EARLY CLINICAL AND LABORATORY MARKERS OF DENGUE FEVER IN PEDIATRIC PATIENTS IN AND AROUND KOLAR REGION

By

Dr. GAYATHRI DEVI N.

Dissertation Submitted to the

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in partial fulfillment of the requirements for the degree of

DOCTOR OF MEDICINE IN PEDIATRICS

Under the guidance of

Dr. K. N. V. PRASAD MD

Professor

DEPARTMENT OF PEDIATRICS

SRI DEVARAJ URS MEDICAL COLLEGE

TAMAKA, KOLAR – 563101

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Date: **Signature of the Candidate**

Place: **Dr. GAYATHRI DEVI N.**

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Signature of the Guide

Date:

Dr. K. N. V. PRASAD MD
Professor,

Place:

Department of Pediatrics
Sri. Devaraj Urs Medical College
Tamaka, Kolar.

CERTIFICATE BY THE CO-GUIDE

This is to certify that the dissertation titled **"EARLY CLINICAL AND LABORATORY MARKERS OF DENGUE FEVER IN PEDIATRIC PATIENTS IN AND AROUND KOLAR REGION"** is a bonafide and research work done by **Dr. GAYATHRI DEVI N.**, under the guidance and supervision of **Dr. K. N. V. PRASAD** MD, Professor, Department of Pediatrics submitted to the Sri Devaraj Urs Academy of Higher Education and Research, Tamaka, Kolar, Karnataka, in partial fulfillment of the requirements for the Degree of Pediatrics.

Signature of the Co-Guide

Date:

Dr. BEENA P. M. MD
Professor and Head
Department of Microbiology
Sri. Devaraj Urs Medical College,
Tamaka, Kolar.

Place:

ENDORSEMENT BY THE HOD/PRINCIPAL

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This is to certify that the dissertation titled **"EARLY CLINICAL AND LABORATORY MARKERS OF DENGUE FEVER IN PEDIATRIC PATIENTS IN AND AROUND KOLAR REGION"** is a bonafide and genuine research work carried out by **Dr. GAYATHRI DEVI N.**, under the guidance and supervision of **Dr. K. N. V. PRASAD** MD, Professor, Department of Pediatrics and Co-guidance of **Dr. BEENA P. M.** MD, Professor and Head, Department of Microbiology Sri. Devaraj Urs Medical College, Tamaka, Kolar, in partial fulfillment of the requirements for the Degree of Pediatrics.

Seal and Signature of the HOD
Dr. Y. BEEREGOWDA MD
Professor and Head,
Department of Pediatrics
Sri. Devaraj Urs Medical College
Tamaka, Kolar

Seal and Signature of the Principal
Dr. SANIKOP M. B. MS
Principal,
Sri. Devaraj Urs Medical College
Tamaka, Kolar.

Date:

Place:

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SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR

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This is to certify that the ethical committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has unanimously approved, **Dr. Gayathri Devi N.,** student in the Department of Pediatrics at Sri Devaraj Urs Medical College, Tamaka, Kolar to take up the dissertation work titled **"EARLY CLINICAL AND LABORATORY MARKERS OF DENGUE FEVER IN PEDIATRIC PATIENTS IN AND AROUND KOLAR REGION"** to be submitted to the Sri Devaraj Urs Academy of Higher Education and Research, Tamaka, Kolar.

Date:

Place:

Signature of Member-Secretary
Ethical committee

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Date: **Signature of the Candidate**

Place: **Dr. ARCHANA B. R.**

ABSTRACT

OBJECTIVES OF THE STUDY

Study the clinical profile of dengue fever associated with complications like shock, ARDS, dengue encephalitis and hemorrhagic dengue fever.

Study the laboratory factors influencing complications of dengue fever.

SOURCE OF DATA

This study is conducted on seropositive cases of dengue less than 18years of age admitted in the R. L. Jalappa Hospital, Kolar from October 2010 to October 2011. An observational clinical study with 50 patients presented with dengue fever is undertaken to study the clinical profile and factors associated and influencing the dengue fever.

CONCLUSION

As Kolar is an endemic area there is less number of tourniquet positive cases. This is a unique finding of this study in compatibility with the WHO findings which also states that tourniquet positive cases are less in endemic areas.

Out of the various different early predictors studied leucopenia found to be statistically significant and a guide to the prognosis of patient.

Findings from the survey serve as a cornerstone to understand the evolution of breastfeeding practice in rural areas of India.

In DSS, 50% of the complications were pleural effusion, 16% was bleeding manifestations and 33% was ARDS. In DHF, 60% of the complications were bleeding manifestations and rests were pleural effusion and encephalitis.

As seen in our study the superadded infections lead to increase in mortality of the patients instead of dengue only hence one should be also aware of the possible complications.

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INTRODUCTION

Dengue fever is an acute febrile viral disease characterized by sudden onset of fever of 3-5 days, intense headache, myalgia, retro-orbital pain, anorexia, gastrointestinal disturbances and rash. DHF is characterized by increased vascular permeability, hypovolemia and abnormal blood clotting mechanisms.[1]

Dengue viruses are flavivirus, which include four serotypes 1, 2, 3 and 4. These same viruses are responsible for Dengue Hemorrhagic Fever (DHF). The viruses are transmitted to man by the bite of infective mosquitoes, mainly Aedes aegypti. The incubation period is 4-7 days, but range from 3 to 14 days. The disease is now endemic in most tropical, subtropical countries.

Dengue fever (DF) with its severe manifestations such as Dengue Hemorrhagic Fever (DHF) and Dengue Shock syndrome (DSS) has emerged as a major public health problem of international concern. The geographical distribution has greatly expanded over the last 30 years, because of increased potential for breeding of Aedes aegypti.[2] This has been prompted by demographic explosion, rapid growth of urban centers with strain on public services, such as potable water and augmented by rainwater harvesting in diverse types of containers resulting in multiple storage practices.

Today, Dengue ranks as the most important mosquito-borne viral disease in the world. Current estimates report that, atleast 112 countries are endemic for Dengue and about 40% of the world populations (2.5-3 billion people) are at risk in tropics and subtropics. Annually, 100 million cases of dengue fever and half a million cases of dengue haemorrhagic fever occurs worldwide. 90% of DHF subjects are less than 15 years of age.[3]

HISTORY OF DENGUE FEVER

Dengue is a homonym for the African ki denga pepo, which appeared in English literature during an 1827-28 Caribbean outbreak. The word dengue came from denga or dyengo which in Africa means haemorrhage. The exact date when Dengue fever was first recognized in the world is still obscure. Description found in the early literature include an epidemic of "knee fever" in Cairo and its suburbs in 1779 described by Al Jabarti and an epidemic in Asia occurring in the same year in Batavia (Djakarta) described by David Bylon. But these reports are clouded by the similarity of their clinical picture with that of other febrile illnesses. The Dengue like epidemics recorded in 1779 in Batavia, Indonesia, and Cairo, may actually have been caused by chikungunya virus.[4]

Since the geographical distribution of Dengue fever is world-wide, involving nearly all tropical and subtropical countries, it has many names like-dandy fever, Denguero, denga, dunga, break-bone fever, bouguet, seven day fever, bonon, chapenonada, Knieueble, Tok-kive-ana, Mal de genoux, homa mguu, and coup-d-barre.[5]

The first definite clinical report of Dengue is attributed to Benjamin Rush in 1789.[6] Several outbreaks of Dengue or Dengue-like epidemics were reported throughout the 19th and early 20th centuries from all five continents.[7] Generally these epidemics consisted of non-fatal febrile illnesses, often associated with rash and either muscle or joint pains. Deaths occurred during Dengue epidemics in Australia in 1897 and in Greece in 1928, when over 1000 deaths were reported.[8]

Dengue hemorrhagic fever has been recognized as a separate disease entity from classical dengue fever since the second half of twentieth century with the first outbreak called "Philippine Hemorrhagic fever" in 1953. This was followed by outbreak in Thailand in 1958, which was referred to as "Thai hemorrhagic fever". Hemorrhagic manifestations, including gastrointestinal haemorrhage, were described during Dengue epidemics in Texas and Louisiana in 1922.[9]

The term Dengue shock syndrome was coined to describe the cases of DHF with shock. The clinical studies indicated that it was caused by increased vascular permeability and resultant intravascular hypovolemia.[9] Eventually the WHO case definition of DHF was modified to make 'increased vascular permeability' the hallmark of the disease.

Throughout the first half of the 20th century, dengue was generally described as a self-limited, non-fatal febrile illness, with occasional hemorrhagic manifestations such as petechiae, epistaxis, gingival bleeding and menorrhagia, which rarely resulted in more severe or fatal outcomes. Initially, there were long intervals (10-40 years) between major

epidemics, mainly because the viruses and their mosquito vector could only be transported between population centres by sailing vessels.[10] In Southeast Asia, epidemic DHF first appeared in the 1950s, but by 1975 it had become a leading cause of hospitalization and death among children in many countries in this region.[10]

A global pandemic of Dengue began in Southeast Asia after World War II and has intensified during the last 15 years. Epidemics caused by multiple serotypes (hyperendemicity) are more frequent. The geographic distribution of Dengue viruses and their mosquito vectors has expanded, and DHF has emerged in the Pacific region and the Americas.[10]

In the 1980s, DHF began a second expansion into Asia when Sri Lanka, India and the Maldives Islands had their first major DHF epidemics; Pakistan first reported an epidemic of Dengue fever in 1994. The recent epidemics in Sri Lanka and India are associated with multiple Dengue virus serotypes.[10]

From 1997, Dengue has been the most important mosquito-borne viral disease affecting humans; its global distribution is comparable to that of malaria. Each year, tens of millions of cases of dengue fever occur and up to hundreds of thousands of cases of DHF. The case-fatality rate of DHF in most countries is about 5%; most fatal cases are among children and young adults.[10]

MAGNITUDE OF THE PROBLEM: WORLD SCENARIO

As a pandemic in 1998, around 1.2 million cases of Dengue fever and DHF with 3,442 deaths were reported to WHO from 56 countries worldwide in an unprecedented magnitude. Date for 2001-2002 also indicated a situation of comparable quantum. As per estimates, over 50 million infections with about 400,000 cases of DHF are reported annually, out of whom more than 90% are children below 15 years, making it a leading cause of childhood mortality in several Asian countries. The challenge for national and international health agencies is to reverse the trend of this increased epidemic Dengue activity and increased incidence of DHF.

DENGUE IN INDIAN SCENARIO

The first recorded outbreak of Dengue fever in India was in 1812, but serological surveys were first carried out in 1954, which indicated that DEN-1 and DEN-2 were widespread. In 1960, DEN-4 was isolated in Vellore, in the South, without any association with haemorrhagic diathesis.[12]

A double peak haemorrhagic fever epidemic occurred in India for the first time in Calcutta between July 1963 and March 1964. DEN-2 virus strains were isolated form patients with severe haemorrhagic manifestations during the first peak and chikungnya virus was isolated during the second peak.

Further outbreaks occurred in 1965, 1967 and 1968. All four serotypes of Dengue viruses have been isolated form various parts of India. Outbreak of fever of unknown etiology, suspected to be Dengue, have been reported annually, with the affected number ranging from 1,000 to 5,000 and with a case fatality rate of about 0.5 percent.

In New Delhi, outbreaks of Dengue fever were reported in 1967, 1970 and 1982. DEN-2 were isolated during the 1970 epidemic. An explosive outbreak of Dengue fever occurred between August and October 1982. Sera were collected from 36 patients, from which 18 strains of DEN-1 AND two strains of DEN-2 were recovered. This report confirmed the endemicity of Dengue virus infection in New Delhi. It was noteworthy that no haemorrhagic manifestation or fatalities were recorded during those episodes.

OBJECTIVES OF THE STUDY

Study the clinical profile of dengue fever, associated with complications like shock, ARDS, dengue encephalitis and haemorrhagic dengue fever.

Study the laboratory factors influencing complications of dengue fever.

REVIEW OF LITERATURE

EPIDEMIOLOGY AGENT: The Dengue Virus

In 1944, Albert Sabin successfully isolated the virus that causes DF and found that it belongs to the Flavivirdae virus family. In the same year two immunologically distinct but related viruses, now referred to as Dengue 1 (DEN-I) and Dengue 2 (DEN-II), were again isolated by Sabin and his co-workers from patients with clinically diagnosed Dengue.[13]

In 1956, Hammon and co-workers isolated two new serotypes of Dengue virus, designated DEN-3 and DEN-4, as well as the previously recognized DEN-I and DEN-2, during epidemics of severe hemorrhagic illness among children in the Philippines.[14,15]

Four Dengue virus serotypes are recognized. Infection with one serotype is thought to produce lifelong immunity to that serotype but only a few months immunity of the others.[16]

HOST: MOSQUITO

Humans and mosquitoes are the principal hosts of Dengue virus; the mosquito remains infected for life, but the viruses are only known to cause illness in humans. In forest and enzootic cycles in Africa and Asia the virus is probably sustained through vertical (transovarial) transmission in the mosquito, with periodic amplification in non-human primates.[17] The virus is transmitted by bites from Aedes mosquito.

Transmission by Aedes aegypti, first described by Bancroft in 1906, was later proved by Siler et al and Simmons et al.[10] The known natural hosts for Dengue virus are man, lower primates, and mosquitoes.[17] Aedes aegypti, considered the most effective vector, originated in the forests of Africa and is found in between 35 degrees north and 35 degrees south latitude.[1]

THE CHARACTERISTIC FEATURES OF THE DENGUE VIRUS ARE

- It is highly susceptible to Dengue virus.
- It feeds preferentially on human blood.
- Rest indoor, maximizes man vector contact.
- It is a daytime feeder.
- Its bite is almost imperceptible.
- It is a container breeder.

It is restless mosquito as the slightest movement interrupts feeding, thus several people may be bitten in a short period for one blood meal.[18] The female mosquito feeds during the daytime, with peak activity in the mornings and late afternoons.[19]

In many areas, Dengue epidemics occur during the warm, humid, rainy seasons, which favour abundant mosquitoes and shorten the extrinsic incubation period.[20] After feeding on a viraemic individual, the mosquito may transmit the virus directly by change of host, or after 8 to 10 days during this time the virus multiplies in the salivary glands. The infected mosquito then remains capable of transmission for its entire life.

Transovarian transmission of Dengue virus has been documented and A. aegypti eggs are highly resistant to desiccation and can survive for extended periods.[21]

Aedes allbopictus is indigenous to Southeast Asia, feeds during the day and has been shown to have a higher biting frequency than A.aegypti. It was introduced into Nigeria, Europe and the United States, probably by shipments of used automobile tyres.

"Aedes aegypti index" means the ratio, expressed as a percentage, between the number of houses in a limited well-defined area on the premises of which actual breeding-places of Aedes aegypti are found and the total number of houses examined in that area.

HOST: THE HUMAN

The insect vector of Dengue is the most important component in the epidemiological triad of the disease .In the warm environment and humidity at the tropics, the type of clothing makes people more susceptible for mosquito bites. This marks the rapid spread of the disease in a limited geographic area in creating an epidemic. Uncontrolled urbanization, linked most commonly to Dengue, makes its endemicity in the growing cities.

Air travel has enabled infected humans import viruses. These factors can change a region form non-endemic (no virus present) to hypoendemic (one serotype present) to hyperendemic (multiple serotypes present).[17] In South East Asia the mean number of annual cases of Dengue haemorrhagic fever has increased to more than twenty fold in the

past forty years. The same pattern is now unfolding in the Americas.[22] The numbers of reported cases of imported Dengue in countries outside the tropics have also been increasing.[23,24]

ENVIRONMENT

In the past 60 years the incidence, distribution, and clinical severity of Dengue has increased dramatically. Population growth in the tropics provides many susceptible hosts. Uncontrolled urbanization leads to inadequate management of water and waste, providing a range of large water stores and disposable, non-biodegradable containers that become habitats for the larvae. Few control programmes are effective against the mosquitoes.[25]

The monsoon and post-monsoon surge of the disease is very well documented, largely due to an effective breeding opportunity for the mosquito vector. The incidence increases from the monsoon season, reaches a peak in the post-monsoon season before declining.

The reasons for dramatic global emergence of Dengue fever or DHF as a major public health problem are complex and not very well understood. However, several important factors can be identified.

