A STUDY ON SERUM FERRITIN LEVELS IN DENGUE POSITIVE PATIENTS – ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY

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ABSTRACT

Aim: Dengue is a major public health problem worldwide with an estimated 3.9 billion people in 128 countries are at risk of infection. The present study is intended to correlate serum ferritin levels with severity of dengue.

Methodology: The hospital-based cross-sectional study was conducted on patients admitted to the KLES Dr. Prabhakar Kore Hospital, Belgaum between January to December 2020. The inclusion criteria considered were patients of age ≥ 18 years with dengue NS1 / dengue IgM positivity. Patients with diabetes mellitus, HIV, known coagulation disorder, malignancy, alcoholic abuse and those on immunosuppressive drugs and steroids were excluded. A detailed history was taken and clinical features assessed. Complete blood count, liver function tests, renal function tests, PT/INR, USG abdomen and serum ferritin levels were evaluated. Based on the clinical picture and test results patients are divided into dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS).

Significance of different variables namely, age, gender, clinical presentations and serum parameters were evaluated across the 3 different groups using T-test for continuous data and chi-square for categorical data. Correlation of serum ferritin with different variables namely ascites, gall bladder wall edema, pleural effusion, bradycardia, tachycardia, normal sinus rhythm (NSR) and platelet count across different groups were carried out by running python code in Jupyter Notebook (6.2.0).

Results: The study included 60 patients with a mean age of 34.27±14.49, and the male-to-female ratio noted was 1:0.39. Myalgia was noted as the prominent clinical symptom (57%) followed by black stools (33%), headache (28%), body ache (25%),

purpura (25%) and joint pain (9%). Hypertension (12%) was the most prominent comorbidity noted, followed by diabetes (5%) and CAD. The analysis demonstrated that rash/blanching (P=0.00), serum ferritin (P=0.00), T. bilirubin (P=0.00), D. bilirubin (P=0.00), albumin (P=0.01), SGOT (P=0.00), SGPT (P=0.00), PT/INR (P=0.00), APTT ratio (P=0.00) and RBC (P=0.05) were significant across the DF, DHS, and DSS groups. Statistically significant difference in the levels of serum ferritin in DF, DHS, and DSS patients (P=0.00).

Conclusion: Study findings corroborate the association of ferritin levels with the severity of dengue.

ABBREVATIONS

- AST - Aspartate transaminase.
- ALT - Alanine transaminase.
- CAD – Coronary artery disease.
- CRP - C reactive protein.
- DF - Dengue fever.
- DHF - Dengue haemorrhagic fever.
- DSS - Dengue shock syndrome.
- ELISA - Enzyme-linked immunosorbent assays.
- G6PD - Glucose-6-phosphate dehydrogenase.
- HLA - Human leukocyte antigen.
- HDL - High density lipoprotein.
- HIV - Human immunodeficiency virus.
- Ig – Immunoglobulin.
- IL - Interleukin.
- INR - International normalised ratio.
- LDL - Low density lipoprotein.

- NSAIDS- Non steroidal anti inflammatory drugs.
- NS.1 - Non-structural protein-1.
- OFI - Other febrile illness.
- ORS - Oral rehydration therapy.
- PT - Prothrombin time
- aPTT - Partial thromboplastin time
- RT-PCR- Reverse transcriptase–polymerase chain reaction
- SGOT - Serum glutamic oxaloacetic transaminase
- SGPT - Serum glutamic Pyruvic transaminase
- TIBC - Tissue iron binding capacity
- TNF - Tissue necrosis factor
- TGF - Transforming growth factor

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INTRODUCTION

Dengue is the most common viral disease across the world, found in tropical and subtropical areas. According to World Health Organization, the global incidence of dengue has grown rapidly with an estimated 100-400 million infections to occur annually in >100 endemic countries. Nearly half of the world's population is at risk of contracting dengue infection; of which around 5 lakh people require hospitalization every year due to severe dengue and about 2.5% of those affected expired.[1,2]

Dengue virus is transmitted to humans through female mosquitoes mainly of the species *Aedes aegypti.* Dengue virus (DENV) belongs to the family Flaviviridae, genus Flavivirus with four serotypes (DENV-1, DENV-2, DENV-3 and DENV-4) as causing agent. As per World Health Organization, dengue can be classified into severe and non-severe dengue with or without warning signs. The symptoms of dengue include high fever (40°C/104°F), Leukopenia, severe headache pain behind the eyes, muscle and joint pains, nausea, vomiting, swollen glands and rash. Severe dengue is suspected 3-7 days after onset of disease with warning signs such as severe abdominal pain, vomiting, rapid breathing, bleeding gums, fatigue, restlessness, hematemesis .[1] It is characterized by severe plasma leakage which can lead to shock and Fluid accumulation with respiratory distress, severe haemorrhage, severe organ impairment.[3] As per Centers for Disease Control and Prevention, one out of twenty people with dengue will develop severe dengue which can results into shock, internal bleeding, and even death. People with history of dengue, infants and pregnant women are at higher risk for developing severe dengue.[4]

Clinically severe dengue is caused by virulence factors and host factors such as nutritional status of the host, release of cytokine storms consisting of cytokines

such as IL-1β, IL-2, IL-4, IL-6, IL-7, IL-8, IL-10, IL-13, IL-18, TGF-1β, TNF-α, and IFN-γ, which can induce systemic inflammatory effects, activation of T and B cells, and modified endothelial function with elevated vascular permeability.[5]

Early detection of disease through laboratory diagnosis of dengue fever is important to prevent severe dengue potential complications like dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). The commonly used methods for diagnosis of dengue includes virological methods such as reverse transcriptase–polymerase chain reaction (RT–PCR), which include virus isolation by culture and detection of viral nucleic acid, rapid kit test to detect virus-produced protein, called nonstructural protein 1 (NS1) and serological methods, such as enzyme-linked immunosorbent assays (ELISA) detection of dengue-specific IgG or IgM antibodies. Liver tests such as elevated liver enzymes are often seen in dengue fever.[1,6]

