3.MYALGIA	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	22	84.62%
Absent	04	15.38%
Total	26	100%
4. ITCHING	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	10	38.47%
Absent	16	61.53%
Total	26	100%
5. ABDOMINAL PAIN	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	22	84.62%
Absent	04	15.38%
Total	26	100%
6. RETRO-ORBITAL PAIN	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	10	38.47%
Absent	16	61.53%
Total	26	100%
7. BLEEDING DISORDERS	**NUMBER OF PATIENTS**	**PERCENTAGE**
Present	26	100%
Absent	00	0.0%
Total	26	100%

GRAPH –7 : Distribution of clinical features in Dengue Haemorrhagic Fever



In this study, all 26 patients with Dengue Haemorrhagic Fever presented with fever and bleeding disorders. 96.15% presented with rash along with arthralgia in 76.92% patients. Myalgia and abdominal pain was seen in 84.62% of cases, followed by itching and retro orbital pain in 38.47% of cases. (Table-7, Graph-7)

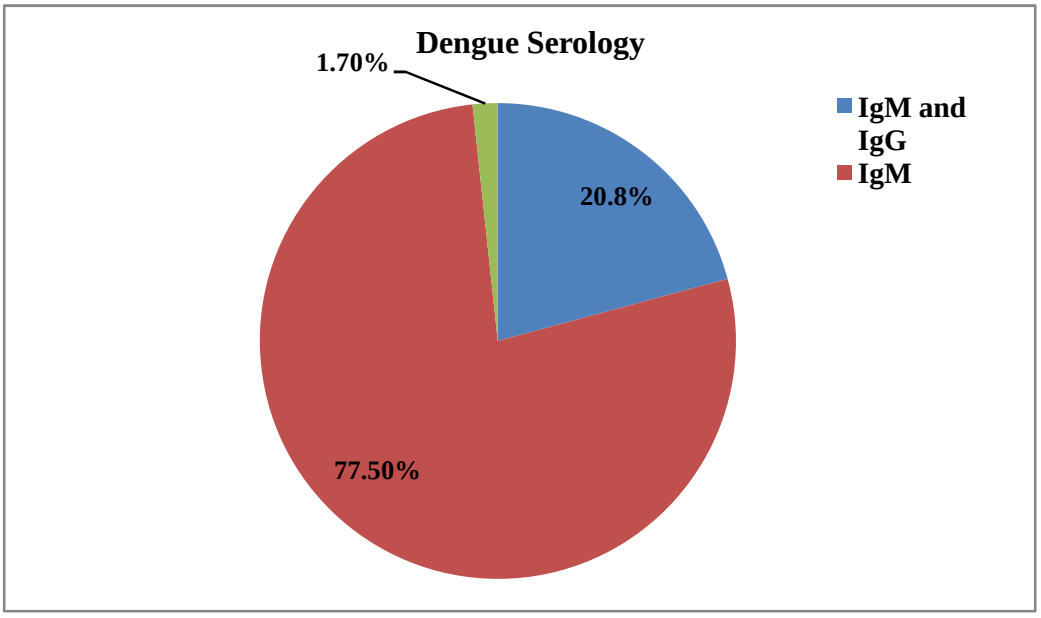
Laboratory assessment :

TABLE – 8 : Distribution according to dengue serology

In this study all 120 patients were NS1 positive.

IgM/IgG	NUMBER OF PATIENTS	PERCENTAGE
IgM	93	77.5
Both	25	20.8
Absent	2	1.7
Total	120	100

GRAPH – 8 : Distribution according to dengue serology

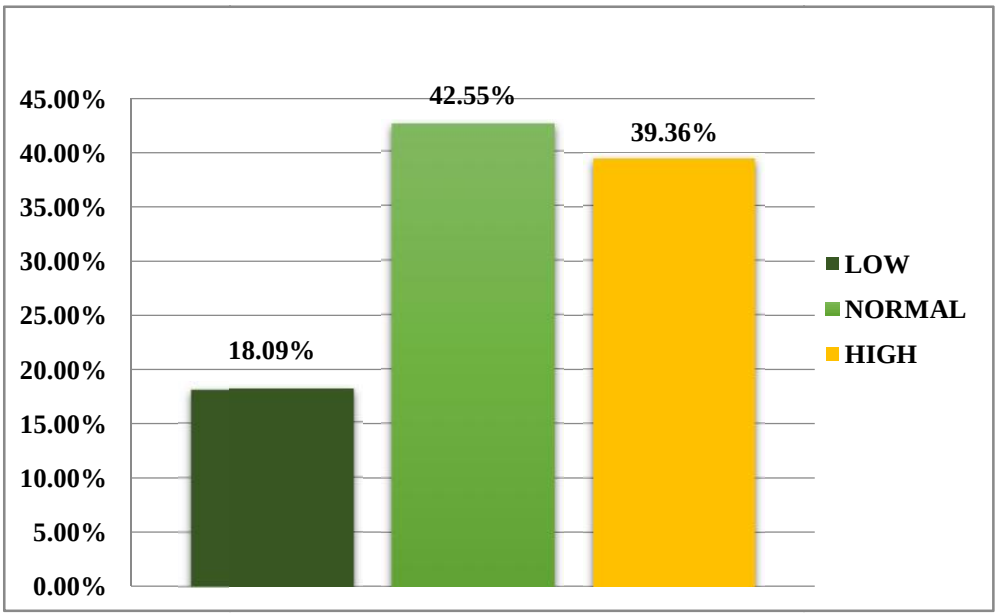


In this study, IgM was positive in 77.50% patients and both IgM and IgG was positive in 20.8% of patients where as 1.70% of patients showed absence of both IgM and IgG. (Table-8,Graph-8)

TABLE –9 :Haemoglobin levels in patients with Dengue Fever

Haemoglobin	Number of patients	Percentage
Low	17	18.09%
Normal	40	42.55%
High	37	39.36%
Total	94	100%

GRAPH - 9 : Haemoglobin levels in patients with Dengue Fever

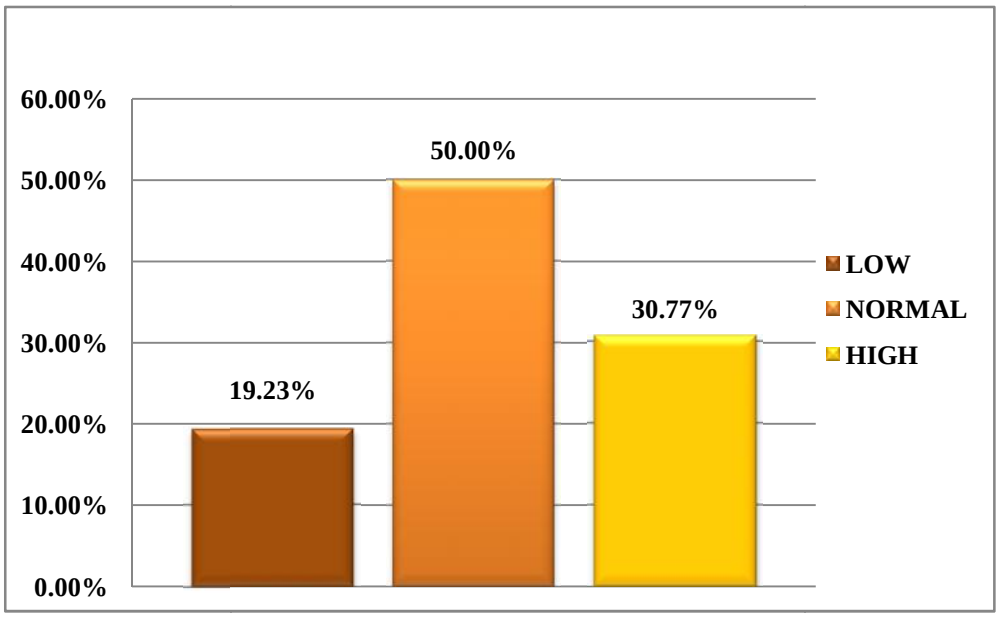


In the present study maximum patients with dengue fever had normal haemoglobin level (42.55%) whereas 39.36% patients had high haemoglobin due to haemoconcentration and 18.09% had low haemoglobin level.(Table-9, Graph-9)

TABLE – 10 :Haemoglobin levels in patients with Dengue Haemorrhagic Fever

Haemoglobin	Number of patients	Percentage
Low	05	19.23%
Normal	13	50%
High	08	30.77%
Total	26	100%

GRAPH – 10 :Haemoglobin levels in patients with Dengue Haemorrhagic Fever

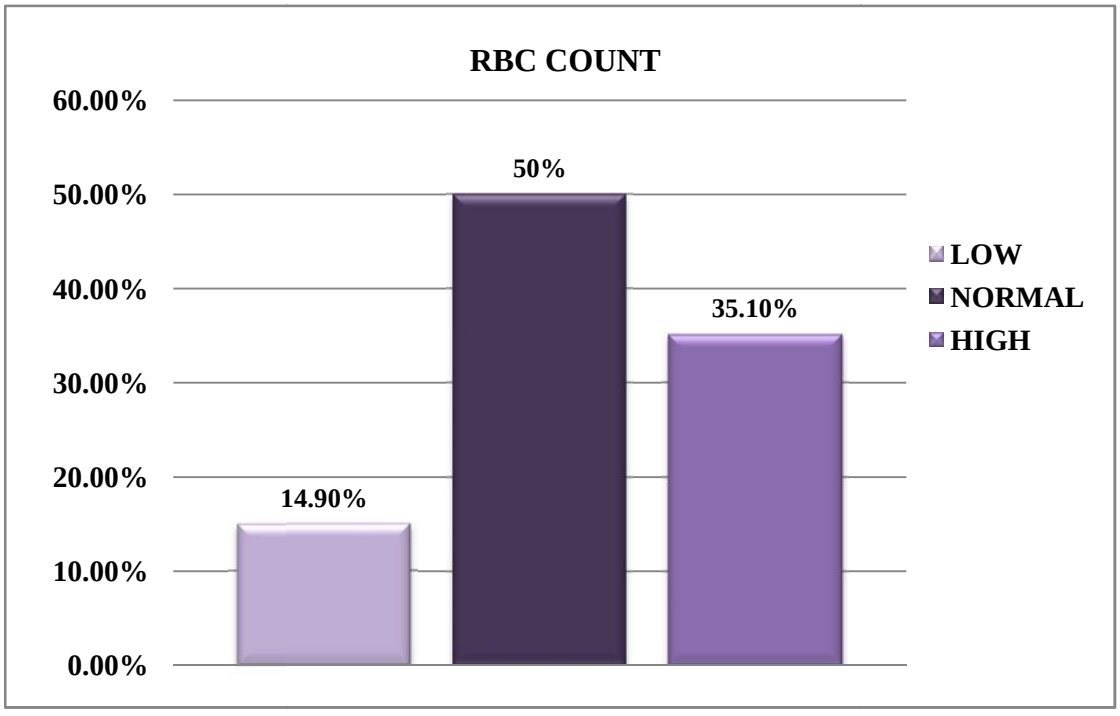


This study showed normal haemoglobin level (50%) in maximum DHF cases. However, 30.77% patients had high haemoglobin and 19.23% had low haemoglobin level.(Table-10, Graph-10)

TABLE – 11 : RBC count of patients with Dengue Fever

RBC	NUMBER OF PATIENTS	PERCENTAGE
Low	14	14.90%
Normal	47	50%
High	33	35.10%
Total	94	100%

GRAPH – 11 : RBC count of patients with Dengue Fever

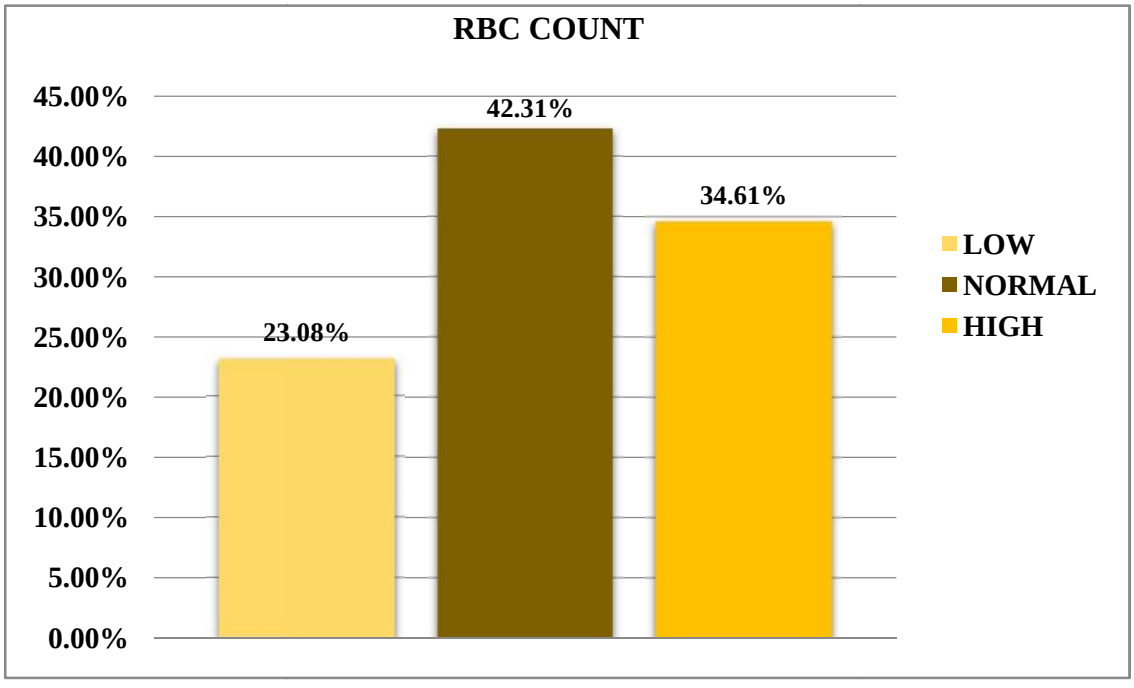


In this study 50% patients had normal RBC count, where as 35.10% patients had high count and 14.90% had low RBC count. (Table-11, Graph-11)

TABLE –12 : RBC count of patients with Dengue Haemorrhagic Fever

RBC	NUMBER OF PATIENTS	PERCENTAGE
Low	06	23.08%
Normal	11	42.31%
High	09	34.61%
Total	26	100%