Firstly, major global demographic changes have occurred, the most important of which have been uncontrolled urbanization and concurrent population growth. These demographic changes have resulted in substandard housing and inadequate water,

sewage, and waste management systems, all of which increase A.aegypti population densities and facilitate transmission of A.aegypti borne disease. Secondly, effective mosquito control is virtually nonexistent in most Dengue-endemic countries. Considerable emphasis for the past 25 years has been placed on ultra-low-volume insecticide space sprays for adult mosquito control, a relatively ineffective approach for controlling A.aegypti.

Thirdly, increased travel by airplane provides the ideal mechanism for transporting Dengue virus between population centers of the tropics, resulting in a constant exchange of Dengue virus and other pathogens.

In most countries the public health infrastructure has deteriorated. Limited financial and human resources and competing priorities have resulted in a "crisis mentality" with emphasis on implementing so-called emergency control methods in response to epidemics rather than on developing programmes to prevent epidemic transmission. This approach has been particularly detrimental to Dengue control, because in most countries, surveillance is very inadequate; the system to detect increased transmission normally relies on reports by local physicians who often do not consider Dengue in their differential diagnoses. As a result, an epidemic has often reached or passed transmission before it is detected.

Dengue has been linked to urbanization, explaining its maximum incidence in middle class. The immediate microenvironment of the patient, consisting of artificial collections of water within the house (as in flower vases, decorative plant pots within the house), forms a fertile breeding place for the mosquito vector. This leads to exposure to the mosquito bites and spread of Dengue.

Finally, international commercial trade has aided geographical expansion of the mosquito, particularly in used tyres, in which rainwater easily accumulates. Increased air travel and breakdown of vector control measures have also contributed greatly to the global burden of Dengue fever.

Nevertheless, Dengue is often asymptomatic or causes a non-specific febrile illness and Dengue is not a reportable disease in most countries.[26] Thus, despite the proliferation of reported cases, it is generally accepted that the incidence of infection and disease is largely under-reported.

ECONOMIC IMPACT OF DENGUE[10]

Few studies on the economic impact of DF, DHF and DSS have been conducted. For children suffering from dengue fever average hospital stays will be about 5 – 10 days. Intensive care is required for severely ill patients, including intravenous fluids, blood or plasma transfusion and medicines. Adults miss work in order to attend to their children's illness. Consequently, there are both direct and indirect costs for each Dengue patient, ranging form inconvenience due to a sick child with uncomplicated Dengue, to substantial costs for hospitalization and significant disruption of earning potential. In

addition, burden to local municipalities for vector control activities, and often revenue is lost through reduced tourism. While the exact cost of each epidemic is difficult to calculate, it is clear that Dengue and DHF/DSS represent a significant economic burden on the societies affected.

It has always been speculated whether the surveillance system in our country has been tight enough to project a proper figure. Hence, any informative study on this disease carries prominence.

PATHOLOGY AND PATHOGENESIS

It is prudent to understand the clinical manifestations of Dengue fever in the background of pathogenesis. Classic Dengue primarily occurs in non-immune, non-indigenous adults and children. Symptoms begin after a 5 to 10 days of incubation period. DHF and DSS usually occurs during a secondary Dengue infection in persons with pre-existing actively or passively (maternally) acquired immunity to a heterologous Dengue virus serotype. Dengue haemorrhagic fever is distinguished from Dengue fever by the presence of increased vascular permeability, not by the presence of haemorrhage.[16]

Patients with Dengue fever may have severe haemorrhage without meeting WHO criteria for Dengue haemorrhagic fever. In these cases the pathogenesis probably derives from thrombocytopenia or a consumptive coagulopathy, not from the vascular leak syndrome seen in Dengue haemorrhagic fever.[27]

Dengue virus antigen has been found in a variety of tissues, predominately the liver and reticuloendothelial system.[20] Although the site of viral replication during Dengue infection remains uncertain, dendritic cells (Langerhans cells) in the skin may be an early target of infection,[28] mononuclear phagocytes may be the most likely site.[29] But infection of megakaryocytes in the bone marrow has also been proposed.

As with yellow fever, focal central necrosis has been found in the liver of patients who have died of Dengue.[29] Autopsies of patients who died of Dengue haemorrhagic fever show diffuse petechial haemorrhages in most organs and serous effusions of pericardial, peritoneal and pleural spaces. Viral particles or antigen have been detected in monocytes in kidney, skin tissue, liver, spleen, thymus and lung.[30] Dengue virus has been isolated by reverse transcription-polymerase chain reaction from peripheral blood leukocytes, as well as from autopsy tissue from liver, spleen, lymph node, bone marrow, thymus, heart, kidney, stomach and lung.

Dengue virus and antibody (including IgM) have also been identified in the cerebrospinal fluid, but direct involvement of Dengue virus in neuronal damage is controversial.[31,32]

All four serotypes have been associated with Dengue haemorrhagic fever. Variations in virus strains within and between the four serotypes may influence disease severity. Secondary infections (particularly with serotype 2) are more likely to result in severe disease, Dengue haemorrhagic fever.[33] This is explained by the theory of antibody dependent enhancement whereby cross reactive but non-neutralizing antibodies from a

previous infection bind to the new infecting serotype and facilitate virus entry into cells resulting in higher peak viral titres.[34] In primary and secondary infection, higher viral titres are associated with more severe disease.[33] Higher titres may result in an amplified cascade of cytokines and complement activation causing endothelial dysfunction, platelet destruction and consumption of coagulation factors, which result in plasma leakage and haemorrhagic manifestations.[35,36]

Several hypotheses have emerged to explain why DHF occurs in some individuals who are infected with Dengue virus. These include:

- Changes or differences in viral virulence between serotypes and/or between strains within serotypes.[37]
- Interactions of Dengue virus with other environmental or infectious agent.
- Differences in genetic susceptibility or other host factors.[38]
- The immunologic enhancement of Dengue infection by antibody acquired from a previous infection with a different Dengue serotype.

The theory of immune enhancement, developed extensively by Halstead,[39] predicts that individuals who have been immunologically sensitized to one Dengue virus serotype may developed non-neutralizing antibodies that actually enhance the entry of different serotype. Entry of Dengue virus into mononuclear phagocytes, resulting in the increased activation of complement and kinins and the release of mediators of vascular permeability. This proposed mechanism has been supported by laboratory investigation and several studies have shown that during outbreaks a majority of DHF patients show secondary immune response patterns.[40]

However, cases of DHF have been described in patients with primary Dengue infection[41] and the denominators for estimating proportions of primary and secondary infections that result in DHF have been difficult to evaluate with certainty. Carefully designed epidemiologic studies are needed to further evaluate this theory and to study the possible interaction of immune enhancement with other risk factors. The recognition of various forms of severe or fatal dengue that are different from DHF as defined by WHO may require revisions or additions to the case definition required for such studies.[42]

CLINICAL FEATURES:

Three to Ten days after the bite of an infective mosquito, the patient typically suffers sudden onset of headache, fever, retro-orbital pain, backache, bone and joint pain, weakness, depression and malaise. Young children with Dengue often have an undifferentiated febrile illness with a maculopapular rash. Upper respiratory infections, especially pharyngitis are common. Most infections in children under[15] years are asymptomatic or minimally symptomatic. A study of school children in Thailand found only 13% of those infected missed more than one day of school because of illness.

Classic Dengue is more commonly seen among older children, adolescents, and adults. They are less likely to be asymptomatic.[43] Dengue is abrupt in onset, typically with high fever accompanied by severe headache, incapacitating myalgias and arthralgias, nausea and vomiting, sore throat, cough, groin pain, hyperesthesia, dizziness, photophobia, eye pain and rash. The decline in fever may be followed by 1 to 3 days later by a resurgence of fever and symptoms, giving a “saddleback” appearance to the temperature curve. Rash, typically macular or maculopapular, often becoming confluent

and sparing small islands of normal skin, has been reported in over half of infected people.[44] Some patients have an evanescent rash over the thorax and joint flexures. There may be flushing of the face and conjunctivitis as well as taste aberrations, anorexia and abdominal pain. Lymphadenopathy and hepatomegaly may occur but splenomegaly is infrequent. Fever and associated symptoms may subside after 3 or 4 days and the patient may recover completely. Recovery may be prolonged and include depression.[16]

Dengue hemorrhagic fever is primarily a disease of children under 15 year of age. Black populations may be at decreased risk. The disease is characterized by increased capillary permeability and haemostatic changes. If major plasma leakage occurs. It usually develops 24 hours before to 24 hours after defervescence. Patients may develop effusions and ascitis with a variable amount of bleeding. Enlargement and tenderness of the liver has been reported in up to 40% of patients. As the fever begins to drop around day 3 to 5, circulatory instability may develop with signs of decreased peripheral perfusion. Profound shock may follow. Disseminated intravascular coagulation and severe gastrointestinal haemorrhage have been described.

Mortality can be as high as 10-20% (over 40% if shock occurs) without early appropriate treatment, but it is as low as 0.2% in hospitals with staff experienced in the disease.

Warning signs that Dengue shock syndrome is impending include:

- Sustained abdominal pain.
- Persistent vomiting,
- Change in level of consciousness (irritability or somnolence),
- Sudden change from fever to hypothermia,
- Sudden decrease in platelet counts.[2]

A second rash, varying in form from scarlatiform and maculopapular to petechial and occasionally purpuric, may appears with the initial decline of the fever. Severe itching, especially of the hands and feet, may accompany this rash, which is sometimes followed by desquamation.

During the course of the illness there is often a relative or paradoxical bradycardia in the face of increased temperature. Patients may have hemorrhagic manifestations such as epistaxis or menorrhagia. Jaundice is rare. Convulsions may occur with the onset of fever. The spinal fluid is almost always clear with no elevation of cell count but the pressure may be increased. Depression, weakness and blurred vision may resolve slowly during convalescence. Patients may take several weeks to recover completely.

Although these symptoms characterize "classical" Dengue fever, Dengue virus infection may also manifest a nonspecific febrile illness which can be confused with influenza, measles or any nonspecific viral syndrome. The lack of a clear clinical pattern for Dengue fever makes laboratory diagnosis a necessary part of any definitive evaluation of the disease.[45] Patients who develop DHF or other severe manifestations of Dengue

generally have an onset of illness similar to that seen in “classical” or non-haemorrhagic Dengue.

In addition to this pattern of DHF, cases of severe Dengue with massive gastrointestinal haemorrhage preceding the onset of shock and without evidence of increased vascular permeability, have been described. Many of these fatal hemorrhagic cases did not meet the WHO case definition for DHF. Severe encephalopathy with convulsions and / or coma has also been described with Dengue infection.

Significant Thrombocytopenia may occur in both DHF and “classical” Dengue. A fall in platelet count associated with a rising hematorit may suggest the development of DHF.

DIAGNOSIS

WHO HAS LAID DOWN THE FOLLOWING CRITERIA FOR THE DIAGNOSIS OF DENGUE FEVER

Diagnosis of Dengue fever and dengue haemorrhagic fever:

Dengue fever

Acute illness with two or more of:

- Headache;
- Retro-orbital pain;
- Myalgia;
- Arthralgia;
- Rash;

- Haemorrhagic manifestations;
- Leucopenia.

Dengue haemorrhagic fever

All of following:

- Haemorrhagic manifestations (shown by positive tourniquet test, petechiae, ecchymosis or purpura, or bleeding from mucosa, gastrointestinal tract, injection sites, or other locations).
- Platelet count <100 000 /mm^3.
- Objective evidence of plasma leakage due to increased vascular permeability shown by either fluctuation of packed cell volume during the course of illness and recovery or clinical signs of plasma leakage such as pleural effusion ascitis, or hypoproteinaemia.

Dengue shock syndrome

- Criteria for dengue haemorrhagic fever and either.
- Pulse pressure <20 mm Hg or
- Hypotension (defined as systolic pressure <80 mmHg for those aged <5 years or <90 mmHg for those aged >5 years).

PROBABLE DIAGNOSIS

Atleast one of following:

- Supportive serology on single serum sample: titre 1280 with haemagglutination inhibition test, comparable IgG titre with enzyme linked immunosorbent assay, or positive for IgM antibody test.
- Occurrence at same location and time as confirmed cases of Dengue fever.

CONFIRMED DIAGNOSIS

Atleast one of following:

- Isolation of dengue virus from serum or autopsy samples
- Fourfold or greater increase in serum IgG (by haemagglutination inhibition test) or increase in IgM antibody specific to Dengue virus.
- Detection of Dengue virus in tissue, serum or cerebrospinal fluid by immunohistochemistry, immunosorbent assay.
- Detection of Dengue virus genomic sequences by reverse transcription-polymerase chain reaction.

WHO case definition of DHF[46]

WHO CLASSIFICATION OF DENGUE INFECTIONS AND GRADING OF SEVERITY OF DHF

DF/DHF	GRADE	SIGNS AND SYMPTOMS	LABORATORY	
DF		Fever with two of the following: • Headache. • Retro-orbital pain. • Myalgia. • Arthralgia/bone pain. • Rash. • Haemorrhagic manifestations. • **No evidence of plasma**	Leucopenia (WBC ≤5000 cells/mm^3). • Thrombocytopenia (Platelet count <150 000 cells/mm^3). • Rising hematocrit (5% – 10%). • No evidence of plasma loss	
DHF	**I**	Fever and haemorrhagic manifestation (positive tourniquet test) and **evidence of plasma leakage**	Thrombocytopenia <100 000 cells/ mm^3; HCT rise ≥20%	
DHF	**II**	As in Grade **I plus** spontaneous bleeding.	Thrombocytopenia <100 000 cells/mm3; HCT rise ≥20%.	
DHF*	**III**	As in Grade **I or II plus** circulatory failure (weak pulse, narrow pulse pressure (≤20 mmHg), hypotension,	Thrombocytopenia <100 000 cells/mm3; HCT rise ≥20%.	
DHF*	**IV**	As in Grade **III** plus profound shock with undetectable BP and pulse	Thrombocytopenia < 100 000 cells/mm3; HCT rise ≥20%.	

Source: http://www.who.int/csr/resources/publications/dengue/Denguepublication/en/
*: DHF III and IV are DSS

Atypical variants

Rare and unusual presentations of Dengue are protean. The atypical variants have been encountered in various studies. To quote a few:

- Acute abdominal pains, diarrhoea, severe gastrointestinal haemorrhage, Irregular pulse and heart rate, acute renal failure, haemolytic uraemic syndrome.[47]
- Severe headache, convulsions, altered sensorium, Encephalitic signs associated with or without intracranial haemorrhage.[48]
- Respiratory distress.[49]
- Fulminant hepatic failure, obstructive jaundice, raised liver enzymes, Reye's Syndrome.[50]
- Disseminated intravascular coagulation.[50]
- Vertical transmission in newborns.[51]
- Dengue virus has been isolated from CSF suggesting direct involvement of the brain.[31]

Multisystem involvement is increasingly being documented during the last 10 years.

Transient reverse in the CD4/CD8 ratio occurred at days 6-10 after the onset of fever. These changes in immune parameters indicate aberrant immune activation during Dengue virus infection.[52]

The haemophagocytic syndrome is characterized by systemic proliferation of non-neoplastic histiocytes showing haemophagocytosis resulting in blood cytopenia. Bone marrow aspirations showed that platelets, red and white blood cells were phagocyted by histoicytes.[53]

Rare presentations of infection include severe haemorrhage, jaundice, parotitis, cardiomyopathy and non-specific ECG changes like ST elevations, premature ventricular complexes and bradycardia.[26]

Unusual neurological presentations include mononeuropathies, polyneuropathies, encephalitis, and transverse myelitis.[1]

Guillain-Barre syndrome has been associated with Dengue.[1]

Encephalopathy occurs occasionally and may result from cerebral edema, cerebral haemorrhage, liver failure or electrolyte imbalances.[1]

LABORATORY DIAGNOSIS

Specific diagnosis of Dengue infection is made by isolating the virus from the patient's blood. Acute serum samples are inoculated into tissue cultures of mosquito cells or directly into live Toxorhynchites or Aedes mosquitoes. Isolates can be identified from 2 to 7 days after inoculation depending on the actual technique used. Viruses are most likely to be isolated from acute serum samples obtained within[5] days after the onset of illness. Specific Dengue serotypes can be identified by the indirect fluorescent antibody test, with the use of type-specific monoclonal antibodies on the isolated virus.[17]

Immunodiagnostic methods for determining Dengue infection include detection of anti-Dengue IgM and IgG by enzyme-linked immunosorbent assay (ELISA) and detection of Hemaglutination inhibition (HI) antibody.[17]

Dengue-induced HI antibody cross-reacts broadly with other flavirirus such as yellow fever and St. Louis encephalitis virus. Complement fixation and neutralization antibody tests are more specific than hemagglutination inhibition.