Various biomarkers suggested by studies for prediction of the severe dengue include soluble receptors, growth factors, cytokines, *von Willebrand factor*, genetic profiling for identifying endothelial cell and immune activation, and biochemical and genetic markers. However, clinical utility of these markers is limited due to technical difficulty and reduced availability.[7]

Apart from the present available laboratory investigations for dengue, serum ferritin level has been associated with dengue. Ferritin is considered to be an imperative inflammatory marker, that is expressed by cells of the reticuloendothelial system secondary to infectious and inflammatory situations. Iron is an essential compound for immunosurveillance and its deficiency augments the immunological capacity of cells of the phagocytic system. The iron metabolism is normally under control of iron-regulatory proteins which bind to sequences on mRNA and protect

their degradation. Due to iron deficiency, enhancement of the expression of Tfr protein by binding of the iron-regulatory proteins to mRNA and, thereby suppressing ferritin synthesis. If the availability of iron is adequate, it promotes ferritin synthesis and iron storage occurs. During acute inflammation, the normal mechanism of iron metabolism is reorganized by the primary mediators of the acute phase response namely TNF-α and IL-1. Induction of ferritin transcription by TNF-α and IL-1 contributes to increase in concentration of serum ferritin, although there are low levels of serum iron, as ferritin mRNA has more sensitivity towards cytokines than iron. The elevation of serum ferritin concentrations facilitates the iron storage as well as retention within the reticuloendothelial system. The dengue virus affects the mononuclear cells like endothelial cells, hepatocytes, Kupffer cells, tissue macrophages, which leads to activation of the regulatory T-cells and then release of pro-inflammatory cytokines like IL-1 and TNF-α. It creates an imbalance between the pro-inflammatory and anti-inflammatory cytokines. There is the formation of the auto antibodies against endothelial cells, plasmin, and platelets. These inflammatory cytokines released in excess will induce ferritin transcription and increase the serum ferritin levels in the blood.[8]

Soundravally et al. reported significantly elevated serum ferritin levels in dengue-infected patients as opposed to the controls. In addition, during the febrile and defervescence stages of the infection cases with severe dengue had higher ferritin levels than milder forms.[9] A study reported by Chaiyaratana had shown elevated serum ferritin associated with severe dengue in children and high serum ferritin levels > or = 1,200 ng/ml as a predictor of dengue hemorrhagic fever.[10] In Aruba dengue outbreak, hyperferritinemia was found to be interrelated with severe immune instigation and coagulation impairment in dengue-inflicted subjects and the

concussion of the study is ferritin can be utilized as a biomarker to differentiate between dengue versus OFI.[11] Nadeem et al. reported that serum ferritin levels can serve as an ideal biomarker for an early detection of disease severity on the day of admission and serum ferritin elevated levels are significantly associated with severe dengue with mean ferritin levels higher in patients with severe dengue as compared to dengue fever.[12]

According to World Health Organization, there is a dearth of specific treatment for severe dengue and to reduce or prevent the disease progression.[1] In a Malaysian study by Sani et al, it was shown that a significant percent of subjects had severe dengue during early febrile stage.[13] Hence it is extremely important to predict the risk factors for advancement to severe dengue at an early stage. Elevated ferritin levels in dengue infection have a longer half-life than cytokines [14] which make it feasible to measure their levels and make ferritin suitable candidate for the present study. The aim of this study was to look into the relation between serum ferritin level in dengue-positive patients and its correlation with severity of dengue.

OBJECTIVES

- To study the serum ferritin levels in dengue-positive patients and correlate with the severity of the disease.

REVIEW OF LITERATURE

Dengue, a fastest spreading arthropod-borne viral infection, is caused by flavivirus and it is a major public health problem worldwide with an estimation of 3.9 billion people in 128 countries are at risk of infection.[15] The symptoms of dengue varies from ultra-mild to those that may require medical intervention and hospitalization.[1] There is no specific treatment found to cure dengue; however the symptoms experienced by patients can be managed. It can cause simple pyrexia to severe complicated conditions similar to DSS and DHS, which can result in higher rate of mortality if not diagnosed in advance and treated promptly. Dengue is epidemic all over the world and has resulted in significant mortality. There is rise in incidence dengue over the years and member states of the World Health Organization (WHO) in South-East Asia reported numbers of cases from 2.2 million in 2010 to 3.2 million in 2015 in Southeast Asia, America, and Western pacific region. Dengue is listed as a potential threat among 10 diseases in 2019 by the World Health Organization (WHO). Severe dengue is a lethal form, which is distinguished by plasma leakage leading to fluid accumulation, respiratory distress, severe bleeding, or organ impairment and if appropriate intervention is not instituted timely it can lead to Rapid deterioration, and even death.[1]

Dengue virus

Dengue viruses belong to the genus flavivirus within the *Flaviviridae* family. DENV consists of 4 serotypes: DENV1, DENV2, DENV3 and DENV4. As per different geographic regions distinct genotypes have evolved & genotypical classification thus imparts a method of deciding the birth and evolution of epidemics.[16]

Table 1: Classification of dengue viruses according to genotype and their distribution [16]