GRAPH – 12 :RBC count of patients with Dengue Haemorrhagic Fever

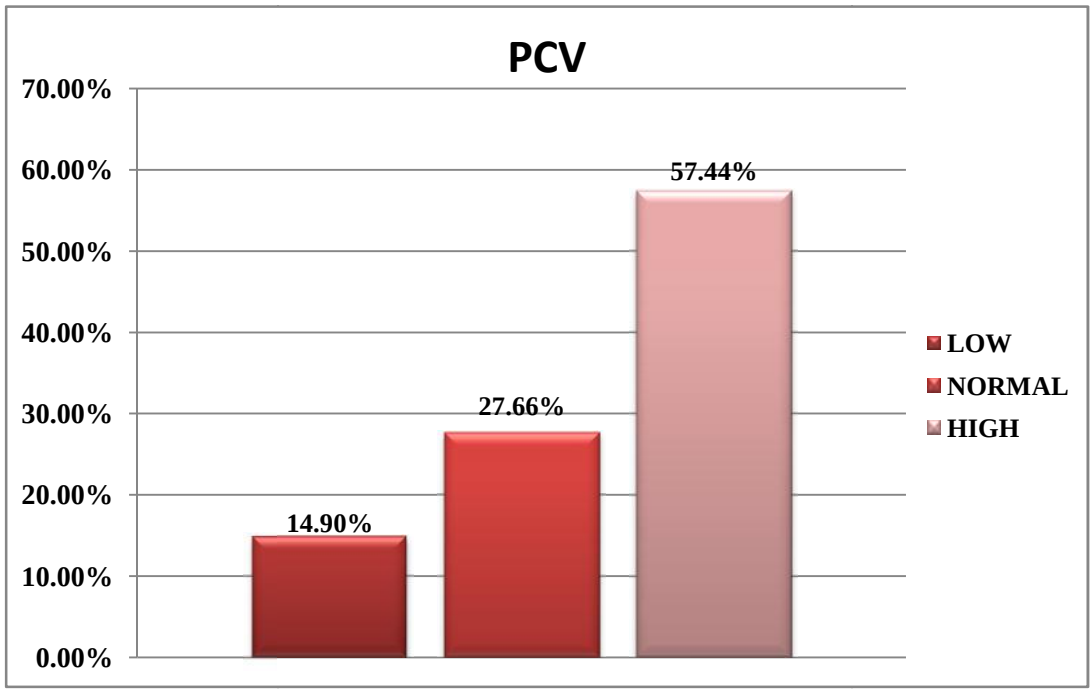


In this study 42.31% patients with DHF had normal RBC count, where as 34.61% patients had high count and 23.08% had low RBC count. (Table-12, Graph-12)

TABLE – 13 : Distribution of patients with Dengue Fever according to PCV levels

PCV	NUMBER OF PATIENTS	PERCENTAGE
Low	14	14.90%
Normal	26	27.66%
High	54	57.44%
Total	94	100%

GRAPH – 13 : Distribution of patients with Dengue Fever according to PCV levels

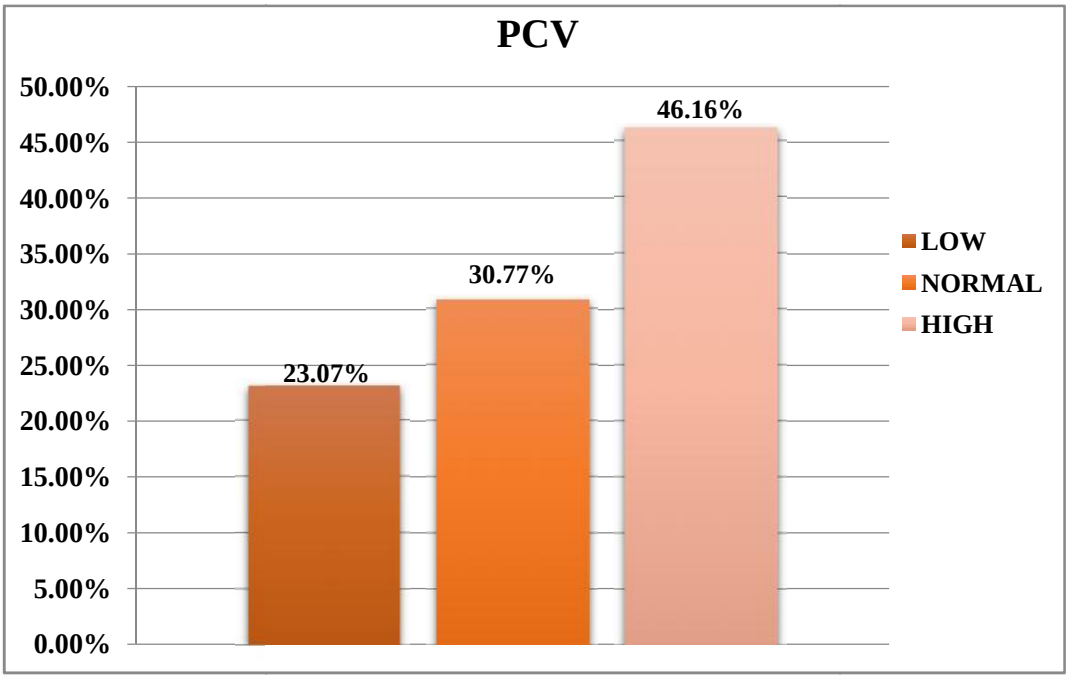


In this study majority of patients (57.44%) showed raised haematocrit (PCV) value. 27.66% patients had normal haematocrit levels and 14.90% had low haematocrit levels. (Table-13, Graph-13)

TABLE–14: Distribution of patients with DHF according to PCV

PCV	NUMBER OF PATIENTS	PERCENTAGE
Low	06	23.07%
Normal	08	30.77%
High	12	46.16%
Total	26	100%

GRAPH–14 : Distribution of patients with DHF according to PCV

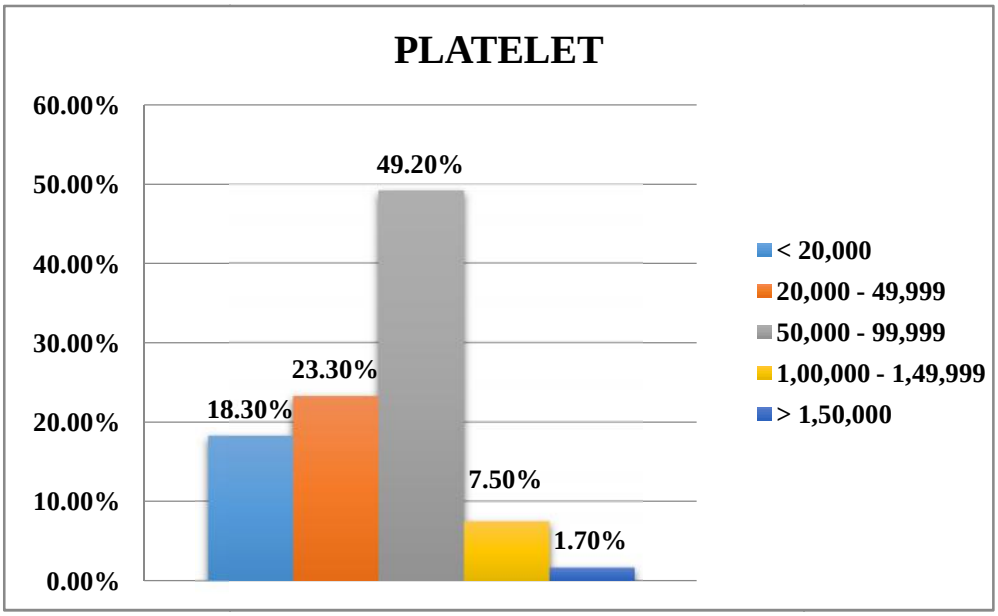


In this study majority of the DHF patients (46.16%) showed raised haematocrit (PCV) value. 30.77% patients had normal haematocrit levels and 23.07% had low haematocrit levels.(Table-14, Graph-14)

TABLE –15 :Platelet count in dengue patients

PLATELET	NUMBER OF PATIENTS	PERCENTAGE
<20,000	22	18.3%
20,000 – 49,999	28	23.3%
50,000 – 99,999	59	49.2%
1,00,000 – 1,49,999	9	7.5%
>1,50,000	2	1.7%
Total	120	100%

GRAPH –15 :Platelet count in dengue patients

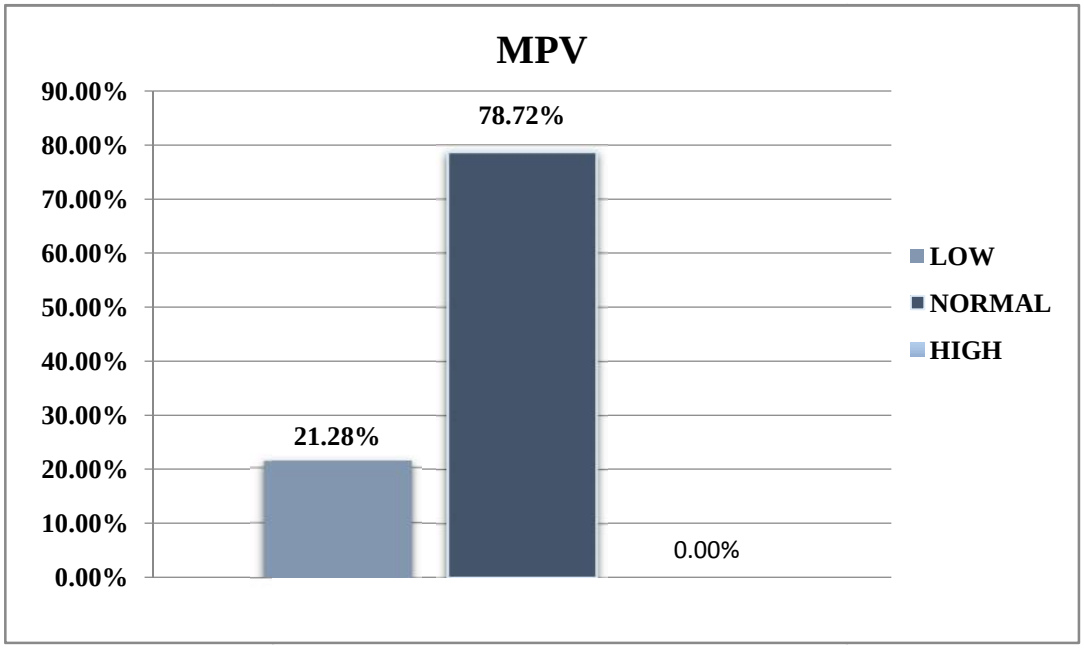


In this study out of 120 patients, maximum number of patients(98.3%) presented with thrombocytopenia, only 2 patients (1.7%) diagnosed with dengue fever had normal platelet count of more than 1,50,000. Majority of the patients with thrombocytopenia (49.2%) had platelet count between 50,000–99,999/cumm, whereas 18.30% patients had platelet count <20,000/cumm. (Table-15, Graph-15)

TABLE–16 :MPV levels in Dengue Fever patients

MPV	NUMBER OF PATIENTS	PERCENTAGE
Low	20	21.28%
Normal	74	78.72%
High	00	00%
Total	94	100%

GRAPH -16 : MPV levels in Dengue Fever patients

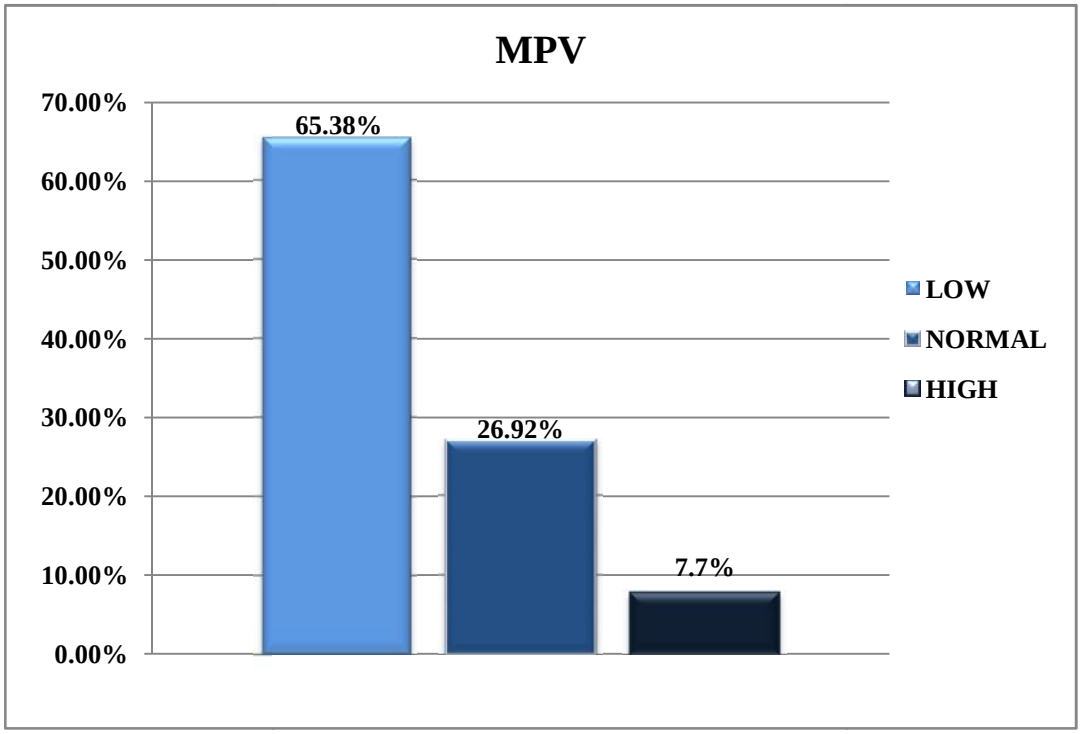


In our study maximum patients (78.72%) showed normal MPV, where as low MPV was seen in 21.28% of patients. None of the patients presented with raised MPV. (Table-16, Graph-16)

TABLE - 17 : MPV levels in Dengue Haemorrhagic Fever patients

MPV	NUMBER OF PATIENTS	PERCENTAGE
Low	17	65.38%
Normal	07	26.92%
High	02	7.7%
Total	26	100%