Most serologic screening for Dengue infection is now done with an IgM ELISA. With appropriately timed samples, the sensitivity and specificity of this test in diagnosing Dengue infection appear to be high.

The pattern of HI response has been used to classify Dengue infections as primary or secondary, based on the concept that initial or primary Dengue infections tend to elicit lower HI titiers than do secondary infections (subsequent infections with a different Dengue serotype or antigenically related flavivirus).

IgM:IgG ratios as determined by ELISA may be an alternative method of distinguishing primary from secondary infections. The rise in neutralizing antibody in primary infection is believed to be relatively type-specific and can be used to determine the infecting serotype. In secondary infections, because the immunologic cross-reactivity to different flavivirus and anamnestic responses may result in heterologus titer elevations, the only reliable method for determining the infecting serotype is virus isolation.[17]

IgM ELISA (serum taken after 5 days of onset):

- IgM antibodies rise quickly and fade down several weeks after the infection.
- Although IgM antibodies can appear very fast after infection, they can be consistently detected in most patients only after the first week. WHO recommends the use of sera taken at least five days after onset. In earlier sera the result is diagnostic only if positive. A positive result indicates that the patient has been exposed to the virus in the recent past. The test is unable to identify the viral type. Strictly speaking, the test is not specific to Dengue as there can be cross-reaction with other Flavivirus as Yellow fever, yellow fever vaccination and other Flavivirus that are not seen frequently in Indian context. However, in conjunction with the clinical presentation and the epidemiological knowledge it can strongly support the diagnosis of Dengue virus infection.[17]

MANAGEMENT

No specific therapeutic agents exist for Dengue; steroids, antivirals, or carbazochrome (which decreases capillary permeability) have no proven role. In patients without shock, oral hydration should be started early. Paracetamol (aspirin and other non-steroidal anti-inflammatory drugs should be avoided owing to the increased risk for Reye's syndrome and haemorrahge) can be used for fever and analgesia. Assessment of the patient's condition includes packed cell volume, platelet count, liver function tests, prothrombin time, partial thromboplastin time, electrolytes, and blood gas analysis. The patient's clinical condition should be monitored until at least 24 hours after defervesence

because of the risk of shock. Patients with signs of severe dehydration or haemorrahge or those who cannot be monitored or return quickly if symptoms worsen should be admitted to hospital. Invasive procedures should be considered carefully because of the risk of haemorrhage. The choice of crystalloid or colloid solutions in Dengue shock syndrome is under debate. No studies have found a difference in clinically significant outcomes, but they do show that appropriate volume repletion is effective in Dengue shock syndrome and that lactated Ringer's solution is no better than normal saline.[54]

Isolation is not necessary in mosquito-free environments. Usual precautions handling blood specimens should be observed.

Criteria for admission (any of the following) in the presence of suspicion of Dengue fever:

- Restlessness or lethargy
- Cold extremities or circumoral cyanosis
- Bleeding in any form
- Oliguria or reluctance to drink fluids
- Rapid and weak pulse
- Narrowing of pulse pressure (< 20 mm Hg or hypotension)
- Haematrocrit of 40 or rising
- Platelet count of less than 100,000/mm3
- Acute abdominal pain
- Evidence of plasma leakage, e.g., pleural effusion, ascites

If patient refuses admission, parent should be advised to:

- Encourage child to drink fluids.
- Observe for coldness / blueness of extremities.
- Administer paracetamol for fever 10-15 m/kg/dose 4-6 hourly (limit to 5 doses in 24 hours).
- Tepid sponging as necessary.
- Avoid aspirin and non-steroidal anti-inflammatory drugs.

Parents must bring the child back immediately to the nearest hospital in the presence of any one of the following situations:

- Not drinking / feeding poorly.
- Passing less urine than usual.
- Abdominal pain.
- Bleeding in any form.
- In older children, inability to sit up, giddiness.
- Irritability, drowsiness, restlessness.
- Child continues to be unwell.

Pointers for early diagnosis of DHF

- Frequent vomiting during first one or two days of febrile illness.
- Leucopenia on day 2.

Management of patients with warning signs

It is important to verify if the warning signs are due to dengue shock syndrome or other causes such as acute gastroenteritis, vasovagal reflex, hypoglycemia, etc. The presence of thrombocytopenia with evidence of plasma leakage such as rising haemotocrit and pleural effusion differentiates DHF/ DSS from other causes. Blood glucose level and other laboratory tests may be indicated to find the causes. Management of DHF/DSS is detailed below. For other causes, IV fluids and supportive and symptomatic treatment should be given while these patients are under observation in hospital. They can be sent home within 8 to 24 hours if they show rapid recovery and are not in the critical period (i.e. when their platelet count is >100 000 cells/mm^3).

WHO Management GUIDELINES of DHF grade I, II (non-shock cases)

In general, the fluid allowance (oral + IV) is about maintenance (for one day) + 5% deficit (oral and IV fluid together), to be administered over 48 hours. For example, in a child weighing 20 kg, the deficit of 5% is 50 ml/kg x 20 = 1000 ml. The maintenance is 1500 ml for one day. Hence, the total of M + 5% is 2500 ml. This volume is to be administered over 48 hours in non-shock patients.

WHO MANAGEMENT GUIDELINES FOR DSS

Infuse 0.9% saline or Ringer's lactate at 10-20ml/kg boluses as rapidly as possible until vital signs return to normal. 2-3 boluses may be needed in profound shock. When vital signs improve, change IV fluids to dextrose 5% and 045% saline at a reduced rate, 1-2 times maintenance (3-6 ml/kg/hour), guided by hematocrit, urine output and vital signs.

If there is not definite improvement in vital signs and if hematocrit remains high, use plasma or plasma expanders. If there is no definite improvement in vital signs and if hematocrit is low or has decreased, transfuse blood because this signifies haemorrhage, occult or obvious. Sudden drop in haemoglobin level is also an indicator of occult haemorrhage.

Continue replacement of further plasma losses with Dextrose 5% and 45% saline over a period of 24-48 hours.

Reduce or discontinue intravenous fluids between 24-48 hours after the onset of shock if vital signs are stable. Reduce intravenous fluids earlier if patient has good urine output (Pulmonary edema and massive pleural effusion will occur if excessive intravenous fluids are given after this stage).

Hyponatraemia and acidosis occur commonly in DSS. These will correct with fluid resuscitation with 0.9% saline. Periodic arterial blood gases and electrolytes should be measured.

BLOOD TRANSFUSION

Blood transfusion is indicated in significant clinical bleeding, most often haematemesis and melena,

WHO GUIDELINES OF MANAGEMENT OF PROLONGED/PROFOUND SHOCK: DHF GRADE 4

The initial fluid resuscitation in Grade 4 DHF is more vigorous in order to quickly restore the blood pressure and laboratory investigations should be done as soon as possible for ABCS as well as organ involvement. Even mild hypotension should be treated aggressively. *Ten ml/kg of bolus fluid should be given as fast as possible, ideally within 10 to 15 minutes.* When the blood pressure is restored, further intravenous fluid may be given as in Grade 3. *If shock is not reversible after the first 10 ml/ kg, a repeat bolus of 10 ml/kg and laboratory results should be pursued and corrected as soon as possible.* Urgent blood transfusion should be considered as the next step (after reviewing the preresuscitation HCT) and followed up by closer monitoring, e.g. continuous bladder catheterization, central venous catheterization or arterial lines.

It should be noted that restoring the blood pressure is critical for survival and if this cannot be achieved quickly then the prognosis is extremely grave. Inotropes may be used to support the blood pressure, if volume replacement has been considered to be adequate such as in high central venous pressure (CVP), or cardiomegaly, or in documented poor cardiac contractility.

If blood pressure is restored after fluid resuscitation with or without blood transfusion, and organ impairment is present, the patient has to be managed appropriately with special supportive treatment. Examples of organ support are peritoneal dialysis, continuous renal replacement therapy and mechanical ventilation.

If intravenous access cannot be obtained urgently, try oral electrolyte solution if the patient is conscious or the intraosseous route if otherwise. The intraosseous access is life-saving and should be attempted after 2–5 minutes or after two failed attempts at peripheral venous access or after the oral route fails.

WHO GUIDELINES OF MANAGEMENT OF SEVERE HAEMORRHAGE

- If the source of bleeding is identified, attempts should be made to stop the bleeding if possible. Severe epistaxis, for example, may be controlled by nasal packing. Urgent blood transfusion is life-saving and should not be delayed till the HCT drops to low levels. If blood loss can be quantified, this should be replaced. However, if this cannot be quantified, aliquots of 10 ml/kg of fresh whole blood or 5 ml/kg of freshly packed red cells should be transfused and response evaluated. The patient may require one or more aliquot.

- In gastrointestinal bleeding, H-2 antagonists and proton pump inhibitors have been used, but there has been no proper study to show its efficacy.

- There is no evidence to support the use of blood components such as platelet concentrates, fresh frozen plasma or cryoprecipitate. Its use could contribute to fluid overload.

- Recombinant Factor 7 might be helpful in some patients without organ failure, but it is very expensive and generally not available.

Management of high-risk patients

- Obese patients have less respiratory reserves and care should be taken to avoid excessive intravenous fluid infusions. The ideal body weight should be used to calculate fluid resuscitation and replacement and colloids should be considered in the early stages of fluid therapy. Once stabilized, furosemide may be given to induce diuresis.

- Infants also have less respiratory reserves and are more susceptible to liver impairment and electrolyte imbalance. They may have a shorter duration of plasma leakage and usually respond quickly to fluid resuscitation. Infants should, therefore, be evaluated more frequently for oral fluid intake and urine output.

- Intravenous insulin is usually required to control the blood sugar levels in dengue patients with diabetes mellitus. Non-glucose containing crystalloids should be used.

- Pregnant women with dengue should be admitted early to intensely monitor disease progress. Joint care among obstetrics, medicine and paediatrics specialities is essential.

- Families may have to be counselled in some severe situations. Amount and rate of IV fluid for pregnant women should be similar to those for non-pregnant woman using pre-pregnant weight for calculation.

- Patients with hypertension may be on anti-hypertensive therapy that masks the cardiovascular response in shock. The patient's own baseline blood pressure should be considered. A blood pressure that is perceived to be normal may in fact be low for these patients.

- Anti-coagulant therapy may have to be stopped temporarily during the critical period.

Haemolytic diseases and haemoglobinopathies: These patients are at risk of haemolysis and will require blood transfusion. Caution should accompany hyperhydration and alkalinisation therapy, which can cause fluid overload and hypocalcemia.

Congenital and ischaemic heart diseases: Fluid therapy should be more cautious as they may have less cardiac reserves.

For patients on steroid therapy, continued steroid treatment is recommended but the route may be changed.

Management of convalescence

- Convalescence can be recognized by the improvement in clinical parameters, appetite and general well-being.

- Haemodynamic state such as good peripheral perfusion and stable vital signs should be observed.

- Decrease of HCT to baseline or below and dieresis are usually observed.
- Intravenous fluid should be discontinued.
- In those patients with massive effusion and ascitis, hypervolemia may occur and diuretic therapy may be necessary to prevent pulmonary oedema.
- Hypokalemia may be present due to stress and diuresis and should be corrected with potassium-rich fruits or supplements.
- Bradycardia is commonly found and requires intense monitoring for possible rare complications such as heart block or ventricular premature contraction (VPC).
- Convalescence rash is found in 20%–30% of patients.

Signs of recovery

- Stable pulse, blood pressure and breathing rate.
- Normal temperature.
- No evidence of external or internal bleeding.
- Return of appetite.
- No vomiting, no abdominal pain.
- Good urinary output.
- Stable hematocrit at baseline level.
- Convalescent confluent petechiae rash or itching, especially on the extremities.

WHO CRITERIA FOR DISCHARGING PATIENTS

- Absence of fever for at least 24 hours without the use of anti-fever therapy.
- Return of appetite.
- Visible clinical improvement
- Satisfactory urine output.
- A minimum of 2–3 days have elapsed after recovery from shock.
- No respiratory distress from pleural effusion and no ascitis.
- Platelet count of more than 50 000/mm^3. If not, patients can be recommended to avoid traumatic activities for at least 1–2 weeks for platelet count to become normal. In most uncomplicated cases, platelet rises to normal within 3–5 days.

METHODOLOGY

This study is conducted on seropositive cases of dengue less than 18years of age admitted in the R. L. Jalappa Hospital, Kolar from October 2010 to October 2011

Probable cases by clinical suspicion (any acute febrile illness with one of the following symptoms myalgia, headache, bleeding, retro-orbital pain, bleeding, altered sensorium, shock or low platelet count) were registered in the study, informed consent was obtained and a detailed clinical history, physical examination and baseline investigations are undertaken (proforma shown as annexure).

Children who were dengue seropositive are stratified into those with or without complications based on symptoms and signs.

Dengue fever includes clinically undifferentiated febrile illness, dengue fever, dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) based on WHO.

Patients included in the study were subjected to routine haematology investigations like haemoglobin, total and differential leukocyte count, hematocrit, platelet count, baseline biochemical investigation including liver function tests. Renal function test and urine examinations are done Chest X-ray and USG abdomen were taken to demonstrate pleural effusion. CSF analysis was done in patients with convulsions or meningeal signs whenever indicated

INCLUSION CRITERIA

- Patients with positive serology for dengue fever(IgG & IgM,or IgM positive).
- Patients positive for NS1 Ag.

EXCLUSION CRITERIA

- Patients with negative serology for dengue fever(IgM)&/or
- Patients negative for NS1 Ag.
- Age more than 18 years.

Statistical Methods: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. The following assumptions on data is made: **Assumptions:** 1. Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent

Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

1 **Sample Size estimation**

Proportion Known populations

$n = [(z^2 * p * q) + ME^2] / [ME^2 + z^2 * p * q / N]$

Proportion Unknown population

$n = [(z^2 * p * q) + ME^2] / (ME^2)$

ME: is the margin of error, measure of precision.

and Z is 1.96 as critical value at 95%CI

N: population size

n: Sample size

σ: Standard deviation

z: Critical value based on Normal distribution at 95% Confidence Interval

Standard deviation: $SD = \sqrt{\frac{\sum (x - \bar{x})^2}{n-1}}$

2. **Chi-Square Test**: The chi-square test for independence is used to determine the relationship between two variables of a sample. In this context independence means that the two factors are not related. In the chi-square test for independence the degree of freedom is equal to the number of columns in the table minus one multiplied by the number of rows in the table minus one

$\chi^2 = \frac{\sum (Oi - Ei)^2}{Ei}$, Where Oi is Observed frequency and Ei is Expected frequency

With (n-1) df

The Assumptions of Chi-square test

The chi- square test, when used with the standard approximation that a chi-square distribution is applicable, has the following assumptions:

- **Random sample**: A random sampling of the data from a fixed distribution or population.

- **Sample size (whole table)**: A sample with a sufficiently large size is assumed. If a chi square test is conducted on a sample with a smaller size, then the chi square test will yield an inaccurate inference. The researcher, by using chi square test on small samples, might end up committing a Type II error.
- **Expected Cell Count**: Adequate expected cell counts. Some require 5 or more, and others require 10 or more. A common rule is 5 or more in all cells of a 2-by-2 table, and 5 or more in 80% of cells in larger tables, but no cells with zero expected count. When this assumption is not met, Fisher Exact test or Yates' correction is applied.

3. **Fisher Exact Test:** The Fisher Exact Test looks at a contingency table which displays how different treatments have produced different outcomes. Its null hypothesis is that treatments do not affect outcomes-- that the two are independent. Reject the null hypothesis (i.e., conclude treatment affects outcome) if *p* is "small".

The usual approach to contingency tables is to apply the χ^2 statistic to each cell of the table. One should probably use the χ^2 approach, unless you have a special reason. The most common reason to avoid χ^2 is because you have small expectation values.