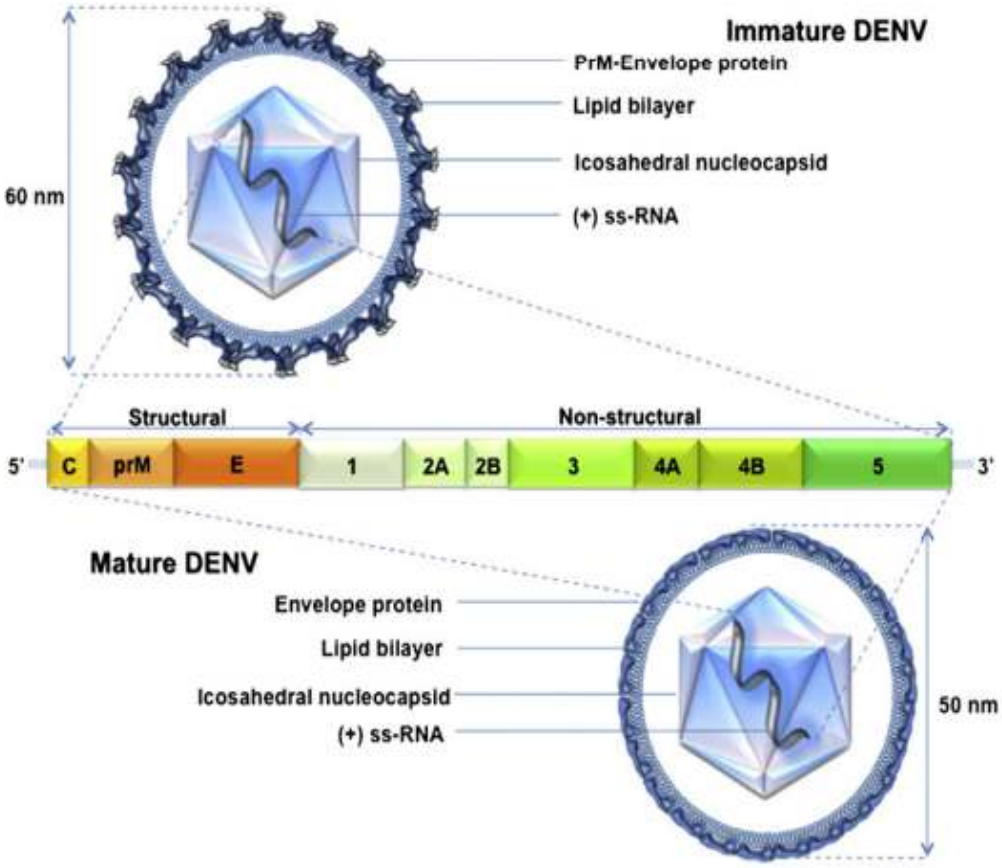
Serotype	Genotype	Geographical Distribution
1	I	· Thailand; Indonesia; Pacific Islands and Malaysia
	II	· Thailand; Caribbean; Pacific Islands and Africa
	III	· Thailand; Philippines and Hawaii
2	I	· Thailand; Vietnam; Burma; Malaysia and Caribbean
	II	· Sri Lanka, Seychelles
	III	· Africa
	IV	· Africa
	V	· Americas
	VI	· Pacific Islands
3	I	· Indonesia; Malaysia and Pacific Islands
	II	· Thailand; Malaysia; Indonesia; Burma; Vietnam and Philippines
	III	· Caribbean; Pacific Islands
	IV	· Thailand
4	I	· Philippines; America; Southeast Asia; Africa and Pacific Islands

The virus is a single stranded, positive sense RNA virus surrounded by an icosahedral nucleocapsid and mature virion of about 50nm in diameter. Its structure consists of relatively smooth surface with diameter of 500 Å and a lipid bilayer surrounding the electron dense core. The genome is 10,700 bases in length, comprising of a single long open reading frame that is translated as a polyprotein of about 3388 amino acids. The genome consists of three structural protein genes encoding the nucleocapsid or core protein (C), a membrane associated protein (M), an envelope protein (E) and seven non-structural (NS) protein genes, which are followed downstream by 7 non-structural (NS) proteins in the sequence NS1, NS2a-NS2b-

NS3-NS4a-NS4b-NS5. Mature virion includes structural proteins, however NS proteins helps in virus replication and polypeptide processing.[17,18,19]

A mature dengue virion comprises of 20-30 nm diameter isometric nucleocapsid, which is enclosed by 10 nm depth lipid bilayer embedding the E and M part. The size of the envelope protein is between 51,000 and 59,000 Daltons mediating penetration, fusion, and a small non glycosylated internal matrix protein of size 8,500 Daltons. In most of the Flaviviruses, the envelope protein is glycosylated and is exposed on the virion surface. The lipid composition of the envelope is dictated by the composition of the host cell membrane from which the viruses bud.[17,20,21]

Fig. 1: Morphology of dengue virus



Source: Herrero et al., 2013

Replication of dengue virus

The entry of dengue virus into the host is mediated by receptor-mediated endocytosis, which is generally employed by flaviviruses, and replication of dengue virus can occur in wide variety of culture cells of both vertebrate and arthropod origin. Whereas mammalian cell-generated virus enters cells mainly by receptor-mediated endocytosis. Antibody-dependent enhancement mediates virus attachment through binding the virus-antibody complex to cellular Fc receptors.8 DEN-2 may also enter to human peripheral blood monocytes by direct fusion with the plasma membrane.[23] Penetration and uncoating of the virus is facilitated by endocytosis with the formation of coated vesicles. Nucleocapsid uncoating is accomplished once the virus enters the cell by an acid-dependent fusion of viral and endosomal membrane. Lysosomotropic amines increase the pH of the endosome and block the acid-dependent fusion, inhibiting the early phase of viral replication. Replication proceeds with the specific virus after uncoating is completed and inside the cells, virus replication is done by translating uncoated messenger sense viral genomic RNA and assembling replication machinery. [24]