GRAPH -17 : MPV levels in Dengue Haemorrhagic Fever patients

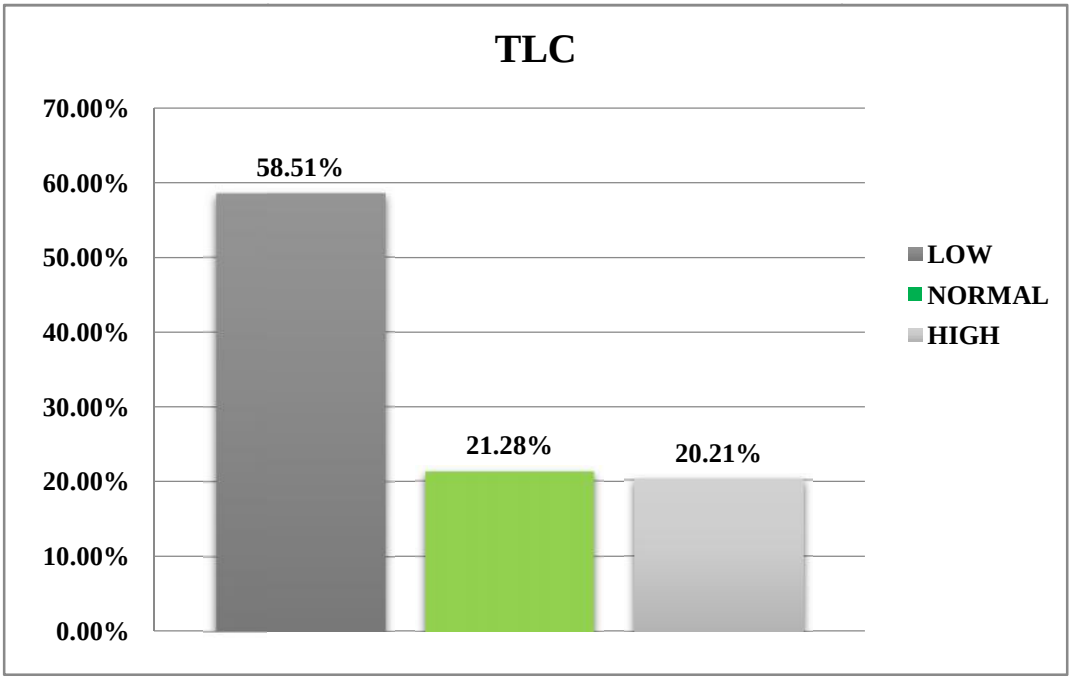


In this study majority of the patients diagnosed with DHF presented with reduced MPV levels (65.38%) , where as normal MPV level was seen in 26.92% and raised MPV was seen in 7.7% patients.(Table-17, Graph-17)

TABLE -18 : Distribution of patients with Dengue Fever according to TLC

TLC	NUMBER OF PATIENTS	PERCENTAGE
Low	55	58.51%
Normal	20	21.28%
High	19	20.21%
Total	94	100%

GRAPH –18 :Distribution of patients with Dengue Fever according to TLC

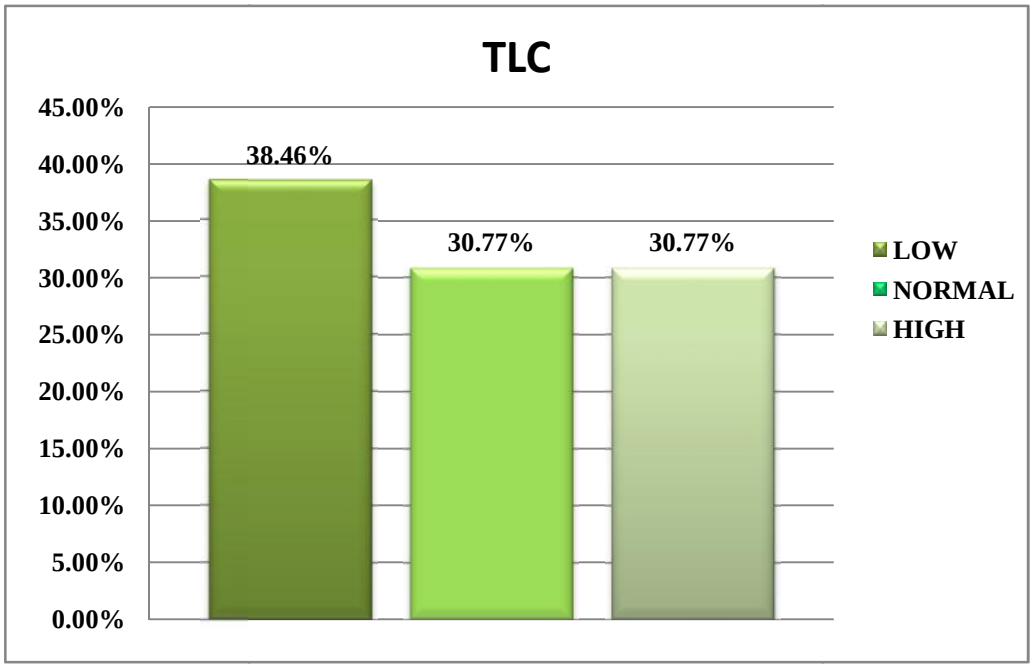


In this study maximum patients (58.51%) presented with leucopenia. However, 21.28% patients had normal total count, where as there was leucocytosis in 20.21% cases. (Table-18, Graph-18)

TABLE -19 : Distribution of patients with DHF ccording to TLC

TLC	NUMBER OF PATIENTS	PERCENTAGE
Low	10	38.46%
Normal	08	30.77%
High	08	30.77%
Total	26	100%

GRAPH –19 :Distribution of patients with DHF according to TLC



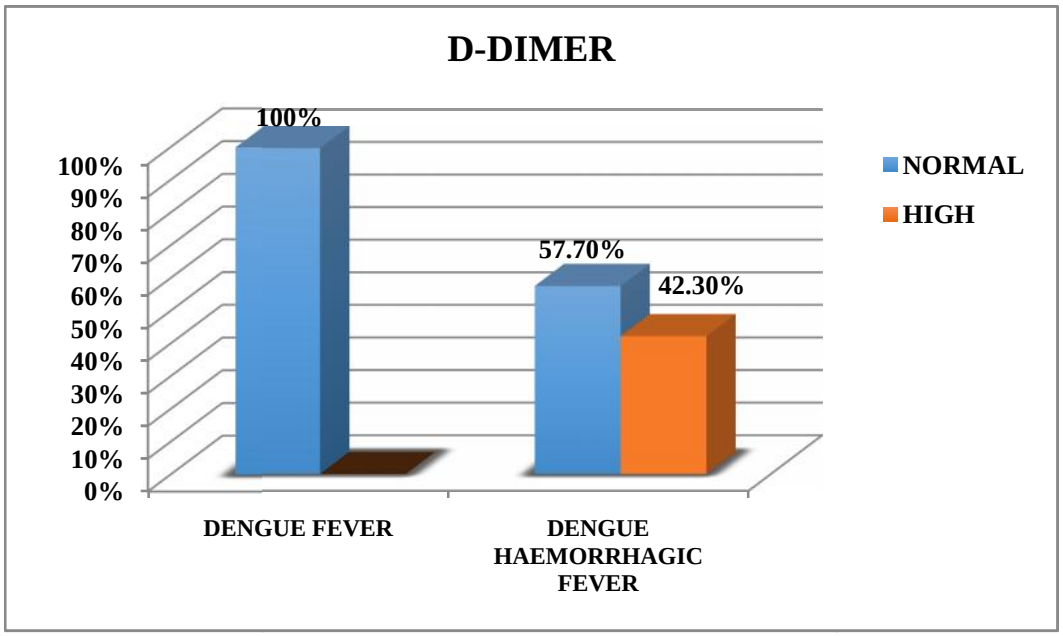
In this study maximum patients (38.46%) presented with leucopenia, whereas 30.77% patients showed leucocytosis and normal count was presented by 30.77% patients. (Table-19, Graph-19)

TABLE –20: Distribution of D-dimer levels in dengue patients

D-dimer was performed only in 35 NS1 positive patients, out of which 26 cases were of DHF and 9 cases were that of DF.

D-DIMER	DENGUE FEVER	DENGUE HAEMORRHAGIC FEVER
Normal	09 (100%)	15 (57.70%)
High	00 (0.0%)	11 (42.30%)
Total	09 (100%)	26 (100%)

GRAPH -20 :Distribution of D-dimer levels in dengue patients

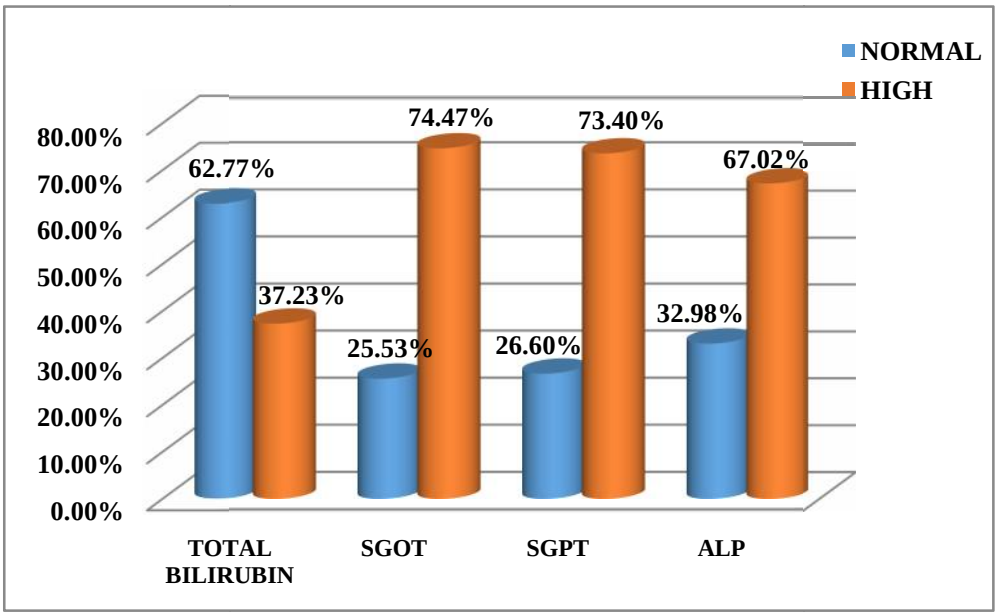


In the present study, among the 26 DHF cases, 57.70% had normal d-dimer levels where as 42.30% cases had high d-dimer levels. And out of the 9 dengue fever cases, all 9 of them had normal d-dimer levels. (Table-20, Graph-20)

TABLE –21: Liver function tests in Dengue fever patients

TOTAL BILIRUBIN	NUMBER OF PATIENTS	PERCENTAGE
Normal	59	62.77%
High	35	37.23%
Total	94	100
SGOT	**NUMBER OF PATIENTS**	**PERCENTAGE**
Normal	24	25.53%
High	70	74.47%
Total	94	100
SGPT	**NUMBER OF PATIENTS**	**PERCENTAGE**
Normal	25	26.60%
High	69	73.40%
Total	94	100
ALP	**NUMBER OF PATIENTS**	**PERCENTAGE**
Normal	31	32.98%
High	63	67.02%
Total	94	100

GRAPH - 21 :Liver function tests in Dengue Fever patients

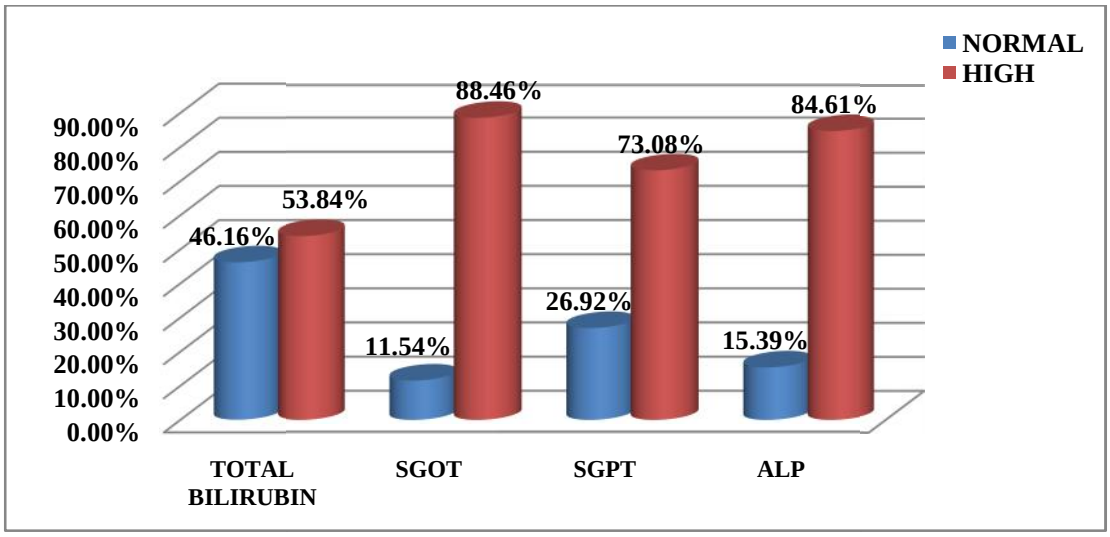


Our study showed marked raise in the liver enzymes. Among the 94 DF patients, 70 patients (74.47%) had raised SGOT, 69 patients (73.40%) had raised SGPT and 63 patients (67.02%) had raised ALP levels. Total bilirubin was normal in majority of patients where as it was raised in 37.23%. (Table-21,Graph-21).