	Class 1	**Class 2**	**Total**
Sample 1	A	b	a+b
Sample 2	C	d	c+d
Total	a+c	b+d	n

2x2 Fisher Exact Test statistic= $\sum p = \frac{(a+b)!(c+d)!(a+c)!(b+d)!}{n!}\frac{1}{\sum a!b!c!d!}$

1. **Fisher Exact test (rxc tables)**

Let there exist two such variables X and Y, with m and n observed states, respectively. Now form an $m \times n$ matrix in which the entries a_{ij} represent the number of observations in which $x = i$ and $y = j$. Calculate the row and column sums R_i and C_j, respectively, and the total sum

$$N = \sum_i R_i = \sum_j C_j$$

of the matrix. Then calculate the conditional probability of getting the actual matrix given the particular row and column sums, given by

$$P_{\text{cutoff}} = \frac{(R_1!\, R_2! \cdots R_m!)\,(C_1!\, C_2! \cdots C_n!)}{N! \prod_{i,j} a_{ij}!},$$

which is a multivariate generalization of the hypergeometric probability function.

3. **Significant figures**

+	Suggestive significance	(p value: 0.05<p<0.10)
*	Moderately significant	(p value: 0.01<p≤ 0.05)
**	Strongly significant	(p value: p≤0.01)

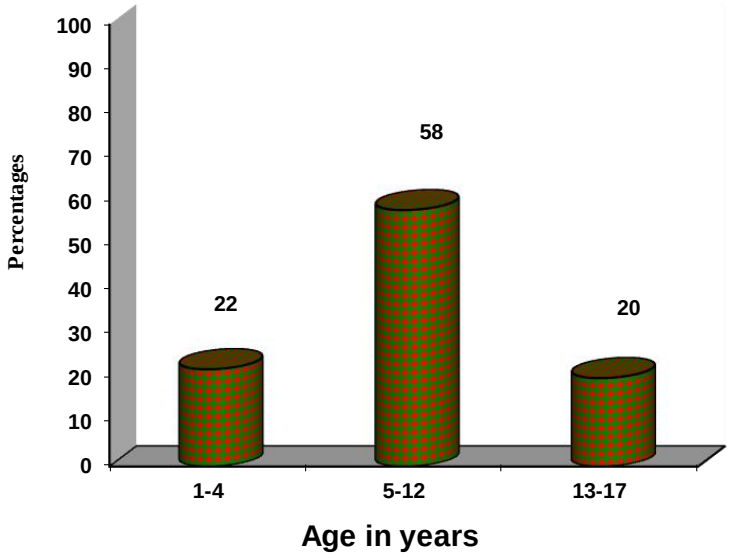
Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

OBSERVATION AND RESULTS

An observational clinical study with 50 patients presented with dengue fever is undertaken to study the clinical profile and factors associated and influencing the dengue fever.

Table 1: Age distribution of patients studied

Age in years	Number of patients	%
1-4	11	22.0
5-12	29	58.0
13-17	10	20.0
Total	50	100.0

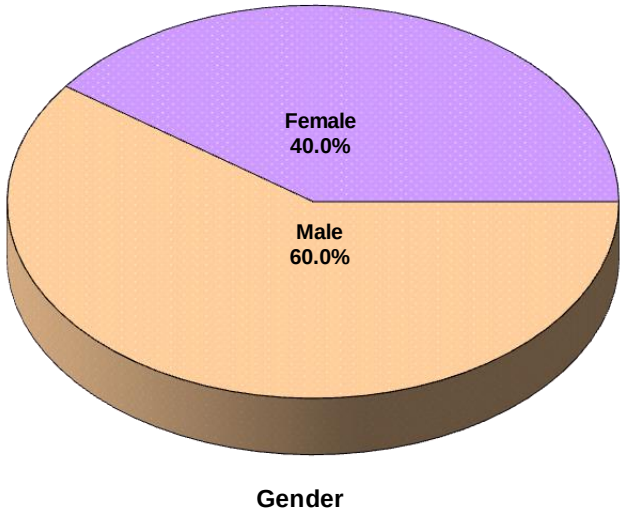


Graph 1: Shows age distribution in the study

In the above study, we can see most of the patients were above 5 years of age.

Table 2: Gender distribution of patients studied

Gender	Number of patients	%
Male	30	60.0
Female	20	40.0
Total	50	100.0

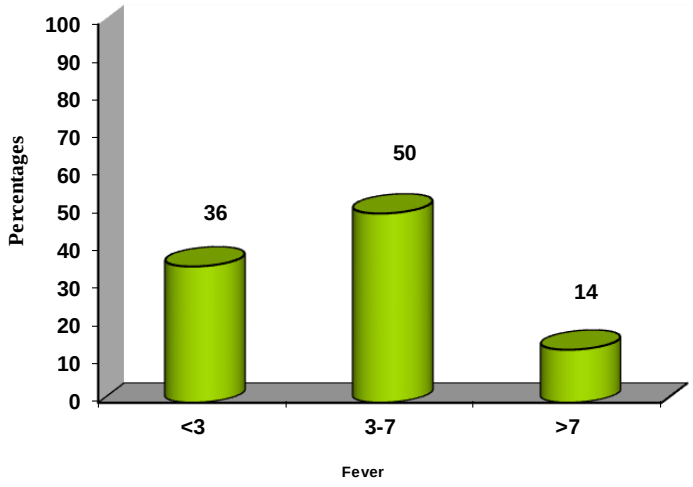


Graph 2: Shows male and female ratio

Male dominance was seen in the gender distribution of cases.

Table 3: Clinical features of patients studied

Clinical features	Number of patients (n=50)	%
Fever		
• <3	18	36.0
• 3-7	25	50.0
• >7	7	14.0
Urine output <0.5ml/kg/hr		
• Normal	35	70.0
• Reduced	15	30.0
Bleeding manifestation		
• Absent	35	70.0
• Present	15	30.0
Rashes		
• Absent	42	84.0
• Present	8	16.0
Facial oedema		
• Absent	44	88.0
• Present	6	12.0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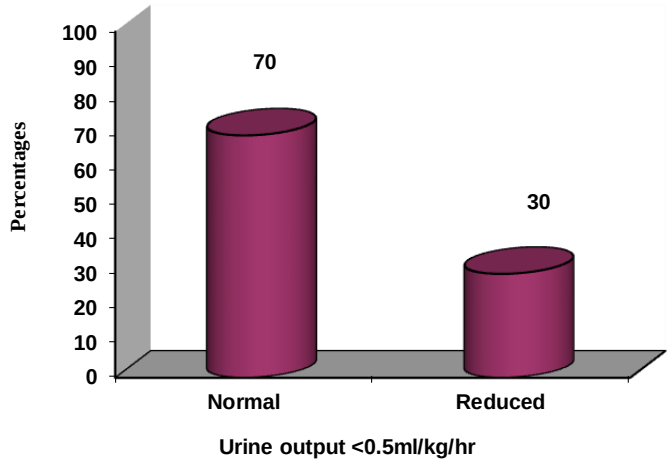
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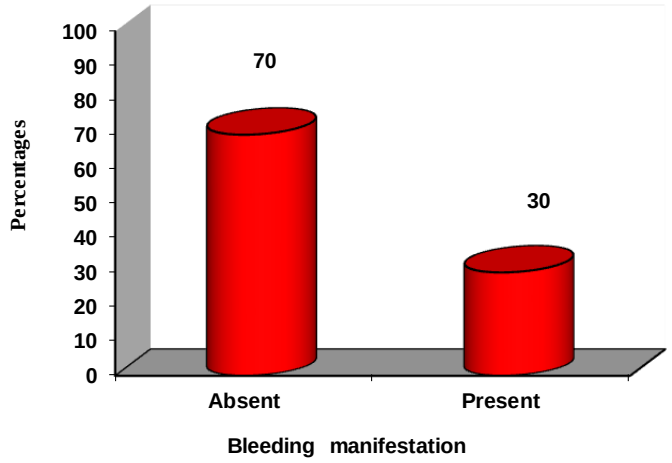
Normal
Reduced
Urine output <0.5ml/kg/hr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Bleeding manifestation

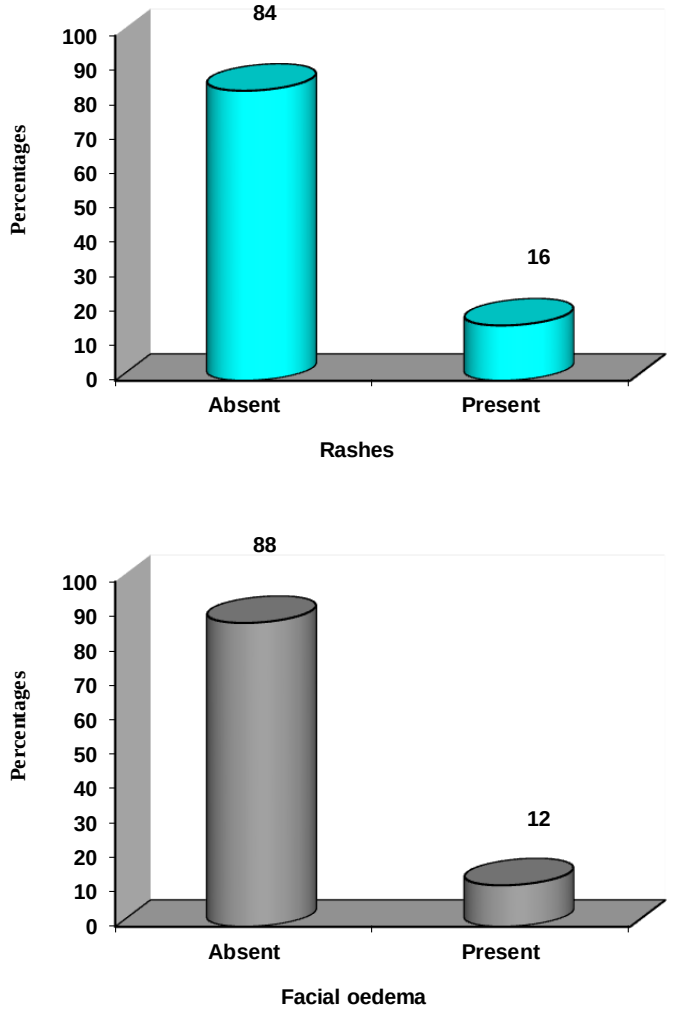
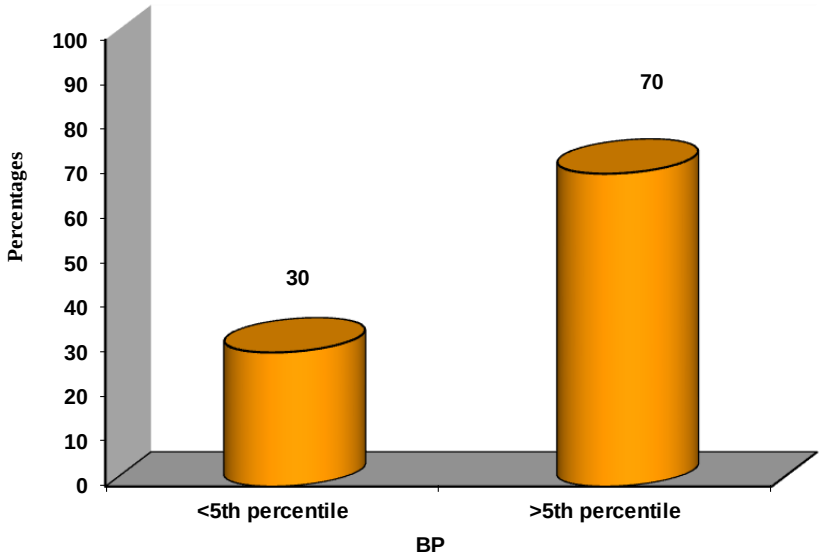


Figure 3: Depicts the different clinical features present in the study

The most common clinical feature patients presented was fever in all cases. The next common presentation was bleeding manifestation which is a distinquishing sign of dengue fever

Table 4: Blood pressure (mmHg) of patients studied

BP	Number of patients	%
<5th percentile	15	30.0
>5th percentile	35	70.0
Total	50	100.0

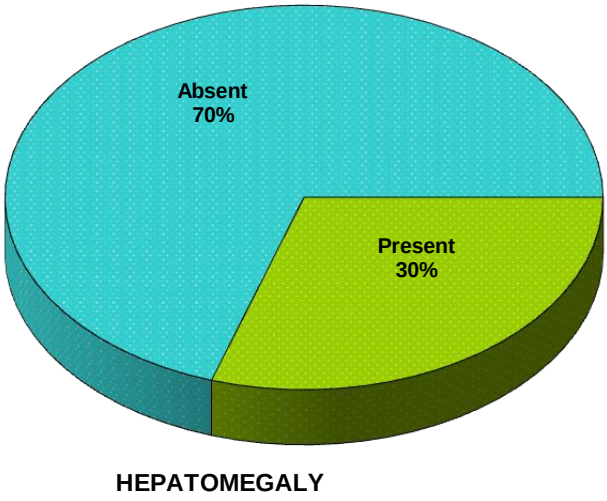


Graph 4: Shows blood pressure percentile of the patients

Of the study 15 patients developed hypotension, among which most of the patients belonged to group of dengue shock syndrome (DSS).

Table 5: Hepatomegaly of patients studied

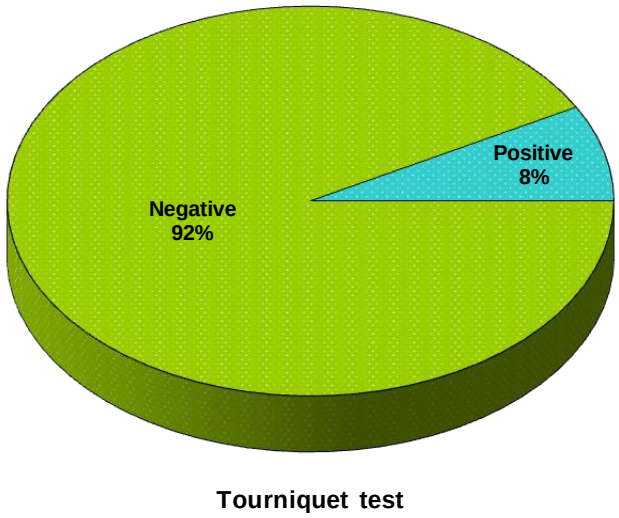
Hepatomegaly	Number of patients	%
Absent	35	70.0
Present	15	30.0
Total	50	100.0



Graph 5: Shows distribution of hepatomegaly in patients

Table 6: Tourniquet test of patients studied

Tourniquet test	Number of patients	%
Negative	46	92.0
Positive	4	8.0
Total	50	100.0

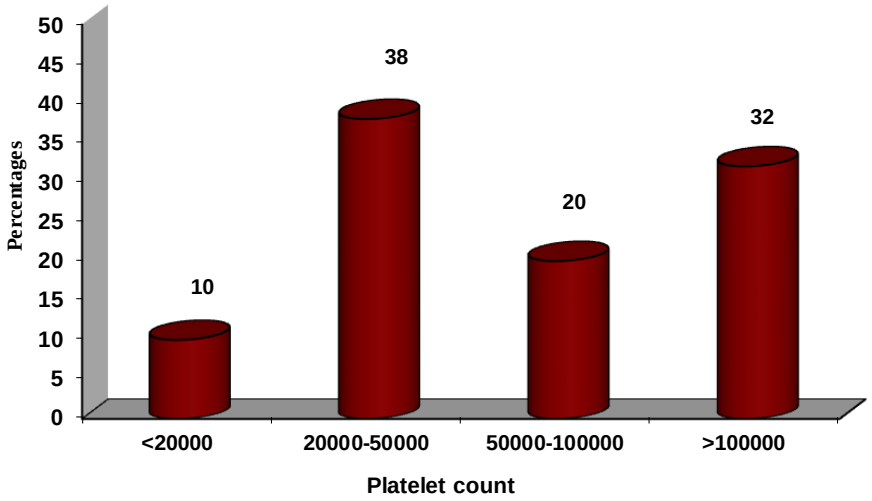


Graph 6: Showing percentage of tourniquet test positivity in patients

Only 4 patients of the study had tourniquet positive, as Kolar is an endemic area there is less number of tourniquet positive cases. This is a unique finding of this study in compatibility with the WHO findings which also states that tourniquet positive cases are less in endemic areas.