Dengue illness

Symptoms

Dengue infections mostly are symptomless or very mild characterized by undifferentiated fever with or without rash. Early clinical features of dengue are variable among patients, and initial symptoms are non-specific. Mild febrile syndrome or typical dengue fever comprises of high fever, severe headache, myalgia, arthralgia, retro-orbital pain, and maculopapular rash in older children and adults. Initial dengue fever symptoms may closely resemble chikungunya fever, influenza-like illness,

leptospirosis, typhoid fever, acute tonsillitis, and malarial symptoms. The symptoms in early febrile stage include fever, malaise, headache, body pains and rash. symptoms such as thrombocytopenia, bleeding, pleural effusion, haematocrit >20%, ascites and clinical warning signs, such as restlessness, and persistent vomiting. Sudden reduction in temperature is associated with profuse perspiration, adynamia, severe and continuous abdominal pain, which are indications towards plasma extravasation, and the imminence of shock is seen in defervescence stage.[25] Dengue fever is the mildest form of clinical dengue infection and due to its broad spectrum of signs and symptoms, it was suggested by World Health Organization to not consider a rigid definition of dengue fever as it may be accompanied by bleeding complications such as epistaxis, gingival bleeding, gastrointestinal bleeding, haematuria and menorrhagia.[26] The symptoms of dengue haemorrhagic fever consists of fever or history of acute fever persisting for 2-7 days, haemorrhagic tendencies evidenced by at least a positive tourniquet test, and increased vascular permeability evidenced by haemoconcentration which is defined by 20% or greater rise in haematocrit above baseline value.[27]

The important laboratory findings associated with dengue haemorrhagic fever are leucopenia, thrombocytopenia, neutropenia, and internal bleeding such as bleeding from mucosa, gastrointestinal tract,, injection sites or other locations. Dengue shock syndrome symptoms comprise of all the criteria for dengue haemorrhagic fever along with evidence of circulatory failure manifested by rapid and weak pulse, narrow pulse pressure (<20 mmHg), hypotension for age and cold, clammy skin and restlessness.[27]

Dengue classification

The World Health Organization criteria 2009 classified dengue according to the levels of severity that is dengue without warning signs, dengue with warning signs (abdominal pain, persistent vomiting, fluid accumulation, mucosal bleeding, lethargy, liver enlargement, increasing haematocrit with decreasing platelets), and severe dengue (dengue with severe plasma leakage, severe bleeding, or organ failure). Non-severe dengue is considered in those patients who recover following defervescence and those who deteriorate tend to manifest warning signs. Further patients are probably will recover with intravenous rehydration and further deterioration is classified as severe dengue.[28]

Global distribution of dengue

The data for the recent decades show that the prevalence of dengue has been increasing substantially worldwide. The prevalence of dengue is estimated to be around 3.9 billion. World Health Organization has reported 8-fold increase in dengue cases from 505,430 cases in 2000, to over 2.4 million in 2010, and 5.2 million in 2019, and the death reported due to dengue has been increased from 960 in the year 2000 to 4032 in 2015. Dengue is found in around hundred countries in African, the Eastern Mediterranean, South-East Asian, American, and the Western Pacific subcontinents.[1]

In 19th and 20th centuries, several dengue epidemics had been reported in America, Southern Europe, North Africa, the Eastern Mediterranean, Asia, and Australia, various islands in the Indian Ocean, the South, Central Pacific, and the Caribbean. The distribution of dengue hemorrhagic fever/dengue fever have steadily increased in the past decade and all four serotypes of dengue emerging and spreading from Asia to the America, Africa and Eastern Mediterranean indicating possible

pandemic threat of disease in near future. Due to large availability of vectors, the prevalence of dengue hemorrhagic fever and dengue fever is more in tropical and subtropical region. In 2020, Increased cases were reported in Bangladesh, Brazil, Cook Islands, Ecuador, India, Indonesia, Maldives, Mauritania, Mayotte (Fr), Nepal, Singapore, Sri Lanka, Sudan, Thailand, Timor-Leste, and Yemen and in 2021 regions of Brazil, Cook Islands, Colombia, Fiji, Kenya, Paraguay, Peru and Reunion Island continues to be affected by Dengue. [1,29]