TABLE –22 :Liver function tests among Dengue Haemorrhagic Fever patients

TOTAL BILIRUBIN	NUMBER OF PATIENTS	PERCENTAGE
Normal	12	46.16%
High	14	53.84%
Total	26	100%
SGOT	**NUMBER OF PATIENTS**	**PERCENTAGE**
Normal	03	11.54%
High	23	88.46%
Total	26	100%
SGPT	**NUMBER OF PATIENTS**	**PERCENTAGE**
Normal	07	26.92%
High	19	73.08%
Total	26	100%
ALP	**NUMBER OF PATIENTS**	**PERCENTAGE**
Normal	04	15.39%
High	22	84.61%
Total	26	100%

GRAPH - 22 :Liver function tests among Dengue Haemorrhagic Fever patients

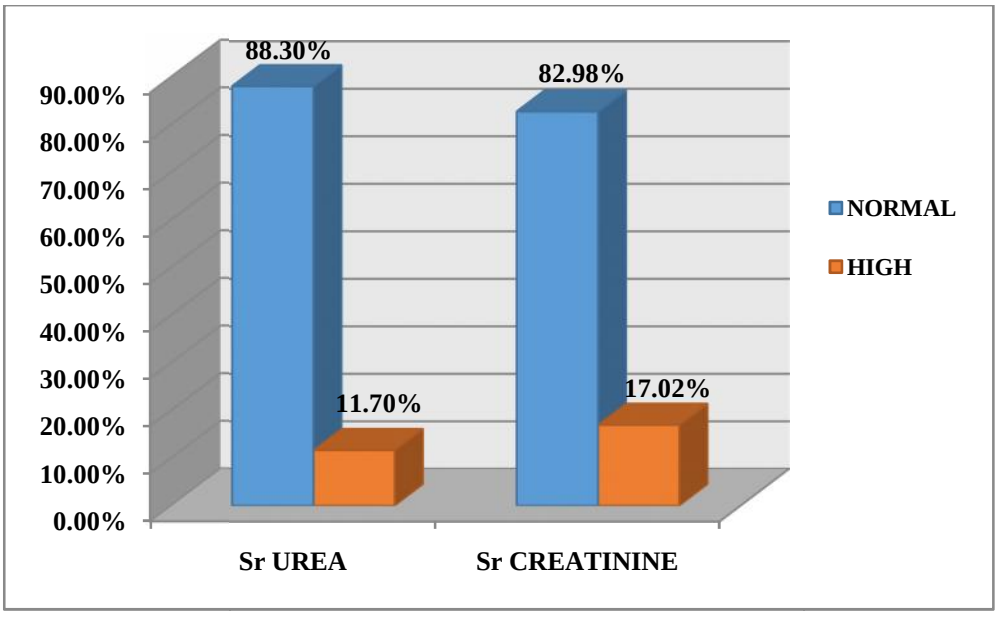


In this study, there was marked increase in all the liver enzymes. Out of 26 DHF patients, 23 patients (88.46%) had raised SGOT, 19 patients (73.08%) had raised SGPT and 22 patients (84.61%) had raised ALP levels. 53.84% patients showed raised total bilirubin. (Table-22, Graph-22)

TABLE –23 : Distribution of Dengue Fever cases according to renal function tests

SR.UREA	NUMBER OF PATIENTS	PERCENTAGE
Normal	83	88.30%
High	11	11.70%
Total	94	100%
SR. CREATININE	**NUMBER OF PATIENTS**	**PERCENTAGE**
Normal	78	82.98%
High	16	17.02%
Total	94	100%

GRAPH – 23 : Distribution of Dengue Fever cases according to renal function tests

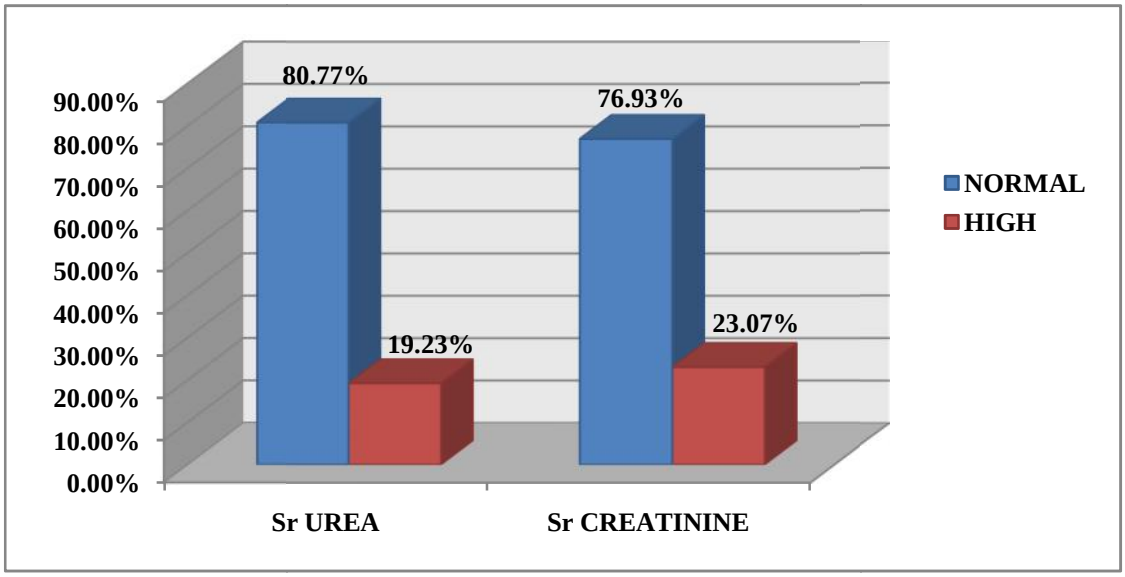


Our study showed majority of the patients with normal serum urea and serum creatinine. Only 11.70% patients had raised serum urea levels and 17.02% patients had raised serum creatinine levels (Table-23, Graph-23)

TABLE –24 :Distribution of Dengue Haemorrhagic Fever cases according to renal function tests

SR.UREA	NUMBER OF PATIENTS	PERCENTAGE
Normal	21	80.77%
High	05	19.23%
Total	26	100%
SR. CREATININE	**NUMBER OF PATIENTS**	**PERCENTAGE**
Normal	20	76.93%
High	06	23.07%
Total	26	100%

GRAPH - 24 : Distribution of Dengue Haemorrhagic Fever cases according to renal function tests

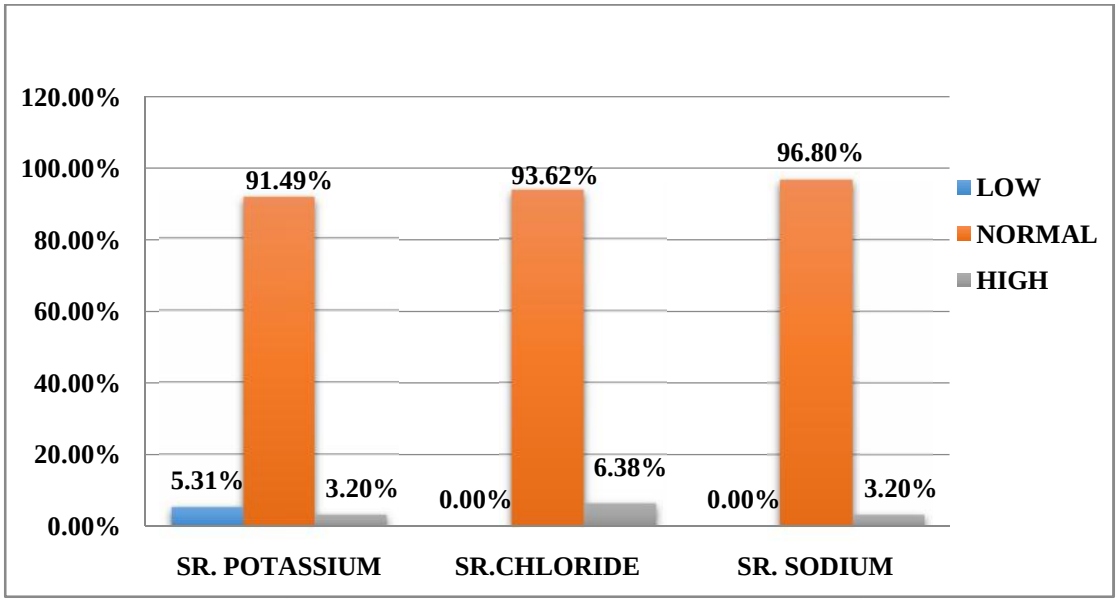


The present studyshowed all 26 DHF patients with normal serum urea and serum creatinine. Only 19.23% patients had raised serum urea levels and 23.07% patients had raised serum creatinine levels. (Table-24, Graph-24)

TABLE –25: Electrolyte levels among Dengue Fever patients

SR. POTASSIUM	NUMBER OF PATIENTS	PERCENTAGE
Low	05	5.31%
Normal	86	91.49%
High	03	3.2%
Total	94	100%
SR. CHLORIDE	**NUMBER OF PATIENTS**	**PERCENTAGE**
Low	00	00%
Normal	88	93.62%
High	06	6.38%
Total	94	100%
SR. SODIUM	**NUMBER OF PATIENTS**	**PERCENTAGE**
Low	00	00%
Normal	91	96.80%
High	03	3.2%
Total	94	100%

GRAPH–25 :Electrolyte levels among Dengue Fever patients

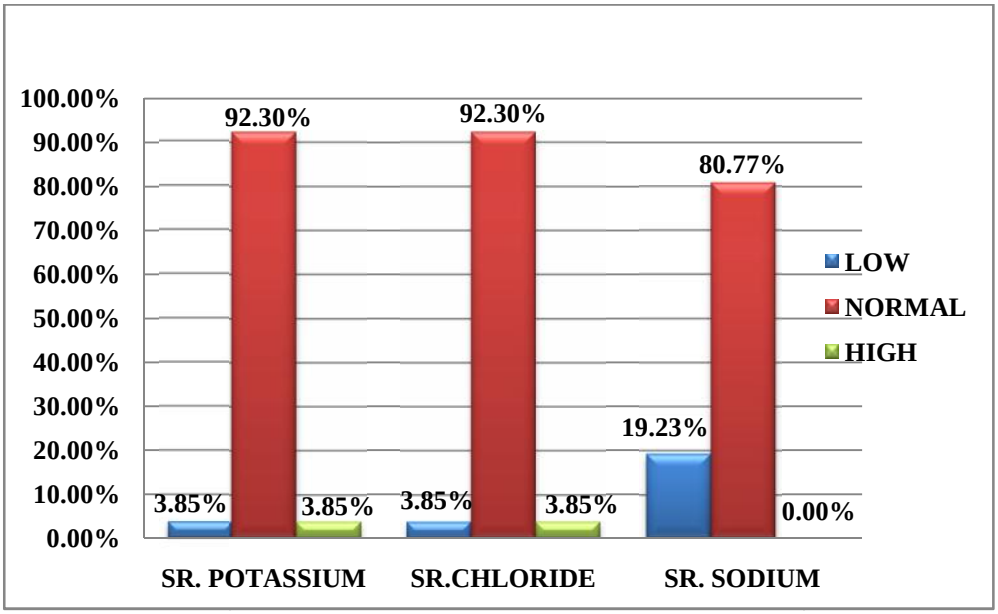


In the present study, maximum cases of DF had normal electrolyte levels. Only 3.20% patients had raised serum potassium, 6.38% patients had raised serum chloride levels and 3.20% patients had raised serum sodium levels.(Table-25, Graph-25)

TABLE –26: Electrolyte levels among Dengue Haemorrhagic Fever patients

SR. POTASSIUM	NUMBER OF PATIENTS	PERCENTAGE
Low	01	3.85%
Normal	24	92.30%
High	01	3.85%
Total	26	100%
SR. CHLORIDE	**NUMBER OF PATIENTS**	**PERCENTAGE**
Low	01	3.85%
Normal	24	92.30%
High	01	3.85%
Total	26	100%
SR. SODIUM	**NUMBER OF PATIENTS**	**PERCENTAGE**
Low	05	19.23%
Normal	21	80.77%
High	00	00%
Total	26	100%

GRAPH–26 :Electrolyte levels among Dengue Haemorrhagic Fever patients



In our study, maximum DHF cases presented with normal serum potassium, serum chloride and serum sodium levels. Raised serum potassium and serum chloride levels were seen in 3.85% patients. 19.23% patients presented with hyponatraemia. (Table-26, Graph-26)

Table – 27 :Haematological and Biochemical profiles of the patients

Sl No	Variables	Mean (n =120)		Median	Range	
		Mean	SD		Minimum	Maxiumum
1.	AGE (Years)	29.38	17.740	25	2	80
2.	HAEMOGLOBIN(gm/dl)	14.58	3.587	14	6	21
3.	RBC (million/cumm)	4.97	1.159	5	2	7
4.	PCV(%)	48.28	10.782	55	22	60
5.	PLATELET (cells/cumm)	60,316.67	35164.67	63,000	8000	158000
6.	MPV(fL)	10.16	1.432	10	8	14
7.	TLC (cells/cumm)	5714.67	3883.983	3750	1900	19000
8.	TOTAL BILIRUBIN(mg/dl)	1.01	.815	1	0	3
10.	SGOT(IU/L)	310.67	408.237	87	10	1220
11.	SGPT(IU/L)	318.07	418.072	90	10	2000
12.	ALP(IU/L)	436.42	256.065	385	90	1152
13.	SR.UREA(mg/dL)	28.72	11.478	25	13	52
14.	SR. CREATININE(mg/dL)	.56	.765	0	0	2
16.	SR. SODIUM(mEq/L)	141.04	6.639	140	119	155
17.	SR. POTASSIUM(mEq/L)	4.22	.667	4	2	6
18.	SR.CHLORIDE(mEq/L)	99.80	8.212	98	89	150

Table – 28 :Correlation between Clinical and Haematological findings using Spearman's correlation coefficient

Clinical features		Haematological findings						
		HB	RBC	PCV	MPV	TLC	D-DIMER	PLATELET
FEVER	r	NA	NA	NA	NA	NA	NA	NA
	p	NA	NA	NA	NA	NA	NA	NA
	n	120	120	120	120	120	34	120
RASH	r	-.098	-.019	-.169	.200	-.054	-.475	.409
	p	.286	.837	.065	.028*	.555	.005*	.0001*
	n	120	120	120	120	120	34	120
MYALGIA	r	.133	.164	.160	.083	.085	-.126	.130
	p	.148	.074	.080	.370	.353	.479	.182
	n	120	120	120	120	120	34	120
ARTHRALGIA	r	-.172	-.023	-.057	.078	.042	-.184	-.193
	p	.060	.805	.539	.398	.648	.298	.045*
	n	120	120	120	120	120	34	120
ITCHING	r	.000	.142	.168	.104	.023	-.377	.077
	p	.998	.121	.067	.261	.800	.028*	.427
	n	120	120	120	120	120	34	120
ABDOMINAL PAIN	r	.096	.144	-.049	.323	.075	-.199	.090
	p	.299	.116	.599	.0001*	.417	.259	.356
	n	120	120	120	120	120	34	120
RETRO ORBITAL PAIN	r	-.020	.018	.004	-.010	-.007	-.276	.099
	p	.830	.841	.967	.913	.940	.114	.308
	n	120	120	120	120	120	34	120
BLEEDING DISORDER	r	-.119	.008	-.012	.207	-.131	-.520	-.541
	p	.196	.928	.895	.024*	.153	.002*	.0001*
	n	120	120	120	120	120	34	120

r = Correlation Coefficient, p = p value (probability value), n = number of study participants

* = Statistically significant

Interpretation:

All the clinical features - fever, myalgia, arthralgia, itching, rash, pain in abdomen, retro orbital discomfort and bleeding disorder were correlated using "Spearman's correlation".