Table 7: Platelet count of patients studied

Platelet count	Number of patients	%
<20000	5	10.0
20000-50000	19	38.0
50000-100000	10	20.0
>100000	16	32.0
Total	50	100.0

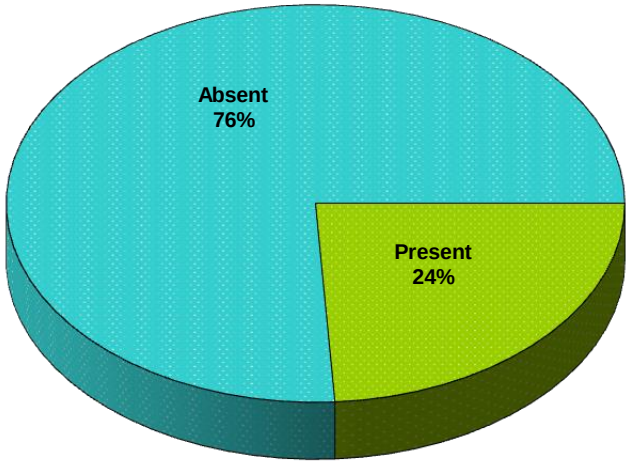


Graph 7: Shows distribution of platelet range in the patients

Majority of patients were between 20000-100000 but 5 patients had platelet count <20000 who had symptoms of DSS.

Table 8: Pleural effusion of patients studied

Pleural effusion	Number of patients	%
Absent	38	76.0
Present	12	24.0
Total	50	100.0

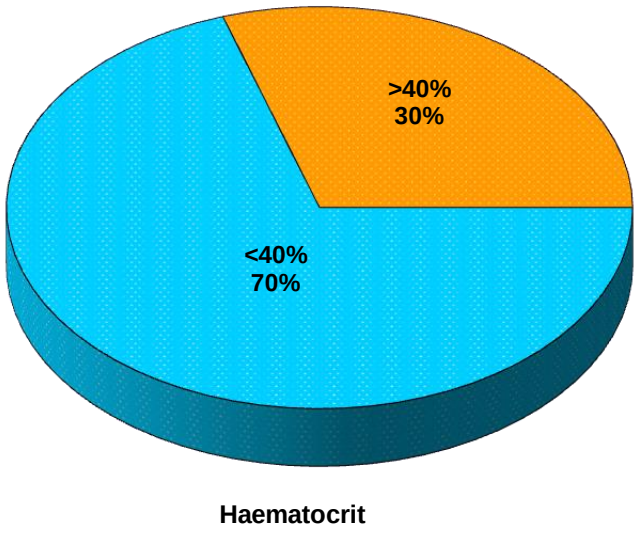


Graph 8: Shows cases of pleural effusion in the study

12 patients had pleural effusion out which 9 patients belonged to the group of DSS. DSS had the major share which resulted in fall of BP.

Table 9: Hematocrit of patients studied

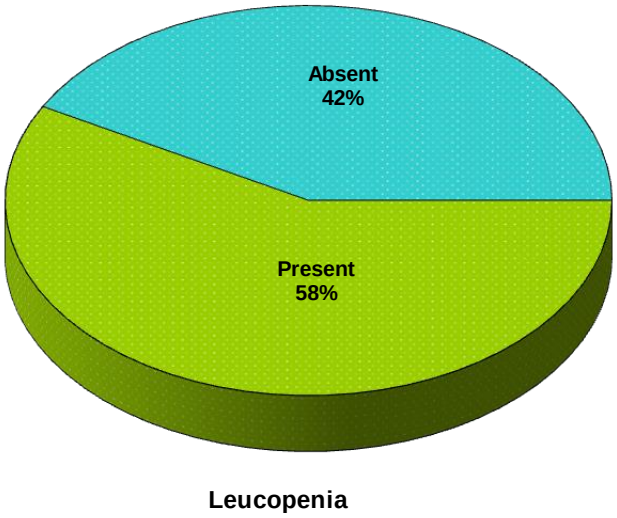
Hematocrit	Number of patients	%
<40%	35	70.0
>40%	15	30.0
Total	50	100.0



Graph 9: Shows distribution of hematocrit in the patients

Table 10: Leucopenia of patients studied

Leucopenia	Number of patients	%
Absent	21	42.0
Present	29	58.0
Total	50	100.0

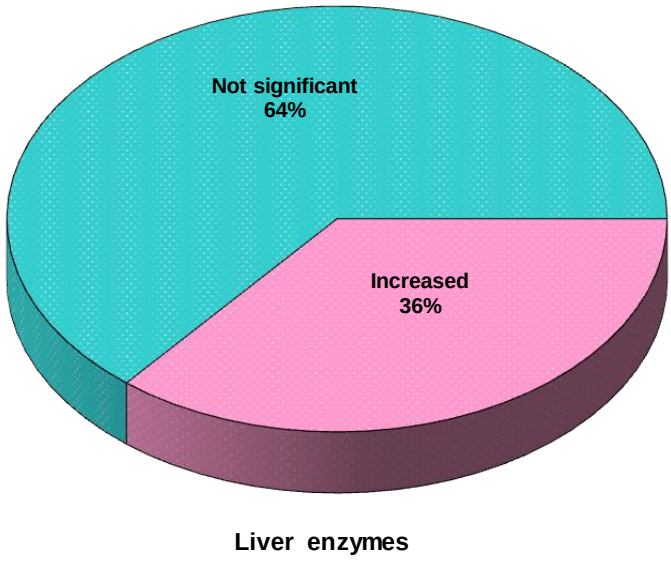


Graph 10: Showing percentage of patients with leucopenia

Majority of the patients suffered from leucopenia. Leucopenia was found to be an significant early diagnostic marker with a p value of 0.040.

Table 11: Liver enzymes of patients studied

Liver enzymes altered	Number of patients	%
Significant	18	36.0
Not significant	32	64.0
Total	50	100.0

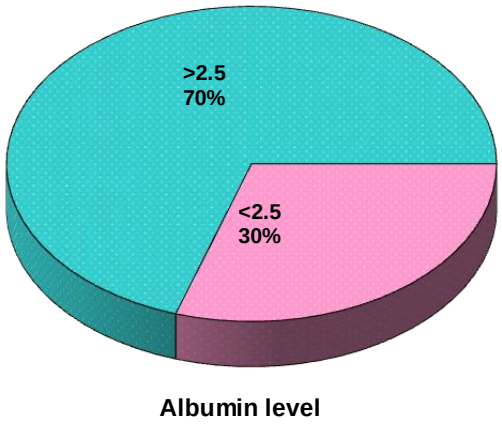


Graph 11: Showing percentage of patients with altered liver enzymes

Increase of liver enzymes by four fold is considered as significant in Dengue. In our study 18 patients had significant increase in liver enzymes.

Table 12: Albumin level of patients studied

Albumin level	Number of patients	%
<2.5	15	30.0
>2.5	35	70.0
Total	50	100.0

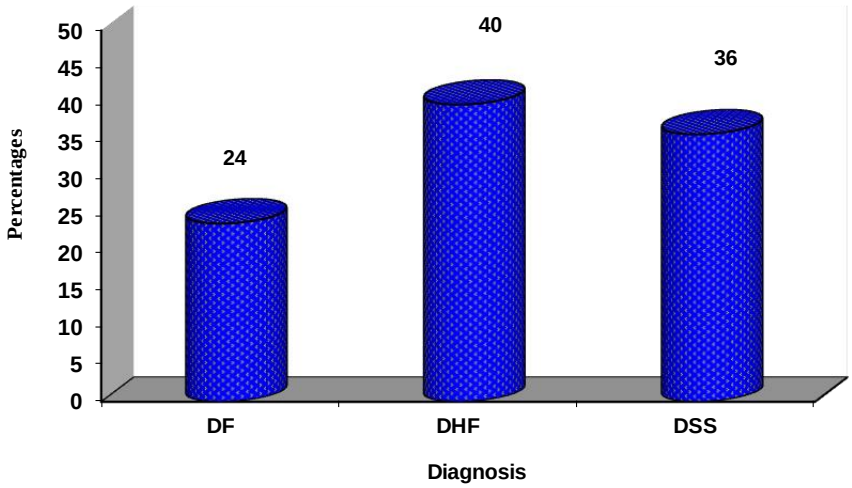


Graph 12: Showing distribution of albumin level in the patients

Most of the patients with decreased albumin levels belong to the group of DSS and DHF which is due to the involvement of liver.

Table 13: Diagnosis of patients studied

Diagnosis	Number of patients	%
DF	12	24.0
DHF	20	40.0
DSS	18	36.0
Total	50	100.0

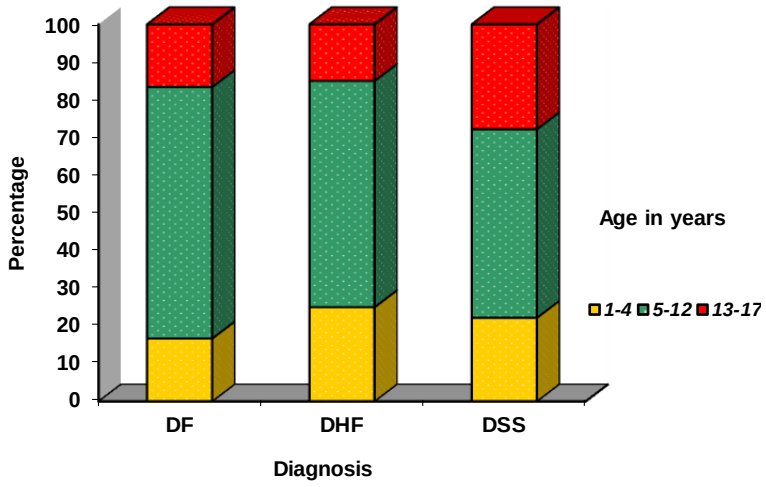


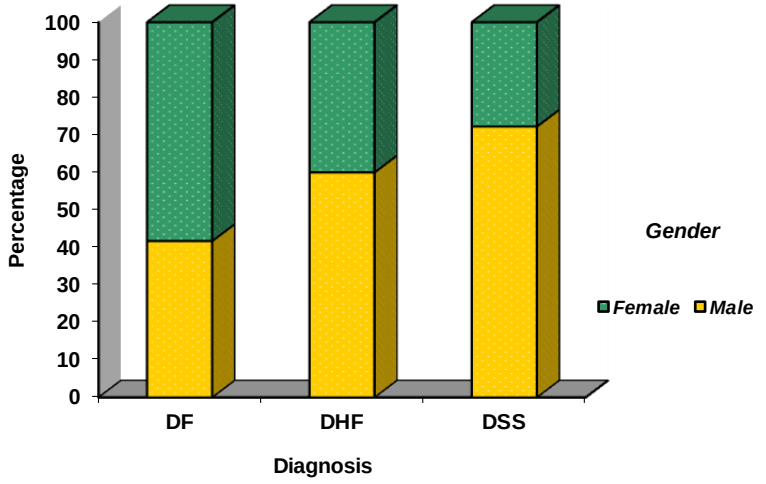
Graph 13: Showing percentage of patients with different types of dengue fever

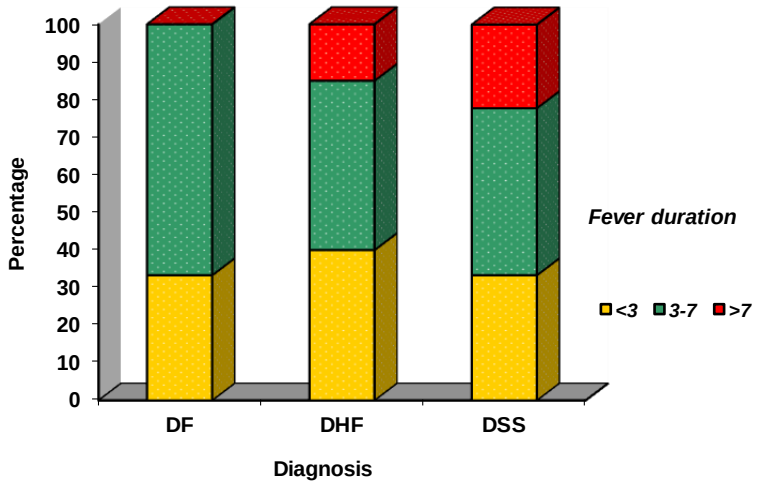
As per the WHO classification of Dengue fever DHF had the major share than the DF and DSS i. e. out of 50 patients 20 were suffering from DHF when 18 had DSS and 12 with DF.

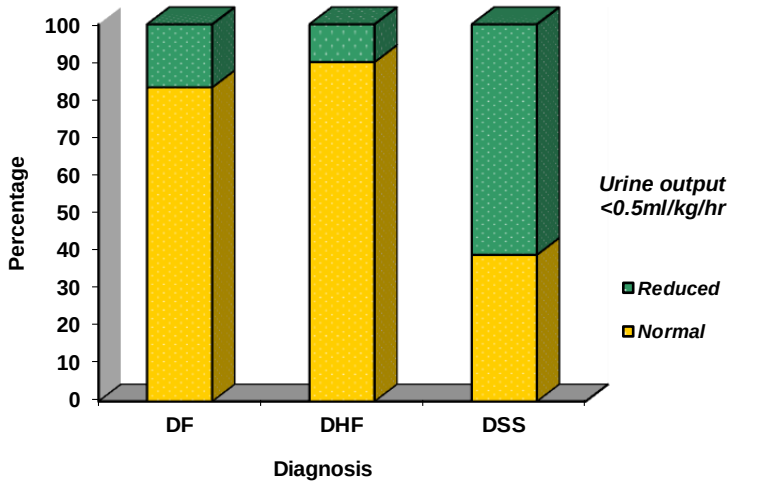
Table 14: Correlation of clinical variables with Diagnosis and severity of Dengue fever

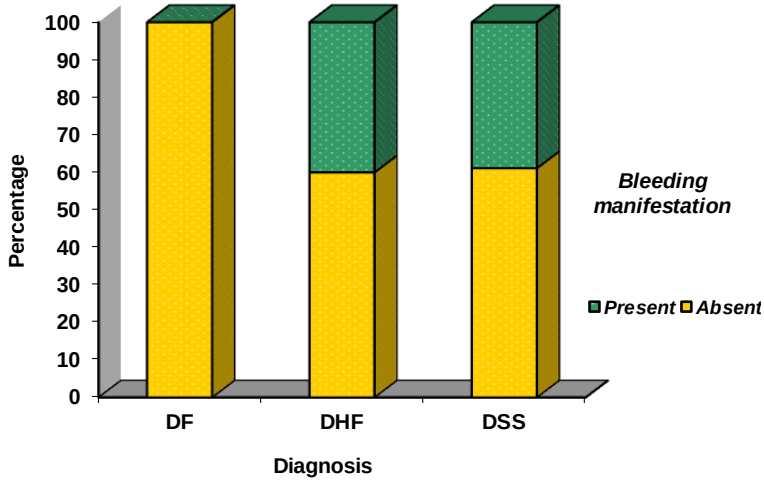
Variables	Diagnosis			p value
	DF (n=12)	DHF (n=20)	DSS (n=18)	
Age in years				
• 1-4	2(16.7%)	5(25%)	4(22.2%)	0.859
• 5-12	8(66.7%)	12(60%)	9(50%)	
• 13-17	2(16.7%)	3(15%)	5(27.8%)	
Gender				
• Male	5(41.7%)	12(60%)	13(72.2%)	0.284
• Female	7(58.3%)	8(40%)	5(27.8%)	
Fever duration				
• <3	4(33.3%)	8(40%)	6(33.3%)	0.501
• 3-7	8(66.7%)	9(45%)	8(44.4%)	
• >7	0(0%)	3(15%)	4(22.2%)	
Urine output <0.5ml/kg/hr				
• Normal	10(83.3%)	18(90%)	7(38.9%)	0.001**
• Reduced	2(16.7%)	2(10%)	11(61.1%)	
Bleeding manifestation				
• Absent	12(100%)	12(60%)	11(61.1%)	0.022*
• Present	0(0%)	8(40%)	7(38.9%)	
Rashes				
• Absent	10(83.3%)	19(95%)	13(72.2%)	0.159
• Present	2(16.7%)	1(5%)	5(27.8%)	
Facial oedema				
• Absent	11(91.7%)	19(95%)	14(77.8%)	0.259
• Present	1(8.3%)	1(5%)	4(22.2%)	
BP				
• $<5^{th}$ percentile	2(16.7%)	2(10%)	11(61.1%)	0.001**
• $>5^{th}$ percentile	10(83.3%)	18(90%)	7(38.9%)	
Hepatomegaly				
• Absent	9(75%)	13(65%)	13(72.2%)	0.857
• Present	3(25%)	7(35%)	5(27.8%)	
Tourniquet test				
• Negative	11(91.7%)	19(95%)	16(88.9%)	0.822
• Positive	1(8.3%)	1(5%)	2(11.1%)	