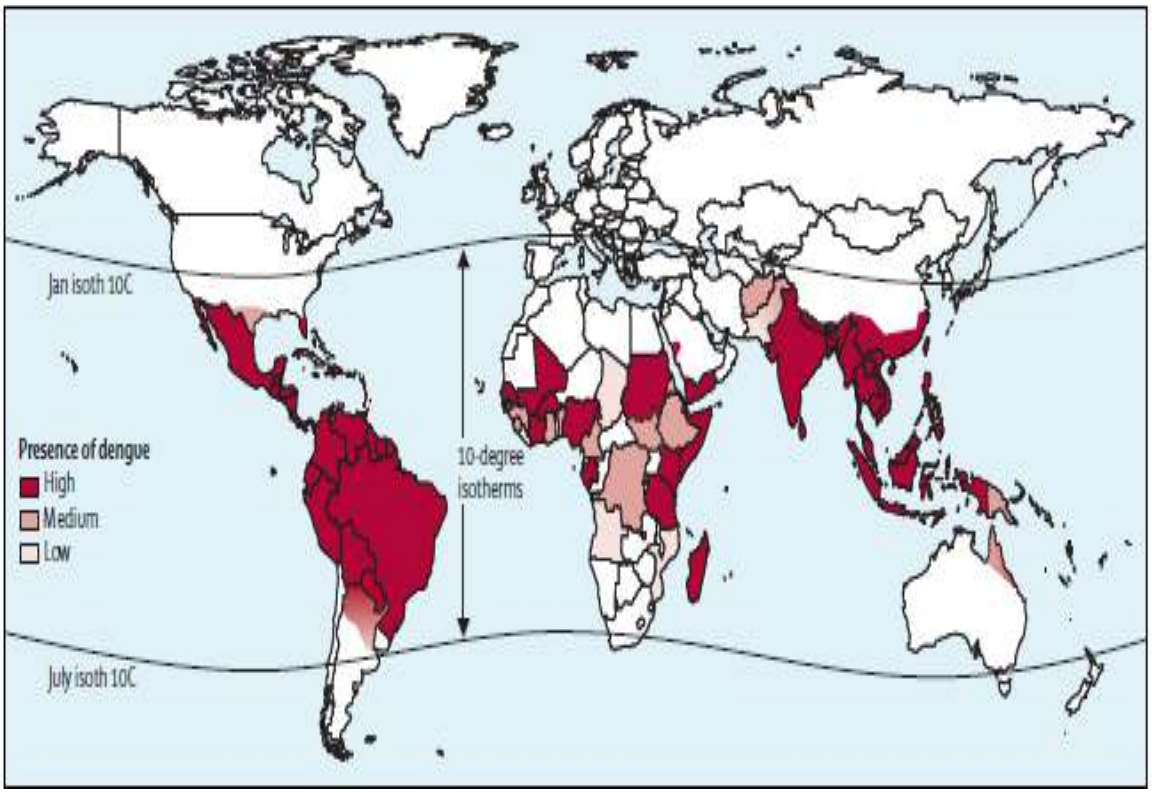
Dengue in Asian region

Asia represents ~70% of the global burden of dengue, apart from Korea. Epidemic dengue is a important public health problem in the tropical monsoon and equatorial zone like some south east Asian countries, where *Ae*. *aegypti* is extensively prevalent in both built-up and country areas. Increased frequency of cyclic epidemics of dengue has been found in Bangladesh, India, Pakistan, and Maldives where it is a leading cause of hospitalization. Around 130 million people live in ten countries consisting of dengue endemic areas of the southeast Asian region. There has been increased cases of dengue by 46% from 451,442 to 658,301 from 2015 to 2019 in Southeast Asian region. However, the number of deaths has been reduced by 2% from 1584 to 1555. Factors such as high population growth, poor management of storage practices, sewer, and waste system, increased global commerce and tourism, changes in public health policy, and the development of hyper-endemicity in urban areas can be responsible for expansion and distribution of dengue mosquito vector and viruses in Southeast Asian region. [1,28,30]

Dengue in Indian region

In 2010 alone, the epidemics in the country has accounted for nearly 34% of global burden. The disease is prevalent in almost all of the metropolitan places, and has endemic status in 18 out of 35 states. In 1996, Delhi had witnessed a severe outbreak of dengue and DHF with 10,252 cases and 423 deaths. India witnessed outbreak of dengue in 21 states with 12,317 cases and 184 deaths in 2006. Serotypes 2 or 4 were found to be responsible for initial epidemics in India. Whereas, serotype 1 was predominant the epidemic in Delhi during 2007-2010. Cyclic epidemics linked to good monsoon rains occur once in every few years. Geographic expansion and increase cyclic epidemic frequency have been reported in arid and tropical climatic zones in india with spread of a plethora of virus serotypes. As per National Vector Borne Disease Control Programme (NVBCP) in 2015, cases were reported maximally from Delhi and then from Punjab. Following closely were Haryana, West Bengal, Gujarat, Karnataka, Maharashtra, Kerala, Tamil Nadu, Rajasthan, Andhra Pradesh, Uttar Pradesh, Orissa, Madhya Pradesh, Arunachal Pradesh, Bihar, Uttarakhand and Telangana. However, there has been decline in dengue cases and deaths from 188401 to 89974 and 325 to 144 during 2017-2018.[31,32,33] Global distribution of dengue has been shown in figure 2. [29]