Correlation coefficient (r) was seen between -1 to +1. A negative 'r' value indicated negative correlation and positive 'r' value indicated positive correlation. Zero signifies no correlation. 'p' value of less than 0.05 was considered to be statistically significant.

If 'r' was less than 0.3 it signified weak correlation, if 'r' was between 0.3 to 0.7 it signified moderate correlation and if greater than 0.7 then strong correlation exists between two variables.

Fever was present in all the study participants, therefore the correlation coefficient could not be obtained in relation to the haematological findings. Also D-Dimer values were obtained in 34 patients out of 120. Hence the correlation with this variable was done among those who showed the presence of it.

Patients with rash showed weak negative correlations with parameters like Haemoglobin, RBC, PCV and TLC. A moderate correlation existed between rash and D-dimer (r = -0.475) and it was found to be statistically significant. However, patients with rash showed positive correlations with MPV and platelet which was found to be statistically significant.

Myalgia and retro-orbital pain showed very weak correlations with haematological counterparts and none of the variables were found to have statistically significant p values.

Arthralgia showed mild haematological correlation, however the correlation with platelet was found to be statistically significant even though it exhibited weak negative correlation coefficient.

Similar kind of weak correlation pattern were observed with itching, but it was noted to have statistical significant and a moderate negative correlation with D-Dimer.

Abdominal pain showed a moderate positive correlation ($r = 0.32$) with MPV and it was found to be statistically significant.

Correlations between the other variables were very weak and hence were not statistically significant.

Those with bleeding disorders showed a weak positive statistically significant correlation with MPV where as with platelet it showed a moderate negative highly statistically significant correlation.

Table – 29 : CORRELATION OF PLATELET WITH CLINICAL FEATURES

Correlation coefficients	Fever	Type Of Fever	Rash	Arthralgia	Myalgia	Itching	Abdominal Pain	Retro-Orbital Pain	Bleeding Disorder
r	NA	-.738	.409	-.193	.130	.077	.090	.099	-.541
p	NA	**.0001**	.0001*	.045*	.182	.427	.356	.308	.0001*
n	120	120	120	120	120	120	120	120	120

The table depicts the correlation between platelet count and the clinical findings using spearman's correlation coefficient. It was observed that the type of fever, arthralgia and bleeding disorder was negatively correlated with platelet count, with correlation coefficients (r) as -0.738, -.193 and -.541 respectively. Among all these findings platelet count was found to be strongly correlated with the type of fever the patient had and bleeding disorder. These were highly statistically significant. ($p = 0.0001$).

All other clinical findings i.e., Rash, Itching, Myalgia, Abdominal discomfort and Retro orbital region pain were positively correlated and all of them were significant statistically. ($p<0.05$)

DISCUSSION

Early diagnosis of dengue is a challenge as it begins with nonspecific symptoms, like fever, arthralgia and myalgia mimicking those of malaria, typhoid and leptospirosis which are endemic in the country.

Detection of dengue by molecular methods (RT-PCR) or virus isolation are considered as confirmatory tests for the diagnosis of dengue infection. However, the requirement for necessary infrastructure, technical expertise and high cost of the test, make these methods limited. Rapid and early diagnosis is essential for speedy management as there is no specific vaccine or treatment for dengue. Serological tests detect virus late in the course of the disease. Haematological investigations help in rapid and early diagnosis of dengue and also forecast the onset of severe dengue. These investigations are very useful in rural setup having limited resources.[83]

However, to date several studies[22,31] have reported the clinical profile of dengue fever using NS1. Hence our study attempted to evaluate and correlate the role of clinico haematological profile in Dengue diagnosis and to know the relationship of the relevant haematological parameters and clinical manifestations during the course of the disease which can be used as markers to suspectand diagnose early dengue infection specially in rural/peripheral areas.

This one year observational study was conducted in the Department of Pathology, J N Medical College and KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi in the year 2018 from January - December. Total 120 dengue fever cases confirmed through dengue serology with NS1 antigen were studied.

Table – 30 : Comparison of age with other studies

S.NO.	STUDIES CONDUCTED	COMMON AGE GROUP AFFECTED	RANGE OF AGE GROUP	TOTAL CASES
1.	Patel M et al[84]	26-35 years (35.38 %)	15-75 years	250
2.	Gitika, et al [85]	21-40 years (52%)	1-70 years	100
3.	Tahlan A et al[86]	21-30 years (39.13%)	14 - 60 years	46
4.	Shaheen S et al[87]	18– 40 years (71.90%)	18- > 50 years	210
5.	Present study	14-50 years (70%)	1 - > 50 years	120

The common age group in the present study was 14-50 years (70%). Studies done by Patel M et al[84], Gitika, et al[85], Tahlan A et al[86] and Shaheen S et al[87] correlated with our study and was seen that the most commonly affected age was the middle age between 20 to 50 years. This is the working class of age group and thus these people are more susceptible to mosquito bites.[85]

Table – 31 :Comparison of sex with other studies

S.NO.	STUDIES CONDUCTED	MALE	FEMALE	MALE TO FEMALE RATIO	TOTAL CASES
1.	Joshi, et al[83]	73 (55%)	59 (45%)	1.2:1	132
2.	Yaseen, et al[88]	59 (59%)	41(41%)	1.4:1	100
3.	Patel M et al[84]	52 (63%)	30 (37%)	1.7:1	82
4.	Present study	79 (66%)	41 (34%)	1.9:1	120

The present study showed 66% males and 34% females. The male to female ratio was 1.9:1. Studies done by Joshi et al[83], Yaseen, et al[88] and Patel M et al[84] also showed similar results with male preponderance. Majority of the patients were males, due to occupational exposure during day time hours either at their work place or during travelling to and from work and increased recreational activity leading to greater exposure to dengue carrying mosquitoes as compared to females.[84]

Table – 32 : Comparison of socio economic status with other studies

S.NO	STUDIES	UPPER	UPPER MIDDLE	LOWER MIDDLE	UPPER LOWER	LOWER	TOTAL CASES
1.	Nijhawan DM et al[62]	0 (0%)	58 (29%)	84 (42%)	58 (29%)	0 (0%)	200
2.	Anand, et al[89]	1 (1%)	68 (68%)	18 (18%)	13 (13%)	0 (0%)	100
3.	Gupta S et al[90]	25 (25%)	56 (56%)	19 (19%)	0 (0%)	0 (0%)	100
4.	PRESENT STUDY	14 (11.67%)	25 (20.83%)	51 (42.5%)	20 (16.67%)	10 (8.33%)	120

In our present study maximum dengue patients (42.5%) belonged to the lower middle socio economic status which correlated with the study conducted by Nijhawan DM et al[62]showing 42% dengue patients from the lower middle socio - economic status. Other studies by Anand et al[89] and Gupta S et al[90] also showed maximum patients from the upper middle and lower middle socioeconomic status.

It is because of less awareness among these class of people that dengue mosquitoes breed in clean standing water along with less knowledge about the preventive measures i.e, mosquito mats, vaporizers, net on the windows, using sprays or repellent creams.[62]

Table – 33 : Comparison of clinical manifestation of dengue fever with other studies

S.NO.	STUDIES CONDUCTED	DF	DHF	DSS	TOTAL CASES
1.	Yaseen, et al[88]	81 (81%)	15 (15%)	4 (4%)	100
2.	Oza J R et al[91]	131 (90.34%)	14 (9.66%)	0 (0%)	145
3.	Gitika, et al[85]	96 (96%)	3 (3%)	1 (1%)	100
4.	PRESENT STUDY	94 (78.30%)	26 (21.70%)	0 (0%)	120

In this study, maximum (78.30%) cases had DF, 21.70% cases manifested with DHF where as none of the cases showed signs and symptoms of DSS.

Yaseen et al[88], Oza J R et al[91]and Gitika et al[85]also showed maximum cases with DF followed by DHF. Studies by Yaseen et al[88] and Gitika et al[85] showed only a few cases of DSS. Hospitals with highly trained staff and resources have reported to have reduced incidence of Dengue shock syndrome.[88]

All these studies correlated with the present study.

Table – 34 : Comparison of clinical features of Dengue Fever with other studies

STUDIES CONDUCTED	FEVER	ARTHRALGIA	MYALGIA	RASH	ABDOMINAL PAIN	RETRO ORBITAL PAIN	ITCHING	BLEEDING DISORDER	TOTAL CASES
Jain A et al[92]	43 (100%)	6 (14%)	24 (55%)	6 (14%)	2 (5%)	9 (21%)	0 (0%)	0 (0%)	43
Patel M et al[84]	82 (100%)	72 (87%)	49 (59%)	13 (15.6%)	29 (35.4%)	0 (0%)	0 (0%)	8 (9.6%)	82
Ram V et al[93]	148 (99.32%)	36 (24.16%)	48 (32.21%)	4 (2.68%)	32 (21.47%)	25 (16.77%)	25 (16.77%)	9 (6.03%)	149
PRESENT STUDY	94 (100%)	69 (73.40%)	74 (78.72%)	36 (38.29%)	51 (54.25%)	48 (51.0%)	59 (62.77%)	11 (11.70%)	94

Among DF patients, our study showed fever (100%) as the commonest clinical presentation followed by myalgia (78.72%), arthralgia (73.40%), itching (62.77%), abdominal pain (54.25%), retro orbital pain (51%) and rash (38.29%).

Studies done by Jain A et al[92], Patel M et al[84] and Ram V et al[93] also showed fever, myalgia and arthralgia as the common clinical features. However itching was not reported by Jain A et al[92] and Patel M et al[84]. In the study by Patel M et al[84] retro orbital pain was not seen in any case where as bleeding manifestation was not obvious in the study by Jain A et al[92].

Hence, the preliminary symptoms like fever, arthralgia, myalgia with rash was observed in all the above studies and correlated with our study.

Table–35 :Comparison of clinical features of Dengue Haemorrhagic Fever with other studies

STUDIES CONDUCTED	FEVER	ARTHRALGIA	MYALGIA	RASH	ABDOMINAL PAIN	RETRO ORBITAL PAIN	ITCHING	BLEEDING DISORDER	TOTAL CASES
Jain A et al[92]	11 (100%)	2 (18%)	7 (63%)	1 (9%)	3 (27%)	2 (18%)	0 (0%)	1 (9%)	11
Chaudhuri NG et al [94]	10 (100%)	4 (40%)	5 (50%)	10 (100%)	2 (20%)	5 (50%)	0 (0%)	10 (100%)	10
Ram V et al[93]	70 (98.59%)	22 (30.98%)	21 (29.57%)	56 (78.87%)	43 (60.56%)	10 (14.08%)	28 (39.43%)	22 (30.91%)	71
PRESENT STUDY	26 (100%)	20 (76.92%)	22 (84.61%)	25 (96.15)	22 (84.61%)	10 (38.47%)	10 (38.47%)	26 (100%)	26

In DHF our study correlated with the studies done by Jain A et al[92], Chaudhuri NG et al[94] and Ram V et al[93]as the predominant clinical feature of DHF was fever, bleeding disorder, retro-orbital pain, myalgia, severe arthralgia and rash. Bleeding disorder and rash mainly correlated with Chaudhuri NG et al.[94]Itching was not seen in Jain A et al[92] and Chaudhuri NG et al.[94]

Hence most of the clinical features in our study correlated with the other studies.

Laboratory assessment

Table – 36 : Comparison of Dengue serology with other studies

S.NO.	STUDIES CONDUCTED	NS1	IgM	IgM and IgG	NS1, IgM and IgG	TOTAL CASES
1.	Patel M et al [84]	200 (80%)	50 (20%)	0 (0%)	0 (0%)	250
2.	Badave GK. et al.[95]	54 (42.9%)	6 (4.7%)	40 (16.87%)	126 (53.16%)	237
3.	Present study	120 (100%)	93 (77.50%)	25 (20.80%)	25 (20.80%)	120

In this study, all 120 cases were NS1 positive, as the inclusion criteria of the present study was all patients with NS 1 positivity. IgM was positive in 77.50% patients, proving these patients became infected with dengue with in recent weeks, where as both IgM and IgG was positive in 21%, suggesting these patients had dengue infection second time (recent secondary infection). There was absence of both IgM and IgG in 1.70% of patients.

In studies by Patel M et al[84] and Badave GK. et al.[95] NS 1 was positive in 80% and 42.9% respectively. Study by Patel M et al[84] did not have any case with IgG positivity. In both these studies the inclusion criteria was patients with either NS1, IgM or IgG positivity.

All the above studies correlated with the present study.

Table – 37 : Comparison of haematological parameters of Dengue Fever with other studies

S.NO.	STUDIES CONDUCTED	HAEMOGLOBIN	RBC	PCV	PLATELET	MPV	TC	TOTAL CASES
1.	Meena KC et al [96]	Normal (57%)	-	Normal (33%)	Thrombocytopenia (90%)	-	Leucopenia (51%)	100
2.	Madhuri K et al[97]	Normal (47.36%)	-	Raised (30%)	Thrombocytopenia (100%)	-	Leucopenia (35%)	57
3.	Shamsunder Khatroth[98]	Normal (33.3%)	-	Normal (33.3%)	Thrombocytopenia (83.33%)	-	Leucopenia (20%)	60
4.	Present study	Normal (42.55%)	Normal (50%)	Raised (57.44%)	Thrombocytopenia (97.87%)	Normal (78.72%)	Leucopenia (58.51%)	94

In this study maximum dengue fever patients presented with normal haemoglobin (42.55%), raised haematocrit (57.44%), thrombocytopenia (97.87%) and leucopenia (58.51%). RBC and MPV were with in normal range. Study conducted by Madhuri K et al[97] showed similar results. Studies by Shamsunder Khatroth[98] and Meena KC et al[96] also showed similar results except haematocrit value which was normal in majority of their patients. Possible reason could be the hospital in which these studies were performed was a tertiary care level; mostly patients came here from other hospital with primary management with I.V fluid. So mostly patients had normal haematocrit.[96] In our study haematocrit was raised due to haemoconcentration attributed to plasma leakage.[88] Madhuri K et al[97], Shamsunder Khatroth[98] and Meena KC et al[96] did not include RBC and MPV in their study, where as our study included the two parameters and both were with normal.