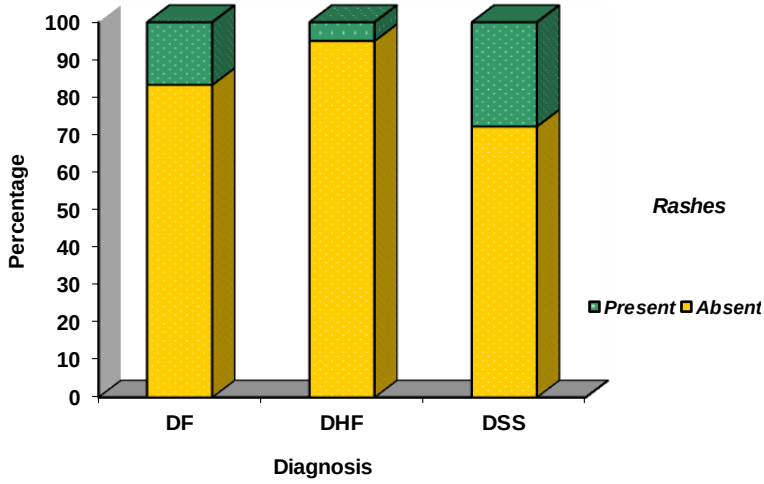

100
90
80
70
60
50
40
30
20
10
0
Percentage
DF
DHF
DSS
Diagnosis
Age in years
1-4
5-12
13-17

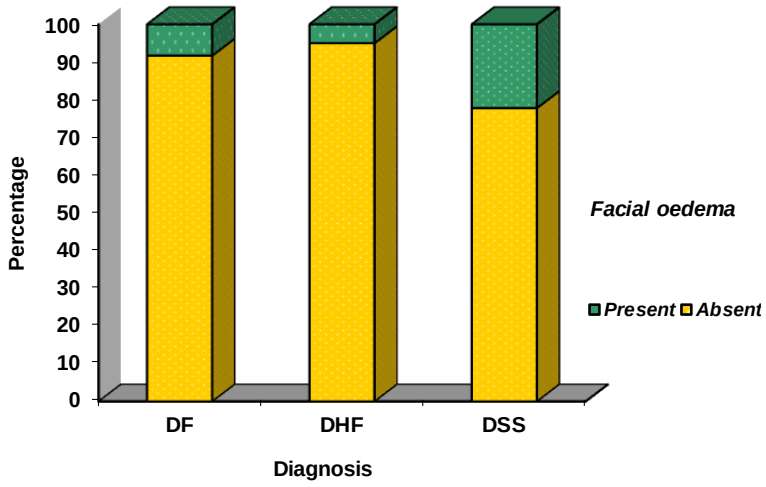

100
90
80
70
60
50
40
30
20
10
0
Percentage
DF
DHF
DSS
Diagnosis
Gender
Female
Male

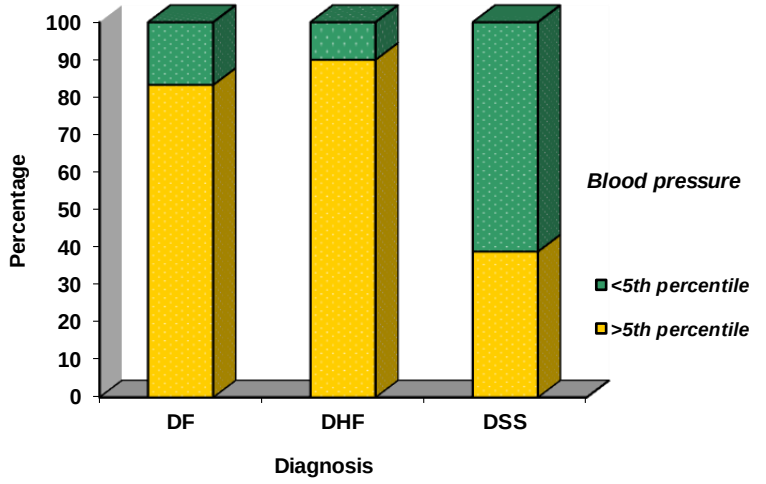

100
90
80
70
60
50
40
30
20
10
0
Percentage
DF
DHF
DSS
Diagnosis
Fever duration
<3
3-7
>7

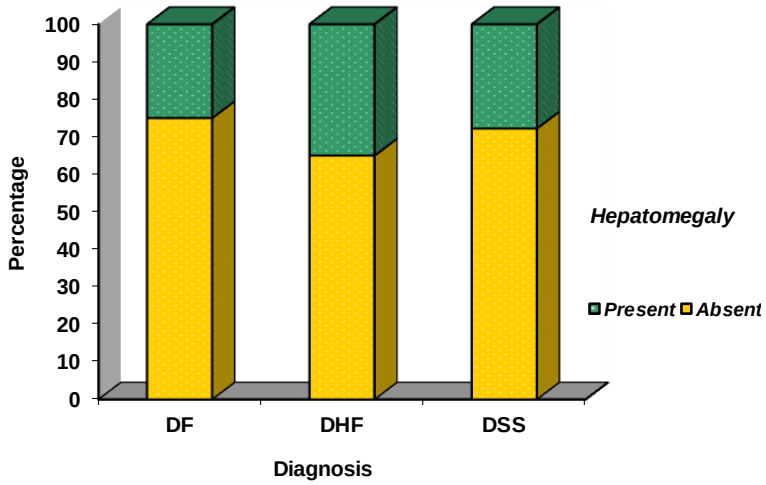

100
90
80
70
60
50
40
30
20
10
0
Percentage
DF
DHF
DSS
Diagnosis
Urine output <0.5ml/kg/hr
Reduced
Normal

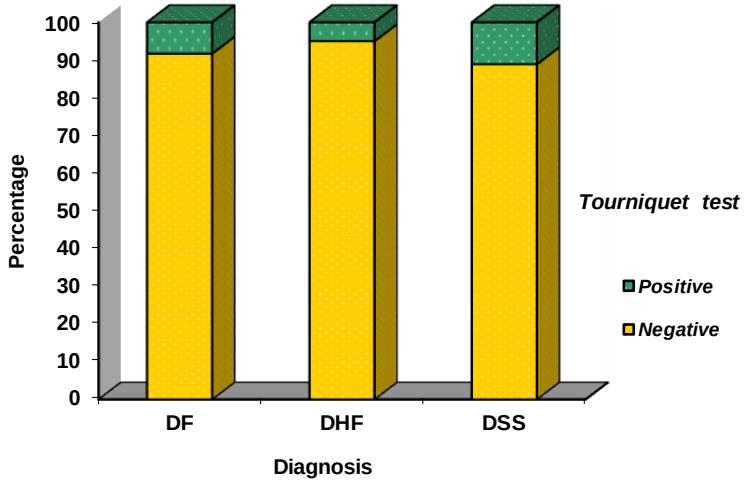

100
90
80
70
60
50
40
30
20
10
0
Percentage
DF
DHF
DSS
Diagnosis
Bleeding manifestation
Present
Absent


100
90
80
70
60
50
40
30
20
10
0
Percentage
DF
DHF
DSS
Diagnosis
Rashes
Present
Absent


100
90
80
70
60
50
40
30
20
10
0
Percentage
DF
DHF
DSS
Diagnosis
Facial oedema
Present
Absent


100
90
80
70
60
50
40
30
20
10
0
Percentage
DF
DHF
DSS
Diagnosis
Blood pressure
<5th percentile
>5th percentile


100
90
80
70
60
50
40
30
20
10
0
Percentage
DF
DHF
DSS
Diagnosis
Hepatomegaly
Present
Absent



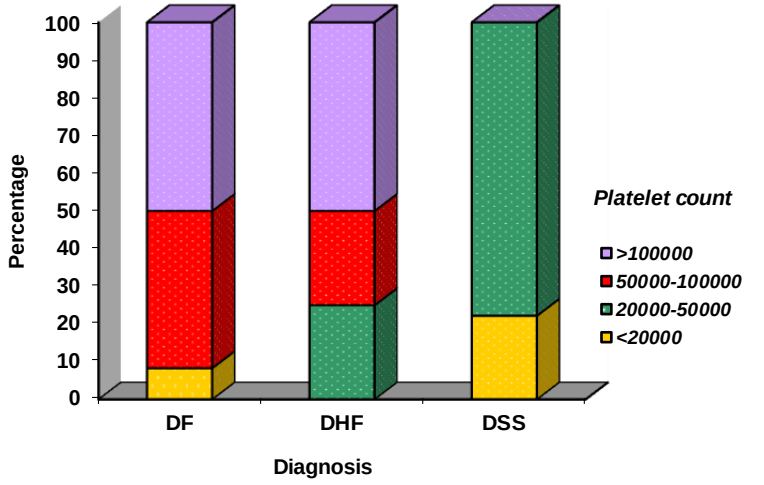
Graph 14a: Showing correlation of clinical variables and predictors with diagnosis of dengue fever

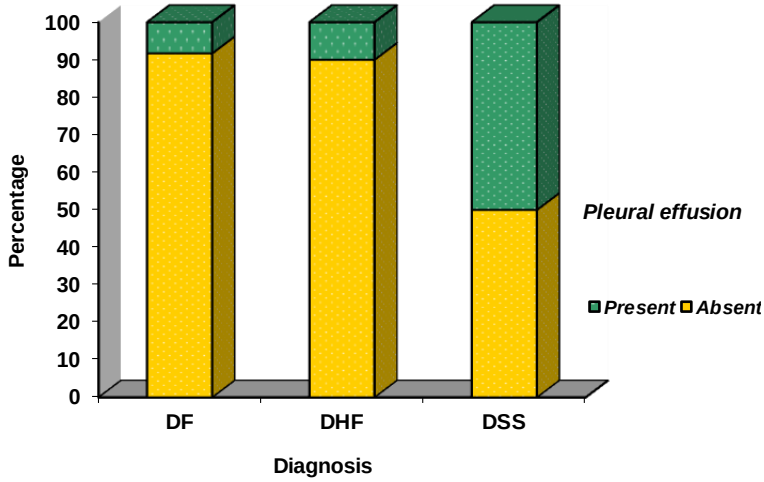
The major and common predictors in DSS were decreased urine output, hypotension and bleeding manifestations, whose p value was significant. Among 18 patients of DSS initially 7 of them presented with BP> 5^{th} percentile but later as the disease progressed the BP went down to <5^{th} percentile.

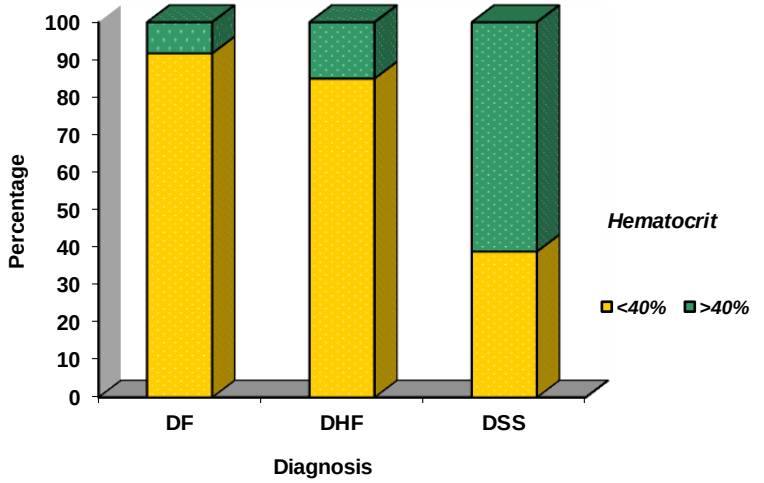
Table 15: Correlation of lab variables with Diagnosis and severity of Dengue fever

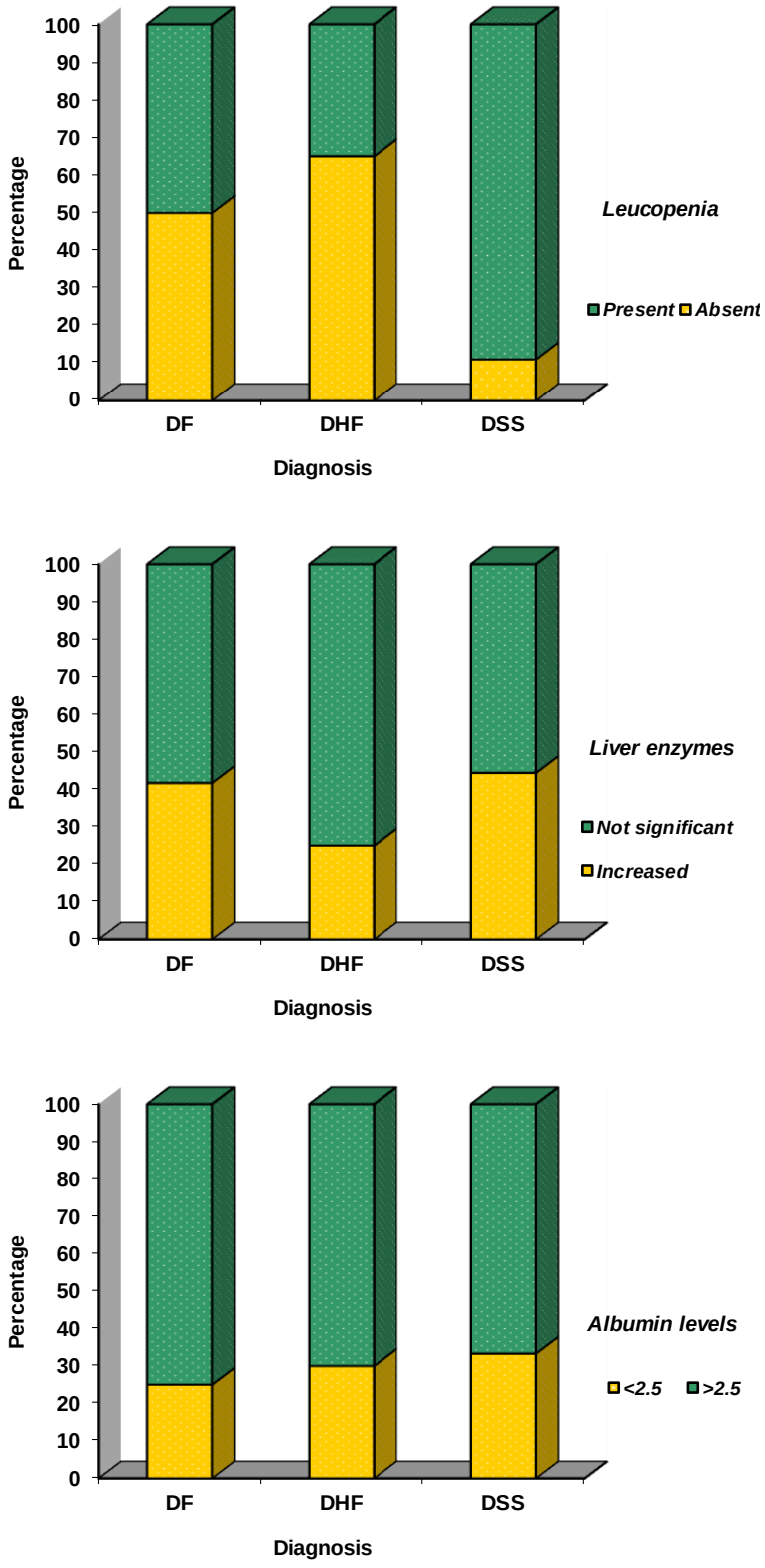
Variables	Diagnosis			p value
	DF (n=12)	DHF (n=20)	DSS (n=18)	
Platelet count				
• <20000	1(8.3%)	0(0%)	4(22.2%)	<0.001**
• 20000-50000	0(0%)	5(25%)	14(77.8%)	
• 50000-100000	5(41.7%)	5(25%)	0(0%)	
• >100000	6(50%)	10(50%)	0(0%)	
Pleural effusion				
• Absent	11(91.7%)	18(90%)	9(50%)	0.006**
• Present	1(8.3%)	2(10%)	9(50%)	
Hematocrit				
• <40%	11(91.7%)	17(85%)	7(38.9%)	0.002**
• >40%	1(8.3%)	3(15%)	11(61.1%)	
Leucopenia				
• Absent	6(50%)	13(65%)	2(11.1%)	0.002**
• Present	6(50%)	7(35%)	16(88.9%)	
Liver enzymes				
• Increased	5(41.7%)	5(25%)	8(44.4%)	0.419
• Not significant	7(58.3%)	15(75%)	10(55.6%)	
Albumin levels				
• <2.5	3(25%)	6(30%)	6(33.3%)	0.927
• >2.5	9(75%)	14(70%)	12(66.7%)	

The majority of patients who had higher grade of dengue fever exhibited significant increase in the value of predictors.