Fig. 2: Global distribution of dengue

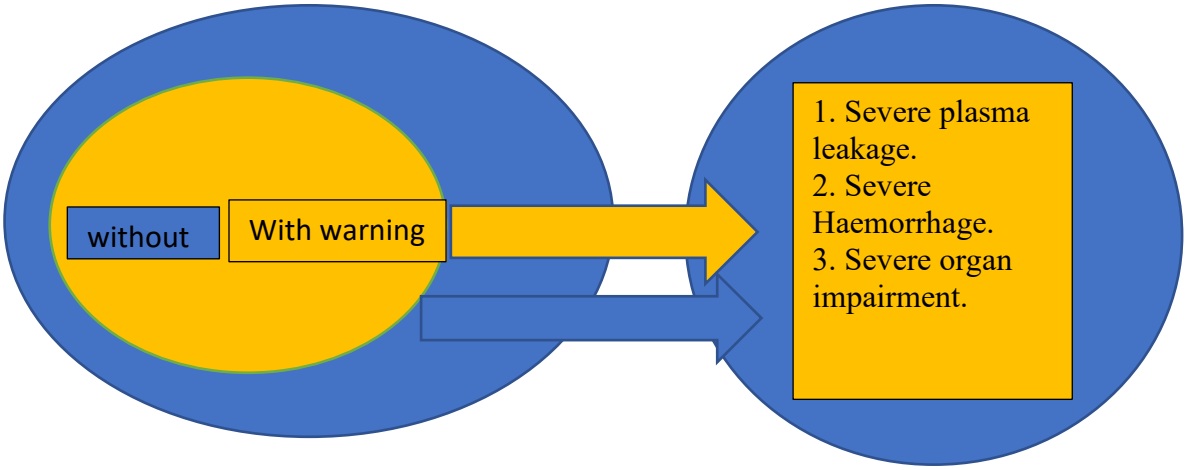


S*ource: Guzman et al., 2014*

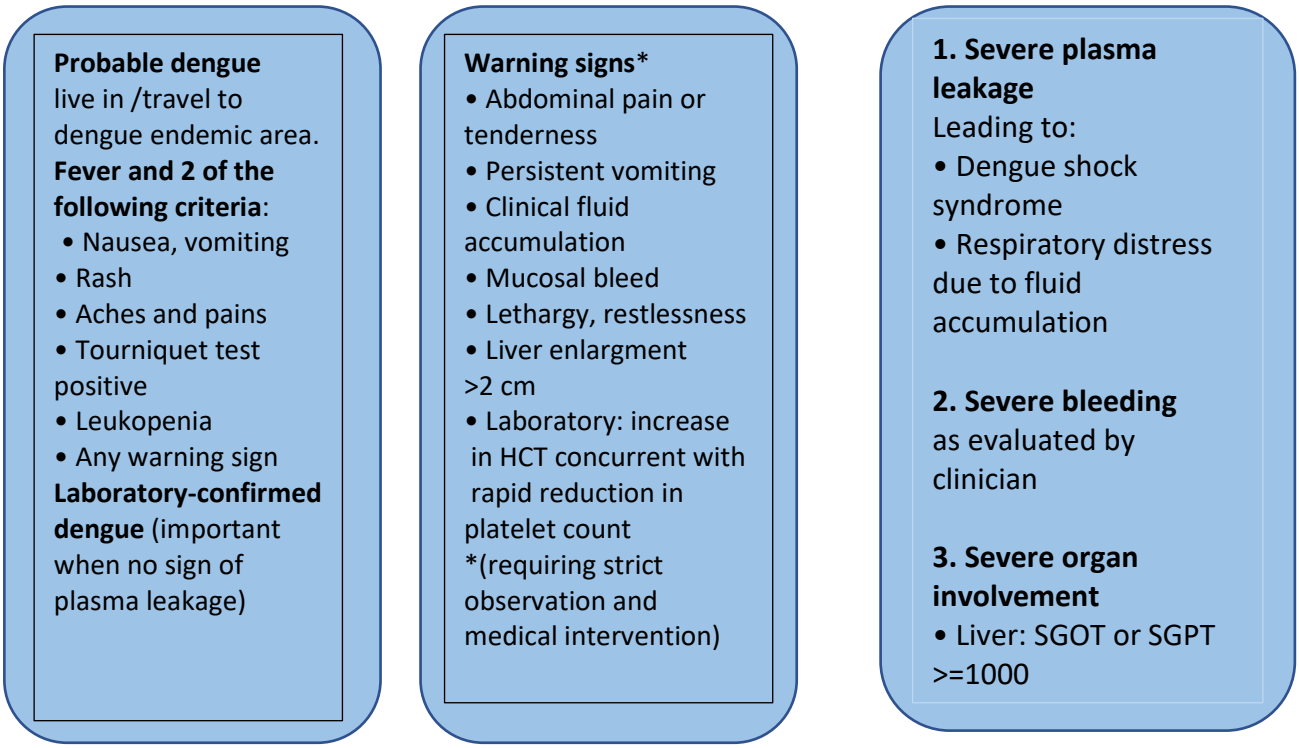
The dengue warning signs and levels of severity have been briefed in figure 3.[28]

Fig. 3: Classification of dengue cases and stages of severity

Dengue ± warning signs **Severe dengue**



Criteria for dengue ± warning signs **Criteria for severe dengue**



EPIDEMIOLOGY

Vector

The vector for dengue virus is female mosquito *Aedes aegypti* and it bites the man mostly during daytime.[1] The transmission of virus may be immediate or after 10-14 days of extrinsic incubation period post feeding on an individual with viremia. Extrinsic incubation period is a key factor influencing the transmission and lower environmental temperature prolongs the extrinsic incubation period, thereby decreasing the transmission. Through the detection of dengue fever antigens, the role of *Aedes aegypti* as the primary vector has been proven. Over the mosquitos' lifetime of 1-4 weeks, several feeding attempts may occur in a day. Adult mosquito residing indoors, and bite in the morning and later afternoon at an interval of 1-2 hrs. The flight range of *Aedes aegypti* in an urban environment is generally around 25-50 metres and it can be transported by land, water, and air resulting in faster transmission

to wide areas. *Aedes aegypti* mosquito generally resides at very high elevated places of around 2,200 metres above the sea level and its survival extended than the summation of the initial non-feeding time post birth and the extrinsic incubation duration helps in infecting another human. *Aedes aegypti* eggs can live for a year in the absence of water, and longevity under natural circumstances ranges between 8-42 days.[34,35,36]

Fig. 4: *Aedes aegypti* mosquito

Source: World Health Organization 2019

Host factor

Although the susceptibility to dengue is not dependant on age, the disease severity is more common among children in Asia, as opposed to America where the infection is usually mild and occurs in adults. Factors such as Asthma, HIV, some HLA types such as HLA-1 (A04, A2, B0, B46), HLA-2 (DQ, DR4, DR1), TGF-β, Glucose-6-phosphate dehydrogenase deficiency, TNF alpha, mutation in MBL

(mannose binding lectin) 2 gene are found to be associated with increase host susceptibility to severe dengue.[37]