Table –38 : Comparison of haematological parameters of DHF with other studies

S.NO	STUDIES CONDUCTED	HAEMOGLOBIN	RBC	PCV	PLATELET	MPV	TC	TOTAL CASES
1.	Nazish Butt et al [99]	Normal (96.15%)	-	Raised (50%)	Thrombocytopenia (100%)	-	Leucopenia (52.89%)	104
2.	Mogra G et al[100]	-	-	Raised (65.90%)	Thrombocytopenia (68.18%)	-	Leucopenia (50.20%)	44
3.	Sudarsi RK et al[101]	Normal (44.44%)		Raised (50%)	Thrombocytopenia (100%)	-	Leucopenia (38.88%)	18
4.	Present study	Normal (50%)	Normal (42.30%)	Raised (46.16%)	Thrombocytopenia (100%)	Low (65.38%)	Leucopenia (38.46%)	26

In our study all dengue haemorrhagic patients presented with raised haematocrit (46.16%), thrombocytopenia (100%), leucopenia (38.46%) and reduced MPV (65.38%), haemoglobin and RBC count was normal. Studies conducted by Nazish Butt et al[99], Mogra G et al[100] and Sudarsi RK et al[101] showed similar reports. However all these three studies did not include RBC count and MPV levels. Mogra G et al[100] did not include haemoglobin in his study. Low MPV was also seen in the study by Mukker P et al[102], Nidhish Kumar et al[103] and Navya et al.[104]

Haematocrit is raised due to haemoconcentration attributed to leakage of plasma which is caused due to cytokine-mediated surge in vascular permeability leading to vascular endothelium damage, which is the main pathophysiological change in DF.[88]

An initial low MPV suggests marrow suppression which is a cause of reduced platelet count and a rising MPV heralds the improvement in platelet count. Therefore, a high MPV indicates increased platelet diameter, this can be used as an indicator for the production rate and activation of platelets.[102]

The inception of thrombocytopenia can be triggered by multiple factors. It can result as a consequence of immune response against platelet which causes the binding of dengue antigens to platelets followed by their immunological destruction, mediated by antibodies.[88] It may also be caused as a result of direct infection of dengue virus on megakaryocytes, which results in increased platelet destruction. In the acute stage of this fever, thrombocytopenia is noted due to the depression of bone marrow.[103] This results in production of cytokines by monocytes infected with dengue virus, B lymphocytes and mast cells.

Leucopenia is caused due to suppression of myeloid series in the bone marrow by dengue virus during the acute phase of the disease.[88]

Table –39 : Comparison of D Dimer levels in Dengue Fever cases with other studies

S.NO	STUDIES CONDUCTED	INCREASED	NORMAL	TOTAL
1.	Bashir AB et al [105]	70 (86.4%)	11 (13.6%)	81
2.	K. Setrkraising, et al [106]	4 (13 %)	8 (87%)	12
4.	PRESENT STUDY	0	09 (100%)	09

In this study D dimer was performed in 9 DF patients and all 9 of them showed normal D dimer levels. Present study correlated with K. Setrkraising, et al[106], whereas Bashir AB et al[105] showed increased D dimer levels (86.4%) in DF patients. Detection of D dimer in the febrile stage of dengue is essential for predicting the clinical course and severity of the disease before the patients progress into toxic stage so that proper managementcan be arranged.[106]

Table –40 : Comparison of D Dimer levels in DHF cases with other studies

S.NO	STUDIES CONDUCTED	INCREASED	NOMAL	TOTAL
1.	Khurshid et al [107]	79 (97.5%)	2 (2.5%)	81
2.	Bashir AB et al[105]	17 (85%)	3 (15%)	20
3.	K. Setrkraising, et al [106]	26 (87 %)	3 (13%)	29
4.	PRESENT STUDY	11 (42.30%)	15 (57.70%)	26

In this study out of the 26 DHF cases 57.70% showed normal D dimer. But the results of Khurshid et al[107], Bashir AB et al[105] and K. Setrkraising et al[106] had increased D dimer levels. D-dimer indicates activation of the coagulation system leading to destruction of cross-linked fibrin, reflecting clot formation and lysis. This informs about the severity of dengue [107]However in our study, all DF cases showed normal D dimer levels, whereas raised D dimer was seen in DHF patients, especially those with severe thrombocytopenia (platelet count < 20,000) as an early indicator of shock or DIC.

Table –41 : Comparison of liver function tests of Dengue Fever with other studies

S.NO	STUDIES CONDUCTED	TOTAL BILIRUBIN	SGOT	SGPT	ALP	TOTAL CASES
1.	Rajaih VN et al[108]	Normal (96.9%)	High (94%)	High (86%)	High (40.6%)	64
2.	Narasimhan D et al [109]	Normal (95%)	High (92%)	High (82%)	High (25%)	100
3.	Rajoo Singh Chhinaa et al[110]	Normal (86.5%)	High (97.1%)	High (92.5%)	High (30.3%)	174
4.	Present study	Normal (62.77%)	High (74.47%)	High (73.40%)	High (67.02%)	94

In this study patients with DF presented with elevated liver function tests except for total bilirubin which was normal in 62.77% patients. SGOT was raised in 74.47%, SGPT in 73.40% and ALP in 67.02% of patients. Comparable results were seen in studies conducted by Rajaih VN et al[108],Narasimhan D et al[109] and Rajoo Singh Chhinaa et al.[110]

The cause for the liver dysfunction is multifactorial and may happen secondary to hypoxia, direct effect of virus or immune mediated damage. Dengue virus directly attacks the kupffer cells and the hepatocytes in the liver. It binds to the receptors while entering the cell and is then taken inside the cell by endocytosis, causing apoptosis of cells.[6,7,109]

ALP is generally raised in hepatobiliary diseases resulting in cholestasis.[109]

Table –42 : Comparison of liver function tests of DHF with other studies

S.NO	STUDIES CONDUCTED	TOTAL BILIRUBIN	SGOT	SGPT	ALP	TOTAL CASES
1.	**Rajaih VN et al[108]**	**High (33.3%)**	**High (100%)**	**High (97%)**	**High (80%)**	**30**
2.	**Rajoo Singh Chhinaa et al[110]**	**High (28.6%)**	**High (100%)**	**High (93.1)**	**High (40%)**	**29**
3.	**Biswas, et al[111]**	**Normal (100%)**	**High (100%)**	**High (100%)**	**High (100%)**	**04**
4.	**Present study**	**High (53.84%)**	**High (88.46%)**	**High (73.08%)**	**High (84.61%)**	**26**

In the present study patients with DHF presented with raised liver function tests. Total bilirubin was raised in 53.84%,where as it was normal in DF, reason being acute blood loss leading to ischaemic injury to the liver.[111] SGPT in 88.46%, SGOT in 73.08% and ALP in 84.61% patients. These results correlated with the studies by Rajaih VN et al[108], Rajoo Singh Chhinaa et al[110] and Biswas, et al[111].

Table –43 : Comparison of renal function tests of Dengue Fever with other studies

S.NO.	STUDIES CONDUCTED	SERUM UREA	SERUM CREATININE	TOTAL CASES
1.	Khan, et al[112]	Normal	Normal (100%)	100
2.	Vakrani GP et al [113]	Normal	Normal (98.6%)	70
3.	Present study	Normal (88.30%)	Normal (82.98%)	94

This study showed all dengue fever patients having with normal serum urea and serum creatinine. Khan et al[112]and Vakrani GP et al[113]also showed normal electrolyte levels in dengue .

Table –44 : Comparison of renal function tests of DHF with other studies

S.NO.	STUDIES CONDUCTED	SERUM UREA	SERUM CREATININE	TOTAL CASES
1.	Khan, et al[112]	Normal	Normal (86%)	50
2.	Vakrani GP et al [113]	Normal	Normal (79%)	19
4.	Present study	Normal (80.77%)	Normal (76.93%)	26

In the present study all 26 dengue haemorrhagic fever patients presented with normal serum urea and serum creatinine. Similar outcomes were found by Khan et al[112]and Vakrani GP et al[113].

Table –45 : Comparison of electrolyte levels of DF with other studies

S.NO.	STUDIES CONDUCTED	SERUM POTASSIUM	SERUM CHLORIDE	SERUM SODIUM	TOTAL CASES
1.	Muhammad Sarfraz et al[114]	Normal (75.7%)	Normal (52.9%)	Normal (60%)	70
2.	Relwani PR et al[115]	Normal (86%)	Normal (87.33%)	Normal (51.33%)	150
3.	Bandaru AK et al[116]	Normal (66.2%)	-	Normal (51.6%)	62
4.	Present study	Normal (91.49%)	Normal (93.62%)	Normal (96.80%)	94

In the present study all 94 dengue fever patients showed normal serum potassium, sodium and chloride levels. Studies conducted by Muhammad Sarfraz et al[114], Relwani PR et al[115]and Bandaru AK et al[116] also showed similar results.

Table –46 : Comparison of electrolyte levels of DHF with other studies

S.NO	STUDIES CONDUCTED	SERUM POTASSIUM	SERUM CHLORIDE	SERUM SODIUM	TOTAL CASES
1.	Muhammad Sarfraz et al [114]	Normal (80%)	Normal (70%)	Normal (55%)	40
2.	Bandaru AK et al[116]	Normal (55.8%)	-	Hyponatremia (53.5%)	43
3.	Lumpaopong A et al[117]	Normal (83%)	-	Hyponatremia (72%)	77
4.	Present study	Normal (92.30%)	Normal (92.30%)	Normal (80.77%)	26

In this study all 26 dengue haemorrhagic patients showed normal serum potassium, chloride and sodium levels. Parallel result was seen in the study by Muhammad Sarfraz et al[114]. Research by Bandaru AK et al[116] and Lumpaopong A et al[117] showed hyponatremia in 53.5% and 72% of the cases respectively. These two studies did not include serum chloride levels. Hyponatremia might be the result of salt depletion, low renal excretion, transient unsuitable antidiuretic hormone or the influx of sodium in the cells leading to dysfunction of sodium potassium pump.[117]

CONCLUSION

The findings of this study highlight significant variations in the clinical profile of DF depending on clinical and laboratory parameters. Clinical features viz. fever, intensearthralgiaand myalgia, abdominal pain, rash, retro orbital ache and itching and laboratory parameters that is platelet count, total count, haematocrit and liver enzymes, showed significant variations.

SUMMARY

Dengue fever has wide variation in clinical profile based on the test used for the detection of dengue also there is scanty data on correlation of clinical profile with different haematological and serological diagnostic parameters in dengue fever patients.

Hence, this study was done in an attempt to assess the clinical as well as the haematological parameters of dengue infected patients in order to increase the screening sensitivity by health care specialists in the most fatal cases and try to highlight the biochemical markers that may demarcate the evolving course and prognosis of the disease.

This observational study was done for a period of one year in the Department of Pathology, J N Medical College and KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 120 dengue fever patients (NS1 positive) from January 2018 to December 2018 were studied. The important observations and implications summarized as below.

- Out of 120 patients, maximum were males (66%) with male to female ratio of 1.9:1.
- Most of the patients were aged between 14-50 years (70%) and mean age was 29.38years.
- IgM was positive in 77.50% patients.
- Maximum cases (42.5%) were from the Lower Middle group of socio economic status.

- DF constituted majority (78.3%) of the cases, and rest of the cases of DHF (21.7%). There were no cases of dengue shock syndrome.
- Clinical features viz. fever along with arthralgia, myalgia, abdominal ache, pain around the retro orbital regionand itching was found in majority of the DF cases.
- Fever along with arthralgia, myalgia, rash and bleeding disorder was more often found in cases of DHF.
- Majority of cases were with normal haemoglobin levels in dengue fever (42.55%) and dengue haemorrhagic fever (50%).
- Normal RBC count was seen in 50% cases of DF and 42.31% cases of DHF.
- Raised haematocrit was seen in 57.44% of the cases with dengue fever and 46.16% of the cases with dengue haemorrhagic fever.
- Leucopenia was seen in 58.51% of dengue fever cases and 38.46% of DHF cases.
- 97.87% of DF patients and 100% of DHF patients showed thrombocytopenia.
- D dimer levels were normal in DF, where as it was raised in 42.30% cases of DHF.
- In liver function tests, majority of cases showed marked increase in the SGOT, SGPT and ALP levels in both, dengue fever as well as dengue haemorrhagic fever cases.

- With regard to renal profile, serum creatinine levels and serum urea levels were normal in maximum cases among both the disease variants i.e; Dengue fever and Dengue haemorrhagic fever.

- Serum sodium, potassium and chloride levels were also normal in majority of the cases in both DF and DHF.

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ANNEXURE I

INFORMED CONSENT

ROLE OF CLINICO HAEMATOLOGICAL PROFILE IN DIAGNOSIS OF DENGUE - ONE YEAR HOSPITAL BASED OBSERVATIONAL STUDY

Purpose of the study: You are being asked to enroll in this study as you are eligible for participation in this study. If you are dengue virus NS 1 positive you will be included in this study.

The purpose of this study is to determine the role of clinico haematological profile in diagnosis of dengue.

Procedure: During this study, you will be asked questions regarding history and background and you are supposed to answer to the best of your knowledge . The principal investigator of the study is _____ under the guidance of _____ (guide).

If you agree to enroll yourself in this study, you will be interviewed regarding your present, past and family history and your clinical manifestations.

Risks and benefits: There are no risks involved in taking part in this study and benefit is we will be able to know the clinico haematological profile of dengue patients for early diagnosis.

Alternatives: Taking part in this study is voluntary. You may choose not to take part in this study or if you decide to take part now, you can later change your mind and

withdraw from the study. The study doctor or sponsor may terminate your participation in this study anytime.

Privacy and confidentiality: All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study will be published but your identity will be confidential in any publication. No information about you or information provided by you during research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

Financial incentives for participation: You will not be paid / offered any gift /incentives for participating in this study.

Authorization to publish results: The results of this study would be forwarded to the KLE University, Belagavi as a part of requirement towards the completion of MD degree, review and publishing.