100
90
80
70
60
50
40
30
20
10
0
Percentage
DF
DHF
DSS
Diagnosis
Platelet count
>100000
50000-100000
20000-50000
<20000


100
90
80
70
60
50
40
30
20
10
0
Percentage
DF
DHF
DSS
Diagnosis
Pleural effusion
Present
Absent

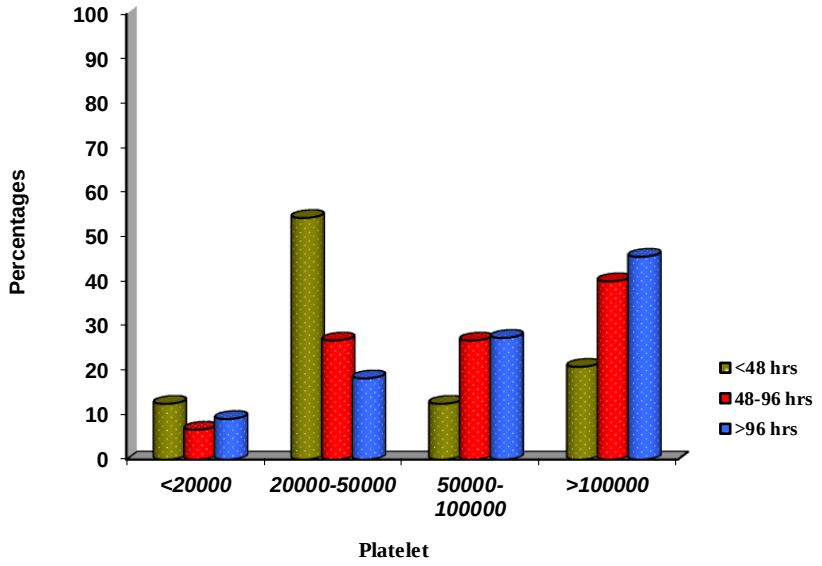

100
90
80
70
60
50
40
30
20
10
0
Percentage
DF
DHF
DSS
Diagnosis
Hematocrit
<40%
>40%



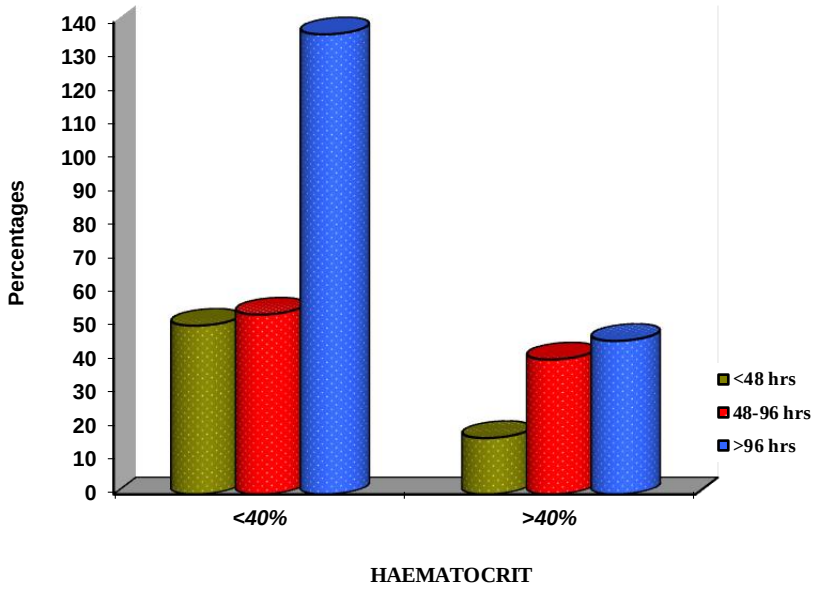
Graph 14b: Showing correlation of clinical variables and predictors with diagnosis of dengue fever

Table 16: Comparison of Predictors based on Time of Presentation to the Hospital

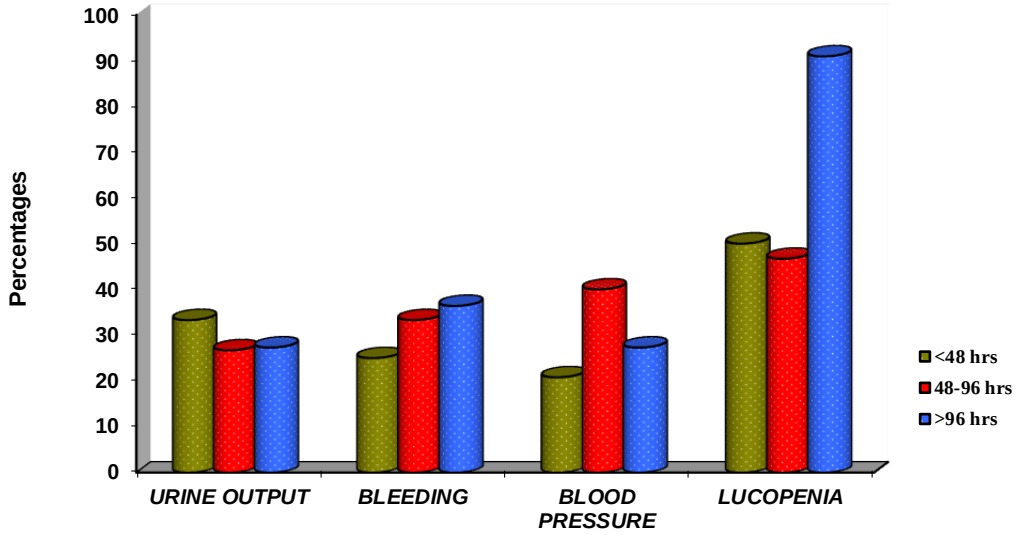
	<48hrs (n=24)	48-96hrs (n=15)	>96hrs (n-11)	p value
Platelet				
<20,000	3(12.5%)	1(6.7%)	1(9.1%)	0.308
20000-50000	13(54.2%)	4(26.7%)	2(18.2%)	
50000-100000	3(12.5%)	4(26.7%)	3(27.3%)	
>1,00000	5(20.8%)	6(40%)	5(45.5%)	
HAEMATOCRIT				
<40%	12(50%)	8(53.3%)	15(136.4%)	0.540
>40%	4(16.7%)	6(40%)	5(45.5%)	
URINE OUTPUT				
Reduced	8(33.3%)	4(26.7%)	3(27.3%)	0.924
BLEEDING	(0%)	(0%)	(0%)	
PRESENT	6(25%)	5(33.3%)	4(36.4%)	0.781
BLOOD PRESSURE				
$<5^{th}$ percentile	5(20.8%)	6(40%)	3(27.3%)	0.463
LEUCOPENIA	(0%)	(0%)	(0%)	
PRESENT	12(50%)	7(46.7%)	10(90.9%)	0.040*



Graph15a: Showing comparison of platelets based on time of presentation to the hospital



Graph 15b: Showing comparison of hematocrit based on time of presentation to the hospital

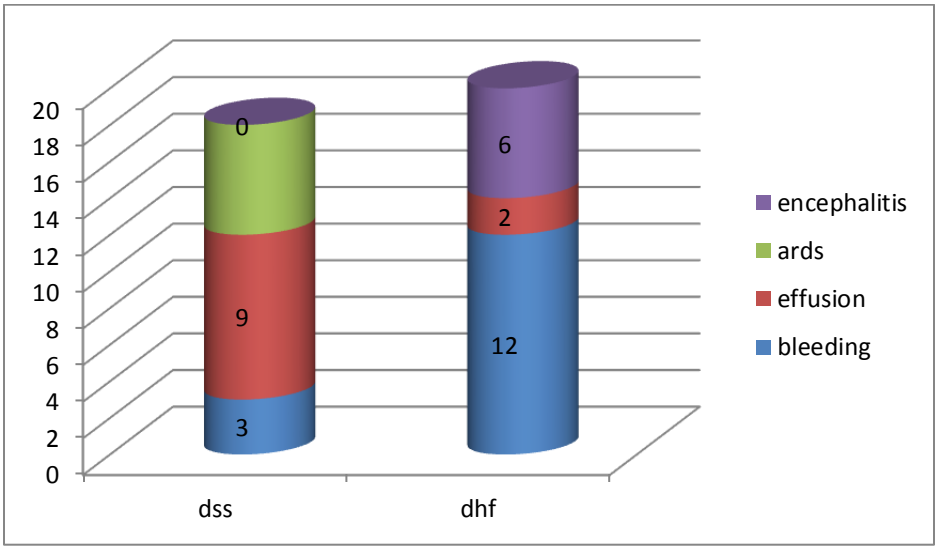


Graph15c: Showing comparison of early predictors based on time of presentation to the hospital

Based on the above values we can draw a conclusion that leucopoenia can be considered as an early predictor and a prognostic marker for early detection of complications.

Table 17: Complications Seen In Dengue Cases

	Bleeding manifestation	ARDS	Pleural effusion	Encephalitis
DSS	3	6	9	0
DHF	12	0	2	6



Graph 16: Showing distribution of complications in dengue

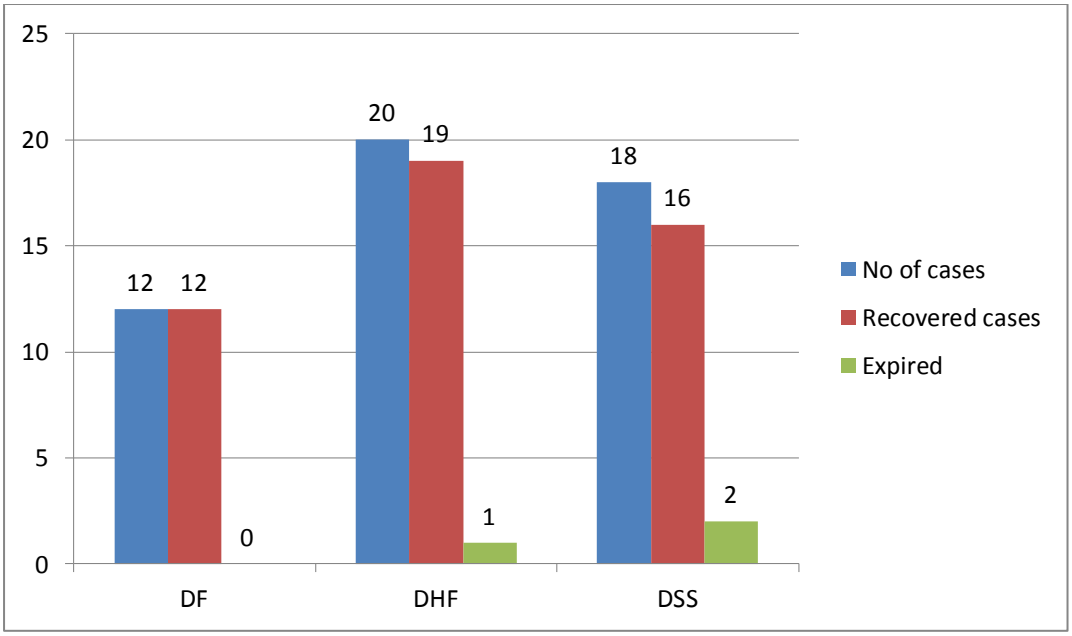
As per the above data it is suggestive that the patients with DSS presented with more number of pleural effusion cases as expected. In DSS 50% of the complications were pleural effusion, 16% was bleeding manifestations and 33% was ARDS. In DHF 60% of the complication were bleeding manifestations and rest were pleural effusion and encephalitis

OUTCOME

Out of 50 children 47 recovered without any sequelae. 3 children who presented in late stages out of which 2 DSS and 1 DHF succumbed.

Table 18: Mortality Pattern of Dengue

	No. of cases	Recovered cases	Expired
DF	12	12	0
DHF	20	19	1
DSS	18	16	2



Graph 17: Showing mortality pattern in dengue

Out of three mortality in the study two cases had a super added infection of leptospira, which suggests that superadded infections leads to increase in mortality of the patients

DISCUSSION

Dengue fever is the most important arboviral infection and has become a major global health problem in India, epidemics are frequent. Involvement of younger age group and increasing in the frequency of epidemics are indicators of higher incidence of infection.

AGE DISTRIBUTION

The 5-12 year age group dominated the present study, accounting for 58% of the total

GENDER DISTRIBUTION

The present study shows increased preponderance in boys as similar to WHO study in 1999.

SYMPTOMS

In the present study, fever (100%) symptoms followed by vomiting, retro orbital pain and rashes.

BLEEDING

In the present study, bleeding manifestations were found in 30% of cases.

TOURNIQUET TEST

The tourniquet test was positive in 8% of cases.

INVESTIGATION

The mean haemoglobin and hematocrit in the present study were 11.2 gm% and 34.7% respectively. There was no significant correlation between hematocrit and severity of the disease among the clinical sub groups of dengue.

FINAL DIAGNOSIS

The present study had DF 12 (24%), DHF 20 (40%) and DSS 18 (36%) cases among total of 50 cases.

NOW WE CAN DISCUSS HOW THIS STUDY IS SIMILAR OR DIFFERENT TO OTHER SIMILAR STUDIES BY COMPARING THEIR VALUES

AGE DISTRIBUTION

The following table gives incidence in age group of 5-11 years among other studies

Sl. No.	Study	Place	Year	%
1	WHO meta analysis[64]	SEAR	1978-88	54
2	Gomber et al[61]	New Delhi	2001	78.9
3	Narayan et al[62]	Chennai	2002	45
4	Present study	Kolar	2011-12	58

The present study correlates with the previous studies in the age incidence. Among the sub group, there is tendency for DSS to occur at younger age.

GENDER DISTRIBUTION

The present study shows increased preponderance in boys as similar to WHO study in 1999.

SYMPTOMS

In the present study, fever (100%) symptoms followed by vomiting, retro-orbital pain and rashes.

The following pattern of symptoms have been observed in other studies.

Study	No of cases	Fever%	Bleeding%	Pain abdomen%
Anuradha et al[63]	515	100	52	56
Narayana et al[62]	59	98	66	54
Present study	50	100	30	34

Of the 50 children in the study all children had fever at the time of examination.

BLEEDING

In the present study, bleeding manifestations were found in 30% of cases.

Other studies have noted the following pattern of bleeding.

Sl. No.	Study	Place	Year	Bleeding (%)
1	Anuradha et al[63]	New Delhi	1998	52.6
2	Kumar et al[66]	Lucknow	2000	31.2
3	Rahman et al[67]	Bangladesh	2002	46
4	Narayan et al[62]	Chenai	2002	66
5	Present study	Kolar	2011-12	30

Majority of patients with bleeding manifestations were in dengue haemorrhagic fever group as expected.

TOURNIQUET TEST

The tourniquet test was positive in 8% of cases. Other studies have got varying results in the test.

Sl. No.	Study	Place	Year	Test positively
1	Nimmanitya et al[38]	SEAR	1969	83.9%
2	Kabra et al[68]	New Delhi	1969	40%
3	Gomber at al[61]	New Delhi	2001	25%
4	Present study	Kolar	2011-12	8%

Tourniquet test is not reliable test for diagnosis as observed in many other Indian studies. As Kolar is an endemic area there is less number of tourniquet positive cases. This is a unique finding of this study in compatibility with the WHO findings which also states that tourniquet positive cases are less in endemic areas.

SYSTEMIC EXAMINATION

Systemic examination revealed non-specific signs as like any other viral illness.

Sl. No.	Study	Place	Year	Hepatomegaly (%)
1	Nimmanitya et al[38]	SEAR	1969	90
2	Mohan et al[69]	New Delhi	2000	74
3	Narayanan et al[62]	New Delhi	2002	52.5
4	Present study	Kolar	2011-12	30

In contrast to other studies hepatomegaly was reported in less number of percentages in the present study.

INVESTIGATIONS

Narayan et al reported the same to be 10.8 g% and 33.2% respectively. The classical description of > 20% rise in hematocrit is difficult to establish as the reference standards have not been established for Indian children.

Although leucopenia has been reported in a number of studies, the present study had a mean leukocyte count of 6300c/mm. The highest and lowest TLC was 15,000 and 2300 respectively.

Platelets counts carry one of the most important key for diagnosis. On taking the WHO limit of <10000c/mm for low platelet count, 68% had in this study.