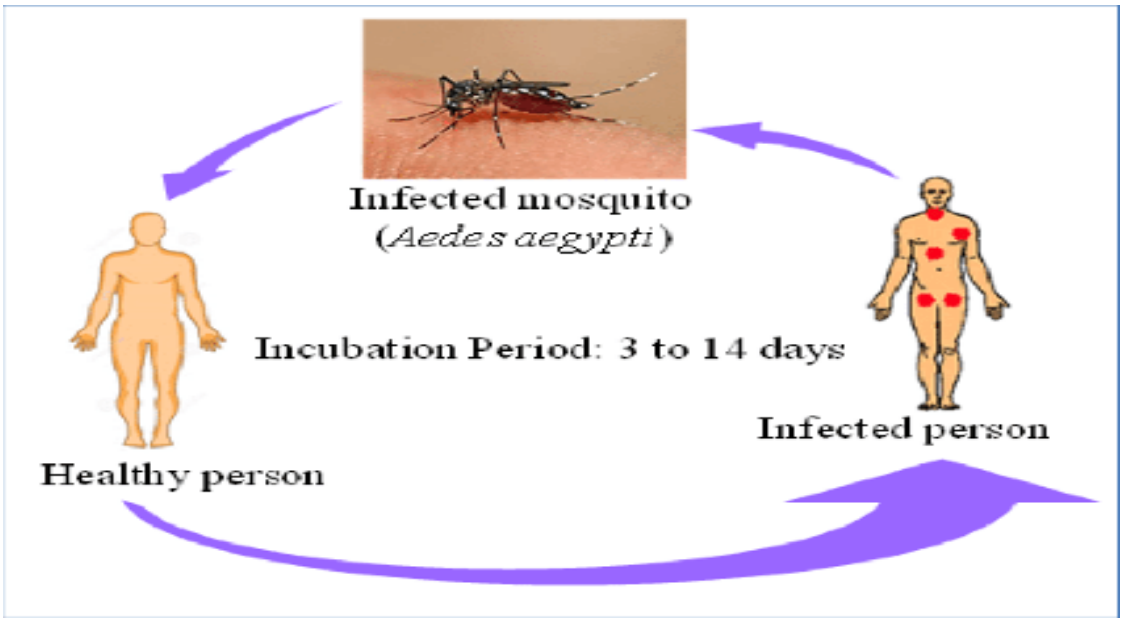
Environmental factor

There exist a favourable connection between monsoon or larval mass and incidence of dengue in tropical countries as the dengue vector can survive at hot and humid temperature. However, the cases have also been reported in areas with minimal rainfall. The rate transmission is very little during winter because of increased extrinsic incubation period beyond the longevity of the insect.[38]

Transmission risk factors

Since the disease transmission is due to vector infestation, ,other family members are also at high risk if any of the household member is infected with dengue (Fig. 5). Movement of infected individuals contributes to the spreading of virus in public places. The infection can pass to foetus through already infected pregnant woman or around the time of birth.[39,40]

Fig. 5: Transmission cycle of dengue



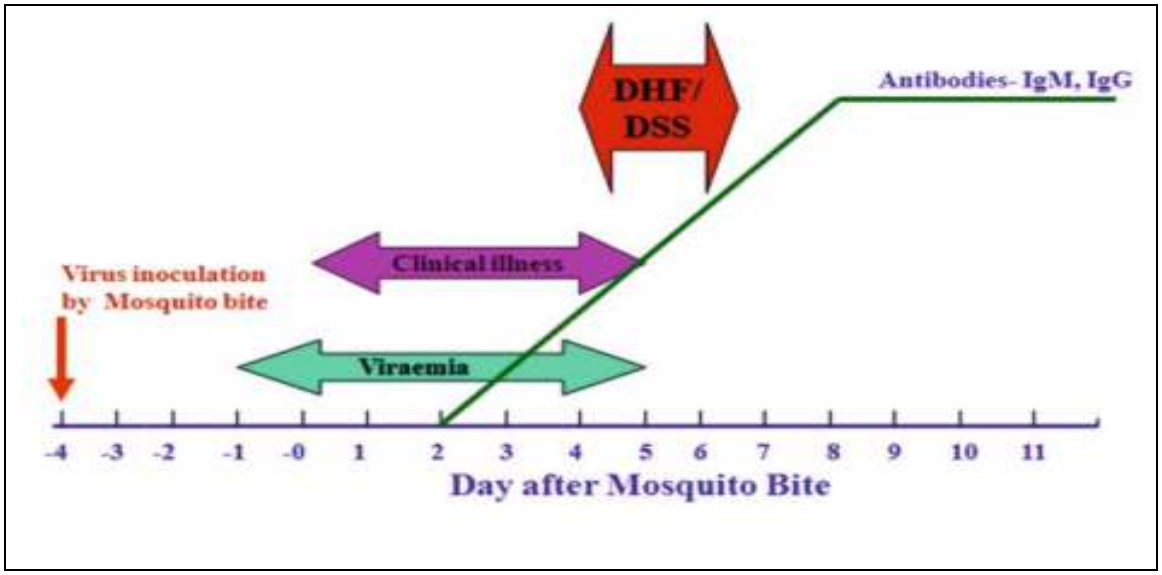
Pathogenesis

The mechanisms leading to the severe manifestations of dengue infection have not been completely explored, but they are likely to be multifactorial involving dengue virus virulence, activation of the complement system, virus tropism, transient autoimmunity, host genetic factors, antibody dependent enhancement (ADE), cross reactive T-cell response and soluble factors.[41] After biting of an infected mosquito, the virus undergoes replication in local lymph nodes and spreads through blood within 2 to 3 days to different tissues and it spreads in the serum classically for five days in affected macrophages/monocytes and to a lesser extent in B cells/ T cells. It also replicates in skin cells, macrophages and reactive spleen lymphoid cells,[42]The immune response towards dengue virus infection can be influenced by genetic background of the host. Langerhans cells and keratinocytes are primarily infected upon inoculation of DV into the dermis. The dengue virus attacks tissue macrophages in many organs, especially those in spleen. Viral load measure in blood is determined collectively by replication efficiency of dengue virus in dendritic cells, monocytes, and macrophages, as well as its tropism for and replication efficiency in endothelial cells (EC), bone marrow stromal cells, and liver cells as viral load represents an important risk factor for development of severe disease. The immune response to dengue is influenced by infection of hepatocytes, macrophages, and endothelial cells. Infected cells undergo mostly apoptosis as well as necrosis, causing release of toxic products and activation of fibrinolytic and clotting systems. Suppression of hemopoiesis and blood thrombogenicity is dependent on the degree of infection of bone marrow stromal cells and concentration of IL-6, IL-8, IL-10, along with IL-18. Dengue hemorrhagic fever is marked by increased capillary fragility (manifested as

petechiae), gastrointestinal mucosal bleeding, and easy bruising due to high viral load, viral tropism, platelet dysfunction and severe thrombocytopenia.[41]