Questions: In case you have any questions related to the study in future you can contact:

1. If you have any queries about your rights as a study subject, you may call Dr. Roopa Bellad, Professor, Department of Paediatrics, Chairman of J.N. Medical College Institutional Ethical Committee of Human Subjects Research, Ph No- 9448113403, at J.N. Medical College, Belagavi

ANNEXURE-II- ETHICAL CLEARANCE LETTER

K.L.E.UNIVERSITY'S
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
(Accredited 'A' Grade by NAAC)

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Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ **Date: 22/11/2017**

To,

REG NO: BN0117001

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"ROLE OF CLINICO HAEMATOLOGICAL PROFILE IN DIAGNOSIS OF DENGUE – ONE YEAR HOSPITAL BASED OBSERVATIONAL STUDY",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

ANNEXURE-III

PROFORMA

NAME:

AGE / SEX :

I.P / O.P Number:

OCCUPATION:

PRESENT HISTORY: - Fever

- Skin rash (Petechaie)
- Arthralgia/ myalgia
- Itching
- Abdominal pain
- Retro orbital pain
- Any other bleeding manifestations

PAST HISTORY:

FAMILY HISTORY:

PERSONAL HISTORY:

CLINICAL DIAGNOSIS:

SOCIO ECONOMIC STATUS : Upper / Upper middle / Lower Middle / Upper Lower / Lower

HAEMATOLOGICAL INVESTIGATIONS

- Hb
- Red cell count
- Platelet count
- MPV
- PCV
- Total leucocytes

DENGUE SEROLOGY

- NS1 positive
- IgM positive
- IgG positive
- Both IgM and IgG positive

BIOCHEMISTRY TEST

- Serum urea
- Serum creatinine
- Total Bilirubin
- SGOT and SGPT
- Alkaline phosphatase
- Serum potassium
- Serum sodium
- Serum chloride

ANNEXURE IV

WRIGHT'S STAINING PROTOCOL

Procedure:

1. Allow the slides to dry and place on the staining rack.
2. Put sufficient Wrights stain on the smear and wait for 3 minutes.
3. Add equal quantity of buffer (distilled water or phosphate buffer pH-6.5)
4. Blow gently
5. Wait for 5 minutes and then discard the stain and the buffer.
6. The back of the slide is cleaned with gauze
7. Excess of water is drained off
8. The stained smear is dried.

Result :

RBC –dark pink

Neutrophils -dark purple nucleus, pale pink cytoplasm with purple granules

Eosinophils - blue nucleus, pale pink cytoplasm with reddish orange granules

Basophils - dark blue nucleus and cytoplasm, dark purple black granules

Lymphocytes –dark purple to deep bluish nucleus, sky blue cytoplasm

Platelets - Violet to purple granules

ANNEXURES V - MASTER CHART

SL.NO	AGE	SEX	FEVER	RASH	MYALGIA	ARTHRALGIA	ITCHING	ABDOMINAL PAIN	RETRO ORBITAL PAIN	BLEEDING DISORDER	SOCIO-ECO STATUS	HAEMOGLOBIN	RBC	PCV	PLATELET	MPV	TLC	NS1	IgM/IgG	TOTAL BILIRUBIN	SGOT	SGPT	ALP	SR.UREA	SR. CREATININE	SR. SODIUM	SR. POTASSIUM	SR.CHLORIDE	TYPE OF FEVER	D-DIMER
1	21	M	P	P	A	A	A	P	P	A	LM	13	5.5	57	44,000	10.2	4500	P	IgM	1	78	48	100	15	0.7	145	3.5	98	DF	245
2	15	M	P	P	A	A	A	A	P	A	LM	17	6.5	55	12000	11.2	5600	P	IgM	1	88	1120	245	22	0.6	150	3.5	96	DF	
3	45	M	P	P	A	A	A	A	A	A	UL	12	5.8	60	1,20,000	9.5	10000	P	IgM	2.5	150	48	220	23	1.5	147	2.8	101	DF	
4	18	F	P	P	A	A	A	A	P	A	LM	12.5	5.5	56	35000	12	3200	P	IgM	2.4	1155	1052	98	18	0.6	146	3.6	95	DF	150
5	13	M	P	P	P	P	P	P	P	P	UL	13	3.9	58	15000	10.5	2500	P	IgM	0.5	40	54	263	50	0.8	139	4.5	99	DHF	1089
6	18	F	P	P	P	P	P	P	P	P	LM	13	4	57	22000	11	3600	P	BOTH	2.1	68	58	300	49	1.1	135	5.1	95	DHF	250
7	48	F	P	P	P	A	A	P	P	A	UL	12	3.6	56	16,000	11	12000	P	IgM	2.1	96	69	250	46	1	142	4.4	95	DF	
8	12	M	P	A	P	P	A	A	A	A	UL	9.8	2.2	52	45000	10.6	5500	P	IgM	1.5	110	750	360	16	0.9	145	4.3	110	DF	150
9	15	F	P	A	P	P	A	A	A	A	LM	9	3.5	33	36000	9.4	8560	P	IgM	1.8	1159	852	1100	15	0.6	135	3.5	95.5	DF	125
10	19	F	P	A	P	P	A	A	P	A	LM	18	6.2	57	25000	12	10000	P	BOTH	1.1	185	460	450	18	1.1	148	3.8	101	DF	
11	60	M	P	P	P	P	A	A	A	A	U	17	6.5	55	28000	10	3600	P	IgM	1.9	980	1222	499	20	1	150	3.1	110	DF	
12	28	M	P	P	A	A	A	P	P	A	L	16	5.2	60	42,000	9.6	9500	P	IgM	2.1	31	31	296	22	0.8	142	2.5	105.5	DF	
13	42	F	P	P	P	P	A	A	P	A	U	14	5.8	56	69000	8.8	3400	P	IgM	1	280	163	630	35	1.1	135	3.9	98.5	DF	
14	36	M	P	A	P	P	A	P	A	A	LM	13	5.7	58	78000	9	2600	P	IgM	2.2	1180	456	582	26	0.6	150	2	96	DF	
15	11	M	P	A	A	P	A	P	A	A	LM	19	5.2	57	1,58,000	10.2	3900	P	BOTH	1.5	39	30	469	22	0.6	147	3.6	94	DF	
16	45	M	P	P	P	P	P	P	P	P	LM	10.2	2.5	34	15000	11	2800	P	IgM	0.6	89	96	280	24	0.6	146	4.5	88	DHF	223
17	48	M	P	A	P	A	A	A	P	A	U	18	6.1	40	90000	12	5200	P	IgM	1.1	100	780	263	16	0.9	139	5.1	94.1	DF	
18	21	M	P	A	P	P	A	P	P	A	LM	6	3.6	42	85000	10.6	6500	P	ABSENT	1	40	26	98	20	0.6	135	4.4	150	DF	

19	32	M	P	P	A	P	A	P	P	A	LM	19	4.8	43	29000	10.8	3600	P	IgM	2.3	78	20	98	32	0.7	142	4.3	102	DF	
20	31	M	P	A	P	P	P	P	P	A	UL	11	3.6	40	80000	9.8	2500	P	BOTH	1.6	119	102	630	33	0.8	145	3.5	104	DF	
21	24	F	P	A	A	P	P	P	A	A	LM	16	4.2	35	94000	9.2	2800	P	IgM	1.3	850	200	700	19	1.1	135	3.8	107.5	DF	
22	42	M	P	P	P	P	P	P	P	P	LM	15	6	38	96000	12.6	3900	P	BOTH	1.7	69	30	100	15	1	148	3.6	98	DHF	645
23	39	M	P	P	P	A	P	P	P	P	LM	10	2.9	33	12000	7.6	7500	P	BOTH	2.4	63	90	300	21	1.1	150	4.5	95	DHF	145
24	65	M	P	P	P	P	P	P	P	P	U	10	3.4	32	79000	7.7	2500	P	BOTH	2.2	78	23	360	23	1	142	5.1	99	DHF	200
25	25	M	P	P	P	A	P	P	P	P	LM	19	6.2	40	14000	8.5	16000	P	BOTH	1.5	95	76	312	22	0.9	150	4.4	106	DHF	1500
26	20	M	P	P	P	P	P	P	P	P	LM	14	5.2	42	8000	8.8	12000	P	BOTH	2.2	36	28	400	20	0.6	147	4.3	98	DHF	>5000
27	27	M	P	P	P	P	P	P	P	P	U	13	3.7	43	26000	7.9	5200	P	IgM	1.6	37	31	852	22	1	146	3.5	96	DHF	150
28	32	F	P	P	P	P	P	P	P	P	LM	12	3.8	40	14000	8.9	19000	P	BOTH	1.4	95	25	360	24	0.6	139	3.8	98.8	DHF	225
29	15	M	P	P	P	A	A	P	P	A	LM	13	5.4	57	79000	9.6	15000	P	IgM	0.4	650	529	420	16	1.1	135	3.8	115	DF	
30	17	M	P	A	P	P	P	A	A	A	LM	13	5.5	55	35000	10.6	12000	P	BOTH	0.8	746	1100	900	20	1	142	4.2	107	DF	
31	42	M	P	A	P	P	A	P	P	A	U	18	4.7	60	68000	11	3900	P	IgM	1.1	1196	1150	456	14	0.6	145	4.1	110	DF	125
32	41	F	P	A	P	P	P	A	P	A	LM	12	3.9	56	1,52,000	12	2500	P	IgM	1.1	85	90	401	52	0.6	135	4.8	100	DF	
33	60	M	P	P	P	P	P	P	P	P	UL	13	6.5	58	15000	8.5	13000	P	BOTH	1	92	69	520	50	1.1	148	5.1	102	DHF	1500
34	45	M	P	P	P	P	A	P	P	P	LM	13	5.9	57	22000	9.1	2800	P	IgM	0.2	118	100	632	46	1.9	150	5.8	100	DHF	200
35	27	M	P	P	P	P	A	P	P	P	UL	13	5.4	56	16000	8.2	5600	P	BOTH	1.6	49	30	612	15	1.5	142	4.3	101	DHF	110
36	24	M	P	P	P	P	A	P	P	P	LM	18	5.8	40	26000	8	4800	P	IgM	2.4	69	79	280	46	1.4	136	3.5	105	DHF	2025
37	19	F	P	A	P	P	P	A	P	A	LM	19	5.7	42	45000	9.1	16000	P	IgM	1.8	86	63	263	26	0.6	143	3.8	95.8	DF	
38	17	F	P	A	P	P	A	P	A	A	LM	12	6.5	43	63000	12	2900	P	BOTH	2.3	190	251	290	22	0.7	152	4.9	112	DF	
39	72	M	P	P	P	P	P	P	A	P	UL	14	5.4	40	13000	9.3	3650	P	BOTH	1.1	1198	850	633	24	1.9	120	5.1	104	DHF	125
40	22	F	P	A	P	P	P	A	A	A	U	12	4.5	30	68000	11.4	10520	P	IgM	2.4	79	76	300	16	2.1	148	4.4	96.2	DF	
41	26	F	P	A	A	P	P	A	A	A	UL	14	4.2	38	89000	10.6	15000	P	IgM	1.1	96	95	450	50	0.6	150	4.7	94	DF	
42	16	M	P	A	A	P	A	A	A	A	UL	16	6.2	46	78000	9.8	16000	P	IgM	1.1	59	63	635	47	1.5	142	4.6	95	DF	
43	62	F	P	A	A	P	P	P	P	A	LM	12	3.8	38	93000	7.6	3600	P	IgM	1	85	100	369	15	0.6	136	3.6	96	DF	
44	6	F	P	P	P	P	P	P	A	P	U	13	3.9	42	14000	8.9	16000	P	BOTH	0.4	84	96	200	22	1.1	122	2.2	102	DHF	172
45	35	F	P	P	P	P	A	A	A	A	UL	18	4.5	40	69000	11.9	12000	P	IgM	0.9	63	86	99	23	1	143	4.3	110	DF	
46	68	M	P	P	P	P	A	P	P	A	UL	11	3.2	46	77000	10.1	2500	P	BOTH	0.3	99	100	220	18	1.8	135	3.5	107	DF	