The serial monitoring of the platelet count can help us to predict the outcome of the patient as in one case in the study extremely low platelet count lead to pulmonary haemorrhage and resulted in death. Hence, it can be monitored as an prognostic indicator. The other factors like platelet dysfunction or disseminated intravascular coagulation may have role in bleeding in dengue fever cases. But platelet count provides a very useful means of diagnosis at the screening level. Hence, the platelet count was a sensitive indicator for diagnosis but it did not correlated with the outcome. Bleeding manifestations are more frequent with low platelet count.

TRANSAMINASES

The range for SGOT was mean of 252.1 IU/lt and for SGPT was 109.8 IU/lt although transminases are said to be non specific for infections and stress. A significant more than fourfold rise was documented in 36% of children. They are not of any prognostic value, but serve as useful marker for diagnosis.

CHEST RADIOGRAPHY

Out of 50 children in the study, 12 of them had pleural effusion.

WHO has mentioned pleural effusion especially on right side as consistent finding of dengue. According to WHO pleural effusion is supporting evidence of plasma leakage, the distinguishing feature of DHF.

DENGUE SEROLOGY

The dengue IgM was tested positive in all 50 children. IgG was positive in 32 cases. The study made use of "**dengue day 1 test kit"** which shows high degree sensitivity and specificity in the global testing centers and were highly recommended for the purpose of serology. IgM has always been one of the sheet anchor for the diagnosis.

FINAL DIAGNOSIS

The present study had DF 12 (24%), DHF 20(40%) and DSS 18(36%) cases among total of 50 cases.

OUTCOME

Out of 50 children 47 recovered without any sequelae. 3 children who presented in late stages out of which 2 DSS and 1 DHF succumbed. The mortality pattern in other studies are as follows:

Sl. No.	Study	Place of study	Year	No	Mortality (%)
1	Anuradha et al[63]	New Delhi	1998	515	6.6
2	Kabra et al[68]	New Delhi	1999	240	7.5
3	Gomber et al[61]	New Delhi	2001	304	4.8
4	Narayanan et al[62]	Chennai	2002	59	3.4
5	Present study	Kolar	2011-12	50	6

Out of three mortality in the study two cases had a super added infection of leptospira, which suggests that superadded infections leads to increase in mortality of the patients

CONCLUSION

The present studies had an objective of studying the clinical manifestation of dengue fever and also study the factors influencing complication of dengue fever.

During epidemic, dengue should be considered on the differential diagnosis of any child presenting with fever.

In children, importance should be given to symptoms like fever vomiting bleeding, musculoskeletal pain flushing and abdominal pain. If these are associated with hepatomegaly, low platelet count, low WBC count and elevated liver enzymes, a strong possibility of dengue to be considered, especially during epidemic.

As Kolar is an endemic area there is less number of tourniquet positive cases. This is a unique finding of this study in compatibility with the WHO findings which also states that tourniquet positive cases are less in endemic areas.

Out of the various different early predictors studied leucopenia found to be statistically significant and a guide to the prognosis of patient.

Blood pressure should be monitored for evaluating the progress of the disease. Bleeding tendencies should be closely watched.

In DSS 50% of the complications were pleural effusion, 16% was bleeding manifestations and 33% was ARDS. In DHF 60% of the complication were bleeding manifestations and rest were pleural effusion and encephalitis.

As seen in our study the superadded infections lead to increase in mortality of the patients instead of dengue only hence one should be also aware of the possible complications.

The treatment of dengue is mainly supportive, but early institutional care and meticulous monitoring are the corner stone for positive outcome.

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PROFORMA

I. **General Data**

I. P. No.:

Name: Age: Sex:

Address:

Similar history in family/neighbours:

Storing water:

Hospital: C. G. H/C. H. I.:

DOA: DOD/DOE:

Socio-economic status:

II. **Clinical history**

Fever

Vomiting

Hemetemesis

Abdominal pain:

Melena:

Arthralgia/Myalgia:

Headache:

Altered sensorium/convulsions:

Retro-orbital pain:

III. **Clinical signs**

Pallor:

Icterus:

Lymphadenopathy:

Purpura/Petechiae/Ecchymosis:

Tourniquet test

Pulse: /min

RR: /min

BP: mmHg

Flushed face/Extremities:

Hepatomegaly/Splenomegaly:

Respiratory system:

Cardiovascular system:

Abdominal examination:

Central nervous system:

IV. **Laboratory findings**

1. CBC:

Hb%:	Platelet count:	/cumm	
HCT%:	TLC:	/cumm	
N:	L:	M:	ESR:

2. LFT:

Serum albumin:	Alkaline phosphatase:
SGOT:	SGPT:

3. Coagulation profile:

PT: Sec APTT: Sec

PI:

4. Chest x-ray:

Pleural effusion: R/L/Both:

5. Dengue serology:

Anti-IgM/IgG: Positive/Negative

6. Others:

V. **Final diagnosis**

Dengue fever:

WHO DHF grade: I/II/III/IV

PROFORMA

"A CLINICAL STUDY OF EARLY MANIFESTATIONS OF DENGUE FEVER AND ITS OUT COME".

I. GENERAL DATA

1. Name
2. Age
3. Sex
4. Similar history in family / neighbours
5. Address
6. Storing of water
7. I.P. No:
8. Hospital : C.G.H/C.H.I
9. DOA
10. DOD/DOE
11. Socio. Economic status

9II. CLINICAL HISTORY

1. Fever
2. Vomiting
3. Hemetemesis
4. Abd pain
5. Melena
6. Arthraligia/Mayalgia
7. Head ache
8. Altered sensorium/Convulsions
9. Retro-orbital pain

III. CLINICAL SIGNS

1. Pallor
2. Icterus
3. Lymphadenopathy
4. Purpura/Petichiae/Echymosis
5. Tourniquest test10
6. Pulse- /min
7. RR /min
8. BP mmhg
9. Flushed face/ Extremities
11. Respiratory system:
12. Cardiovascular system:
13. Abdominal examination

Hepatomegaly / Splenomegaly

14. Central Nervous System.

IV. LABORATORY FINDINGS

1. CBC

Hb% platelet count /Cmm HCT% TLC/ Cmm

N= , L= , M= , ESR mm/ lst hr

2. LFT

S. Albumin Alk.Phosphatase

SGOT

SGPT

3. COAGULATION PROFILE

PT Sec APTT Sec PI

4. CHEST XRAY

Pleural effusion R/L/Both

5. DENGUE SEROLOGY

Anti IgM / IgG Positive/ Negative

6. OTHERS

V. FINAL DIAGNOSIS

Dengue fever.

WHO DHF Grade : I / II / III / IV

MASTER CHART

Sl. No.	name	hospital no	age in yr	sex	fever	urine output<0.5ml/kg/hr	bleeding manifestation	rashes	facial oedema	BP	Hepatomegaly	tournique test	platelet count	pleural effusion	haematocrit	Leucopenia	liver enzymes	albumin level	diagnosis
1	gagan	670867	5	M	<3	reduced	nasal bleed	present	absent	<5th percentile	absent	absent	<20,000	present	35	present	not significant	<2.5	DSS
2	nitin kumar	680811	5	M	3--7	normal	absent	absent	absent	> 5 th percentile	present	absent	20000-50000	absent	36	present	4 folds	>2.5	DHF
3	mukundh	711706	6	M	<7	normal	absent	absent	absent	> 5 th percentile	absent	absent	>100000	absent	33	>4000	not significant	>2.5	DHF
4	manoj kumar	713693	5	M	<3	reduced	nasal bleed	absent	present	<5th percentile	absent	positive	20000-50000	present	>40%	present	not significant	>2.5	DSS
5	pavan	720453	5	M	3--7	normal	absent	present	absent	> 5 th percentile	absent	absent	>100000	absent	35	>4000	not significant	>2.5	DHF
6	hemavathi	720430	5	F	<3	normal	absent	absent	absent	> 5 th percentile	present	absent	50000-100000	absent	32	>4000	4 folds	<2.5	DHF
7	sameer	722533	5	M	3--7	normal	malena	absent	absent	<5th percentile	absent	absent	20000-50000	absent	34	present	not significant	>2.5	DSS
8	pavithra	725613	1	F	<3	reduced	absent	absent	absent	> 5 th percentile	absent	absent	20000-50000	present	>40%	present	not significant	>2.5	DSS
9	naresh	724531	2	M	3--7	normal	nasal bleed	absent	absent	> 5 th percentile	present	absent	50000-100000	absent	36	>4000	not significant	>2.5	DHF
10	naveen kumar	727750	7	M	<3	normal	absent	present	absent	> 5 th percentile	absent	absent	50000-100000	absent	35	present	4 folds	<2.5	DF
11	sudeep	737545	8	M	<7	reduced	absent	absent	absent	<5th percentile	absent	absent	20000-50000	present	>40%	present	not significant	>2.5	DSS
12	amrutha	737838	14	F	3--7	normal	absent	absent	absent	> 5 th percentile	present	absent	>100000	absent	36	>4000	not significant	>2.5	DF
13	chaithra	740255	16	F	<3	normal	absent	absent	absent	> 5 th percentile	absent	absent	>100000	absent	38	>4000	not significant	>2.5	DF
14	syed	740999	9	M	3--7	normal	malena	absent	absent	> 5 th percentile	present	absent	20000-50000	absent	>40%	present	4 folds	<2.5	DHF
15	kiran kumar	743521	12	M	3--7	reduced	absent	absent	absent	<5th percentile	absent	positive	<20,000	present	39	present	not significant	>2.5	DF
16	sravani	747535	14	F	<3	normal	absent	absent	absent	> 5 th percentile	absent	absent	>100000	absent	37	>4000	not significant	>2.5	DHF

MASTER CHART

Sl. No.	name	hospital no	age in yr	sex	fever	urine output<0.5ml/kg/hr	bleeding manifestation	rashes	facial oedema	BP	Hepatomegaly	tournique test	platelet count	pleural effusion	haematocrit	Leucopenia	liver enzymes	albumin level	diagnosis
17	pruthvi	747811	10	M	3--7	normal	nasal bleed	present	absent	> 5 th percentile	present	absent	20000-50000	absent	>40%	present	4 folds	<2.5	DSS
18	nandini	750100	12	F	<3	normal	absent	absent	absent	> 5 th percentile	absent	absent	>100000	absent	38	>4000	not significant	>2.5	DF
19	naveen	751787	13	M	<7	normal	absent	absent	present	> 5 th percentile	absent	absent	50000-100000	absent	37	present	not significant	>2.5	DHF
20	harshini	766443	3	F	<3	normal	malena	absent	absent	> 5 th percentile	present	absent	20000-50000	present	39	present	4 folds	<2.5	DHF
21	mohan kumar	766881	17	M	<3	reduced	absent	absent	absent	<5th percentile	absent	absent	20000-50000	absent	37	present	4 folds	>2.5	DSS
22	hemanth	754952	11	M	3--7	normal	nasal bleed	absent	absent	> 5 th percentile	absent	absent	>100000	absent	>40%	>4000	not significant	>2.5	DHF
23	suma	755077	12	F	<3	normal	absent	present	absent	> 5 th percentile	absent	absent	>100000	absent	38	present	not significant	>2.5	DF
24	nandish	754703	14	M	3--7	reduced	absent	absent	present	<5th percentile	absent	positive	20000-50000	absent	>40%	present	not significant	<2.5	DSS
25	akshay gowda	754142	5	M	<3	normal	hemetemesis	absent	absent	> 5 th percentile	present	absent	20000-50000	present	36	present	not significant	>2.5	DHF
26	meghana	755690	3	F	3--7	normal	absent	absent	absent	> 5 th percentile	absent	absent	50000-100000	absent	38	>4000	4 folds	<2.5	DF
27	lakshmidevi	756444	13	F	3--7	normal	absent	present	absent	<5th percentile	absent	absent	<20,000	absent	35	>4000	not significant	>2.5	DSS
28	mahesh	757451	16	M	<7	reduced	absent	absent	absent	> 5 th percentile	present	absent	20000-50000	absent	>40%	present	4 folds	>2.5	DSS
29	tejaswi	760502	8	F	<3	normal	nasal bleed	absent	absent	> 5 th percentile	absent	absent	>100000	absent	37	>4000	not significant	>2.5	DHF
30	shreyas	761155	8	M	3--7	normal	absent	absent	absent	> 5 th percentile	absent	absent	>100000	absent	36	present	4 folds	<2.5	DF
31	narayana kumari	761668	7	M	3--7	normal	absent	absent	absent	> 5 th percentile	present	absent	20000-50000	present	>40%	>4000	not significant	>2.5	DSS
32	sridhar	762639	4	M	3--7	normal	absent	absent	absent	> 5 th percentile	absent	absent	>100000	absent	39	>4000	not significant	<2.5	DHF

MASTER CHART

Sl. No.	name	hospital no	age in yr	sex	fever	urine output<0.5ml/kg/hr	bleeding manifestation	rashes	facial oedema	BP	Hepatomegaly	tournique test	platelet count	pleural effusion	haematocrit	Leucopenia	liver enzymes	albumin level	diagnosis
33	chandan	763352	5	M	<3	reduced	absent	absent	present	<5th percentile	present	absent	<20,000	present	37	present	4 folds	>2.5	DSS
34	lavanya	762724	14	F	3--7	normal	hemetemesis	absent	absent	> 5 th percentile	absent	absent	>100000	absent	38	>4000	not significant	>2.5	DHF
35	balaji	764203	7	M	3--7	normal	absent	present	absent	> 5 th percentile	present	absent	20000-50000	present	>40%	present	4 folds	<2.5	DSS
36	murugan	764647	5	M	3--7	normal	absent	absent	absent	> 5 th percentile	absent	absent	50000-100000	absent	38	>4000	not significant	>2.5	DHF
37	Vishali	764901	5	F	<3	normal	absent	absent	absent	> 5 th percentile	absent	absent	>100000	absent	39	>4000	not significant	<2.5	DHF
38	chandana	765873	3	F	<7	reduced	nasal bleed	absent	absent	<5th percentile	absent	absent	20000-50000	absent	>40%	present	not significant	>2.5	DHF
39	susheela	765978	6	F	3--7	normal	absent	absent	absent	> 5 th percentile	present	absent	50000-100000	absent	38	>4000	4 folds	>2.5	DF
40	ramu	766087	3	M	3--7	normal	absent	absent	present	> 5 th percentile	absent	absent	>100000	absent	39	present	not significant	>2.5	DF
41	ragavendra	766034	10	M	<3	normal	hemetemesis	absent	absent	> 5 th percentile	absent	absent	20000-50000	present	37	present	4 folds	<2.5	DSS
42	suguna	766356	5	F	3--7	reduced	absent	absent	absent	<5th percentile	absent	absent	50000-100000	absent	>40%	>4000	4 folds	>2.5	DF
43	rajesh	766678	7	M	3--7	normal	absent	absent	absent	> 5 th percentile	present	absent	50000-100000	absent	36	present	not significant	>2.5	DHF
44	laxmi	766987	4	F	<7	reduced	absent	absent	absent	<5th percentile	absent	absent	20000-50000	absent	>40%	present	not significant	>2.5	DSS
45	rahul	767031	8	M	<3	reduced	absent	absent	absent	<5th percentile	absent	positive	>100000	absent	32	>4000	4 folds	<2.5	DHF
46	ramya	767089	3	F	3--7	normal	hemetemesis	absent	absent	> 5 th percentile	absent	absent	20000-50000	absent	38	present	not significant	>2.5	DSS
47	sangeetha	767134	13	F	3--7	reduced	absent	present	present	<5th percentile	absent	absent	<20,000	present	>40%	present	4 folds	>2.5	DSS
48	shankar	767267	9	M	3--7	normal	absent	absent	absent	> 5 th percentile	present	absent	50000-100000	absent	37	present	not significant	>2.5	DF

MASTER CHART

Sl. No.	name	hospital no	age in yr	sex	fever	urine output<0.5ml/kg/hr	bleeding manifestation	rashes	facial oedema	BP	Hepatomegaly	tournique test	platelet count	pleural effusion	haematocrit	Leucopenia	liver enzymes	albumin level	diagnosis
49	ranganath	767326	4	M	<7	reduced	malena	absent	absent	<5th percentile	absent	absent	20000-50000	absent	>40%	present	4 folds	<2.5	DSS
50	deepa	767549	3	F	<3	normal	absent	absent	absent	> 5 th percentile	absent	absent	>100000	absent	38	>4000	not significant	>2.5	DHF