47	28	F	P	P	P	P	P	P	A	A	UL	10	3.6	33	99000	9	11000	P	IgM	2.1	1169	1156	215	26	0.6	145	3.8	108.5	DF	
48	28	F	P	P	P	P	P	P	A	A	UL	12	4.1	40	67000	8.5	3600	P	IgM	2.5	118	88	693	22	0.7	142	4.9	100	DF	
49	32	M	P	P	P	A	P	P	A	A	U	8.5	5.2	42	85000	10.3	14000	P	IgM	1.1	175	200	520	24	0.8	152	5.1	104	DF	130
50	22	F	P	A	P	A	P	P	P	A	U	17	4.9	43	84000	8.6	3650	P	IgM	1	22	25	461	16	0.6	145	4.4	95.8	DF	
51	40	M	P	A	P	P	P	P	P	A	LM	18.5	5.9	40	40000	10.8	2500	P	IgM	1.6	25	30	98	43	1.5	135	4.7	98	DF	
52	19	M	P	A	P	A	P	A	P	A	LM	10	5.5	29	88000	11.6	2800	P	IgM	0.4	19	13	500	32	0.6	136	3.2	95	DF	126
53	12	F	P	A	P	A	A	A	P	A	UM	13	4.3	42	62000	10.4	3400	P	IgM	0.6	68	30	650	35	0.7	140	5.1	96	DF	
54	40	M	P	A	P	P	P	P	A	A	LM	19	5.4	40	45000	8.2	2900	P	BOTH	1.1	14	18	697	40	0.8	150	4.4	95.8	DF	
55	6	M	P	A	P	A	P	A	P	A	UM	16	5.2	41	96000	11	3400	P	IgM	0.3	49	29	460	15	0.7	140	4.3	98	DF	
56	40	M	P	A	P	A	A	A	A	A	UM	10	5.2	33	74000	12	12000	P	IgM	0.4	15	10	900	48	1.5	138	3.5	95	DF	
57	3	F	P	A	P	P	P	P	P	A	LM	12	4.9	39	75,000	11.5	3600	P	IgM	0.6	590	100	850	22	1.7	145	3.8	96	DF	
58	25	F	P	P	P	P	P	P	A	P	LM	9.2	2.8	30	16000	9	18000	P	BOTH	0.8	75	69	361	25	0.7	119	4.9	102	DHF	1025
59	20	F	P	A	P	P	A	P	P	P	UM	18	6.2	40	47000	11	15000	P	IgM	1.1	490	693	466	19	0.6	136	5.1	100	DF	
60	15	F	P	A	P	P	P	A	A	A	UM	18	6.8	37	1,45,000	11	9600	P	IgM	1.9	31	45	300	32	0.6	140	4.4	95	DF	
61	13	M	P	A	P	P	A	A	P	A	LM	16	5.4	46	41000	11.4	11000	P	IgM	1.1	25	30	98	17	2.1	150	4.3	108.5	DF	
62	16	M	P	P	P	P	P	P	A	P	UM	19	5.5	48	12000	8.5	10500	P	BOTH	1.9	21	850	305	40	2	142	3.5	100	DHF	160
63	30	F	P	A	P	P	P	P	A	P	UM	17.5	4.6	35	8000	13	3600	P	BOTH	1.6	78	62	300	43	0.6	139	3.8	104	DHF	>5000
64	38	M	P	A	P	P	A	P	P	P	UM	16	5.8	50	74000	11.4	3900	P	IgM	1.8	58	69	960	32	1.5	155	6.2	95.8	DF	
65	21	M	P	A	A	P	P	P	P	P	LM	14	6.1	56	63000	10.2	2700	P	IgM	0.5	950	189	102	35	1.1	140	5.1	98	DF	
66	52	F	P	A	A	P	P	A	A	A	UM	19	4.2	56	78000	10	10000	P	IgM	0.5	1196	1152	115	40	1.3	138	4.4	95	DF	
67	26	M	P	P	P	P	P	P	A	P	LM	14	6.4	58	14000	9	2800	P	IgM	0.2	1187	2000	998	15	0.7	145	4.3	125	DHF	140
68	35	F	P	A	P	P	P	A	A	A	UM	12	3.8	57	1,35,000	10.6	2900	P	IgM	1.3	528	600	752	18	0.7	135	3.5	100	DF	
69	32	M	P	P	P	P	P	P	P	P	LM	20	4.5	60	15000	8.2	7800	P	BOTH	1.1	496	362	560	15	0.6	136	3.8	100	DHF	215
70	80	M	P	A	A	P	P	A	P	A	LM	18	5.2	56	1,20,000	11.6	12500	P	IgM	1.5	28	36	201	22	1	140	3.8	104	DF	
71	25	M	P	A	A	P	A	P	P	A	LM	10	5.5	35	33000	10.2	2600	P	IgM	1.1	19	15	260	23	0.9	150	5.8	95.8	DF	120
72	25	F	P	A	A	P	P	P	P	A	LM	12	3.5	58	88000	10.1	3500	P	IgM	2.5	752	850	500	18	1.1	142	5.1	98	DF	
73	27	M	P	A	P	P	A	A	P	P	UM	21	6.2	60	74000	8.2	2600	P	IgM	0.3	950	1100	960	26	0.9	139	4.4	95	DF	
74	47	F	P	P	P	P	P	P	P	P	LM	12	6.1	30	13000	10	6500	P	IgM	1.6	1168	1196	899	22	0.6	122	4.3	100	DHF	650

75	78	M	P	A	P	P	A	P	P	P	UL	20	5.8	60	83000	10	11000	P	IgM	0.4	1190	1059	1152	24	0.6	140	3.5	100	DF	
76	17	M	P	A	A	A	A	P	A	A	LM	15	5.2	56	1,18,000	10.1	2600	P	IgM	1.4	78	88	290	16	1	138	3.8	104	DF	
77	13	M	P	A	A	P	P	A	A	A	UM	15	5.5	58	68000	8.6	9500	P	IgM	0.2	96	90	292	22	1.1	145	6.1	96	DF	
78	28	M	P	P	P	P	P	P	A	A	LM	19	5.7	57	64,000	9	16000	P	IgM	0.3	126	150	520	34	1.1	135	4.5	110	DF	
79	32	M	P	A	P	P	P	P	A	A	UL	18	6.2	60	1,31,000	8.8	2500	P	BOTH	0.5	850	750	400	40	0.9	136	5.1	100	DF	
80	65	F	P	A	P	P	P	P	A	A	LM	12	5.9	32	84000	10.4	12500	P	BOTH	0.9	96	100	330	43	0.6	146	4.4	99	DF	
81	16	M	P	A	P	P	A	P	A	A	UM	14	4.5	56	69000	8.2	2900	P	IgM	1	750	133	408	32	0.6	140	4.3	100	DF	
82	42	F	P	A	P	P	A	P	A	A	UM	12.5	5.9	57	74000	11	2400	P	IgM	1.1	126	140	309	35	0.6	138	3.5	101	DF	
83	22	M	P	A	P	P	A	P	A	A	UL	16.1	6	60	56000	12	3700	P	IgM	0.6	30	20	160	40	0.7	145	3.8	105	DF	
84	68	M	P	A	P	A	A	A	A	A	UM	8.2	2.6	30	90000	8	2450	P	IgM	0.5	300	500	782	15	1.8	135	3.8	95.8	DF	
85	72	F	P	A	P	P	A	A	A	A	UM	9	3.5	29	1,16,000	11	9800	P	IgM	2.5	942	1102	450	18	0.9	136	4.2	112	DF	
86	41	F	P	A	A	P	A	A	A	A	LM	14	5.8	56	58000	10.2	6500	P	IgM	3	65	50	99	49	1.3	140	4.1	104	DF	
87	28	F	P	A	A	P	A	A	A	A	UM	18	6.5	60	50000	10.3	2600	P	IgM	2.2	129	230	105	50	1.7	150	4.8	96.2	DF	
88	24	M	P	A	P	P	A	P	P	A	L	17.5	4.5	57	1,25,000	11.2	2500	P	IgM	0.6	50	30	360	51	0.6	142	4.5	100	DF	
89	19	M	P	A	P	A	A	A	A	P	UM	20.2	4.8	57	59000	10	3900	P	IgM	0.5	31	25	250	15	0.6	139	5.1	106	DF	
90	36	M	P	P	P	P	P	A	P	A	L	16	5.5	55	74000	11.1	2700	P	IgM	0.8	15	10	296	46	0.6	146	4.4	99	DF	
91	22	M	P	P	P	P	P	A	A	A	LM	19.5	5.2	60	1,30,000	11.1	2900	P	IgM	2.4	29	39	119	40	0.7	145	4.3	95	DF	
92	42	M	P	P	P	A	A	A	A	A	UM	16.2	5.5	56	55,000	10.3	3650	P	IgM	0.6	10	620	941	16	0.9	135	3.5	98	DF	
93	15	F	P	P	P	A	A	P	A	A	LM	12	5.6	58	89000	10.6	3600	P	IgM	0.5	456	960	685	22	1.5	136	3.8	95	DF	120
94	19	M	P	P	A	P	P	A	A	P	LM	18.4	6.8	57	72000	11.2	2900	P	IgM	1.1	12	15	450	35	1	140	3.8	96	DF	
95	25	M	P	A	A	A	A	A	A	A	L	18	5.2	56	62,000	12	9800	P	IgM	0.3	950	582	590	50	1.1	150	4.2	99	DF	
96	24	M	P	A	P	A	P	A	A	A	L	8.2	3.4	30	69000	10	8500	P	IgM	0.3	28	26	109	28	0.6	142	4.1	98	DF	
97	10	M	P	A	P	A	P	P	P	A	LM	13	4.1	60	82000	8.2	3900	P	IgM	0.2	26	30	99	48	1.6	139	4.8	100	DF	
98	18	M	P	P	P	P	P	A	A	A	LM	20	4.5	56	41000	9.2	2800	P	BOTH	0.1	30	58	98	34	0.9	146	5.1	102	DF	
99	21	M	P	P	P	P	P	A	A	P	UM	19	6.8	58	33000	11	2700	P	IgM	0.3	960	695	299	20	0.6	140	4.5	102	DF	
100	25	M	P	A	P	A	P	A	A	A	UL	15.2	5.7	57	52000	12	3600	P	IgM	0.2	450	500	300	25	1.1	138	5.1	100	DF	
101	17	M	P	A	P	A	A	P	A	P	UL	6.5	2.5	30	38000	9	4900	P	IgM	1.1	1220	1125	1150	14	0.9	145	4.4	95	DF	
102	3	M	P	P	P	P	A	P	P	P	UL	13	4.5	56	22000	8.2	8800	P	IgM	1	25	56	530	25	0.6	135	4.3	99	DHF	195

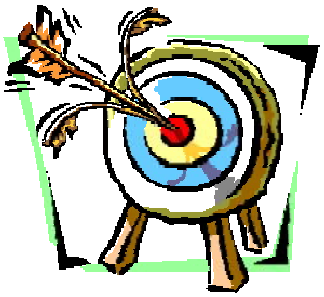
103	19	M	P	A	P	A	P	A	A	A	L	14	5.7	57	41000	12	8700	P	IgM	1.6	85	80	221	40	1.1	136	3.5	112	DF	
104	21	F	P	A	P	A	P	P	A	A	U	9.5	2.1	32	87000	8.6	2600	P	IgM	0.5	31	30	235	43	0.9	140	3.8	104	DF	
105	21	M	P	P	P	P	A	P	A	A	UM	13	5.8	60	64000	8.2	3500	P	IgM	0.8	30	96	560	32	0.6	150	3.8	96.2	DF	
106	36	M	P	P	P	P	P	P	A	A	LM	14.1	4.5	56	92000	11	2900	P	IgM	1.6	56	20	250	35	1.1	142	4.2	100	DF	
107	28	F	P	P	P	P	P	A	A	P	U	18.4	4.8	57	17000	12.5	12000	P	IgM	0.4	750	520	620	42	1.9	139	4.1	106	DHF	742
108	65	M	P	P	P	P	P	A	P	P	LM	19	4.9	55	41000	10.2	3600	P	IgM	0.5	265	200	99	28	1.1	146	4.8	99	DF	
109	13	M	P	P	P	P	P	P	P	P	LM	10	3.2	30	13000	11.6	3700	P	IgM	1.9	1100	960	602	19	0.8	120	5.1	95.8	DHF	980
110	32	F	P	A	P	A	P	A	A	A	U	10.5	3.1	22	87000	9	1900	P	IgM	1.3	456	523	360	39	1.5	138	4.5	98	DF	
111	23	M	P	A	P	P	P	A	A	A	L	10.5	5.6	28	62000	10.1	9800	P	IgM	0.2	90	82	432	38	2	140	5.1	95	DF	
112	32	M	P	P	P	P	P	P	A	P	L	18	4.1	60	36000	10.6	19000	P	IgM	0.3	65	66	580	22	1.1	135	4.4	96.2	DF	
113	13	M	P	P	P	P	P	A	A	P	LM	18.4	5.5	56	19,000	12	3600	P	IgM	0.2	1195	1125	500	25	0.9	136	4.3	100	DF	
114	63	M	P	P	P	P	P	P	A	P	U	18.6	5.5	57	55,000	11.5	8400	P	IgM	0.3	20	25	622	40	0.6	140	3.5	106	DHF	220
115	52	M	P	P	P	P	A	P	P	A	UM	20.5	5.2	55	64000	11	8800	P	IgM	1.5	70	96	364	43	1.1	150	3.8	100	DF	
116	45	F	P	P	P	P	P	P	P	P	UM	16.8	4.8	60	38000	10	8600	P	IgM	2.1	25	20	320	32	0.9	142	3.8	95	DF	
117	21	M	P	P	P	P	P	P	A	A	UM	19	5.8	56	15,000	8.2	2500	P	IgM	1.4	39	45	650	35	0.6	139	4.2	108.5	DF	
118	23	F	P	P	P	P	P	P	A	A	UM	15	3.8	58	89000	8.8	2900	P	IgM	0.2	22	26	600	40	1.1	146	4.1	100	DF	
119	18	F	P	P	A	A	P	P	P	A	L	18	6.2	57	67000	10	7800	P	IgM	1.2	18	18	459	15	1.1	140	4.8	104	DF	
120	17	M	P	P	A	A	A	P	P	A	L	18.6	6.5	56	88,000	11.2	3800	P	IgM	0.6	1145	1169	856	18	0.8	138	5.1	96.2	DF	200

ANNEXURE-VI

KEY TO MASTER CHART

A	-	Absent
ALP	-	Alkaline phosphatase
DF	-	Dengue Fever
DHF	-	Dengue Haemorrhagic Fever
F	-	Female
IgG	-	ImmunoglobulinG
IgM	-	ImmunoglobulinM
L	-	Lower
LM	-	Lower middle
M	-	Male
MPV	-	Mean platelet volume
NS1	-	Non structural protein
P	-	Present
PCV	-	Packed cell volume
RBC	-	Red cell count
SGOT	-	Serum glutamic oxaloacetic transaminase
SGPT	-	Serum glutamic pyruvictransaminase
Sr	-	Serum
TLC	-	Total leucocyte count
U	-	Upper
UL	-	Upper lower
UM	-	Upper middle

Introduction



Objectives

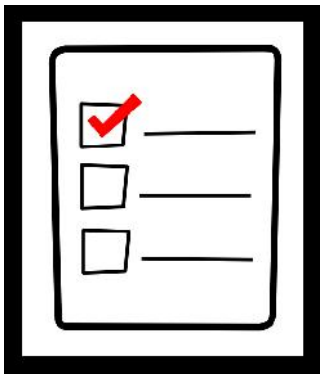
Review of Literature

Methodology

Results

Discussion

Conclusion

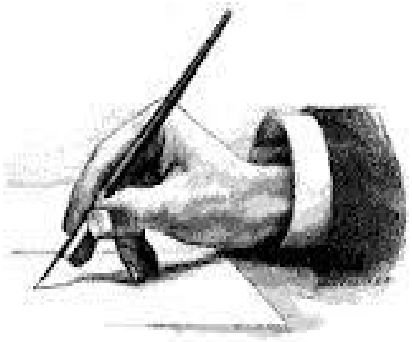


Limitations

Recommendations

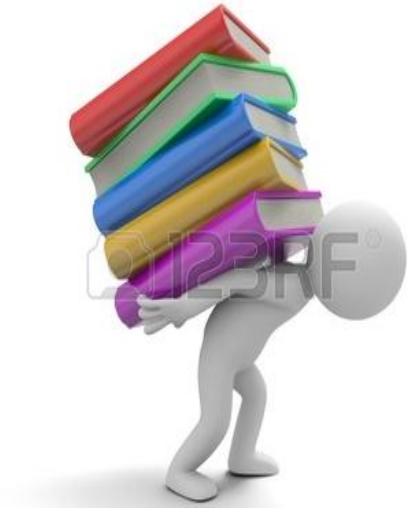
Summary

Bibliography



Annexure-I

Annexure-II



Annexure-III

Annexure-IV

Annexure-V