Anti-dengue virus IgM antibodies are detectable on days 3 to 5 of illness in half of the hospitalized patients developing rapidly and anti-dengue virus IgM levels peak at about 2 weeks post infection and then decline to undetectable levels over 2 to 3 months followed by anti-dengue virus IgG.[43] Whereas, in primary and secondary infections, early presence of the cross-reactive IgG antibodies titres are high and occur before or simultaneously along with the IgM responses.[26] Dengue infection induced antibodies confers defense against infection with a heterologous serotype of DENV which is short lived and neutralization of antibody associated with the protection against dengue virus. [44] Primary dengue viral infection of the Acute phase is defined as having an IgG negative and IgM positive report, and acute secondary dengue viral infection is defined as having an IgM and IgG + or IgG + and IgM negative report. [45]Serology in dengue illness is based on the finding of 'IgM antibodies' during the initial phase of illness.[46]

Fig. 6: Sequence of events following the bite of infected mosquito



Source: Chaturvedi et al, 2008

Phases of dengue fever

Febrile phase

Febrile phase may prolong for about two to five days and during this phase of infection, people can be presented with facial flushing, skin erythema, generalized body ache, myalgia, arthralgia and headache, sore throat, injected pharynx, conjunctival injection, anorexia, nausea, and vomiting. At this phase it is difficult to differentiate dengue fever from other illnesses, as the individual may show progressive reduction in leucocytes with tender hepatomegaly.[3]

Critical phase

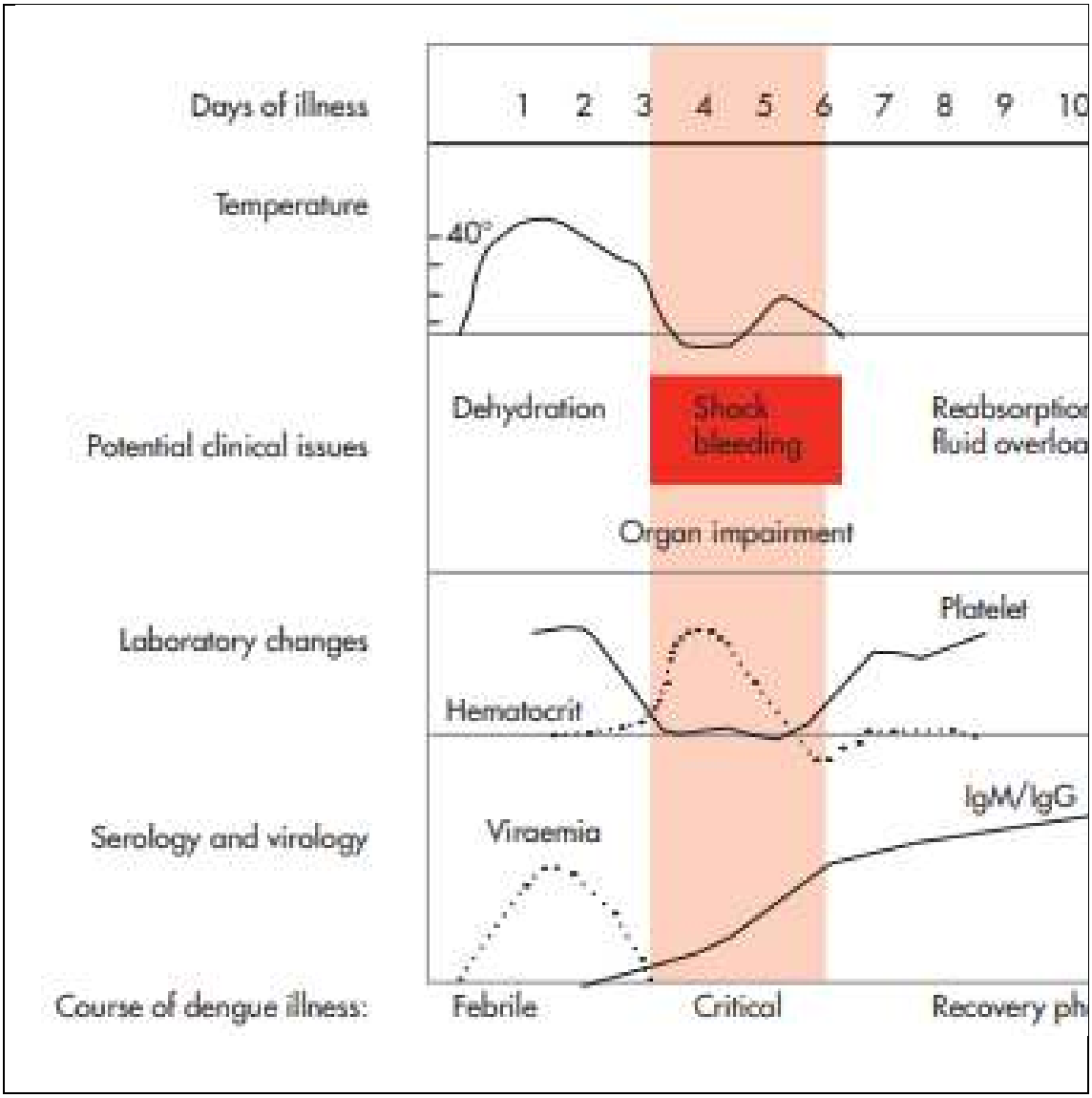
The infected person will subsequently enter the critical phase, this critical phase classically persists from four days to one week with excess capillary leakage and can show warning signs due to capillary leakage. The warning signs include severe pain in abdomen and severe vomiting, attributed to plasma leakage. They may worsen, resulting in shock state. Weakness, mucosal bleeding or bleeding at injection sites and dizziness or postural hypotension, are important haemorrhagic manifestations and appropriate management at this stage is paramount to prevent further complications and mortality.

Recovery phase

Following the survival of the 24–48-hour critical period, the patient enters the recovery phase in which there is ‘resorption of fluid from the extravascular space’. The inpatient may experience a rash of ‘isles of white in the sea of red’, pruritus, bradycardia, and electrocardiographic changes at this stage. White blood cell counts

are usually elevated after defervescence however, recovery of platelet count takes time compared to white blood cell count.[3]

Fig. 7: Course of dengue infection



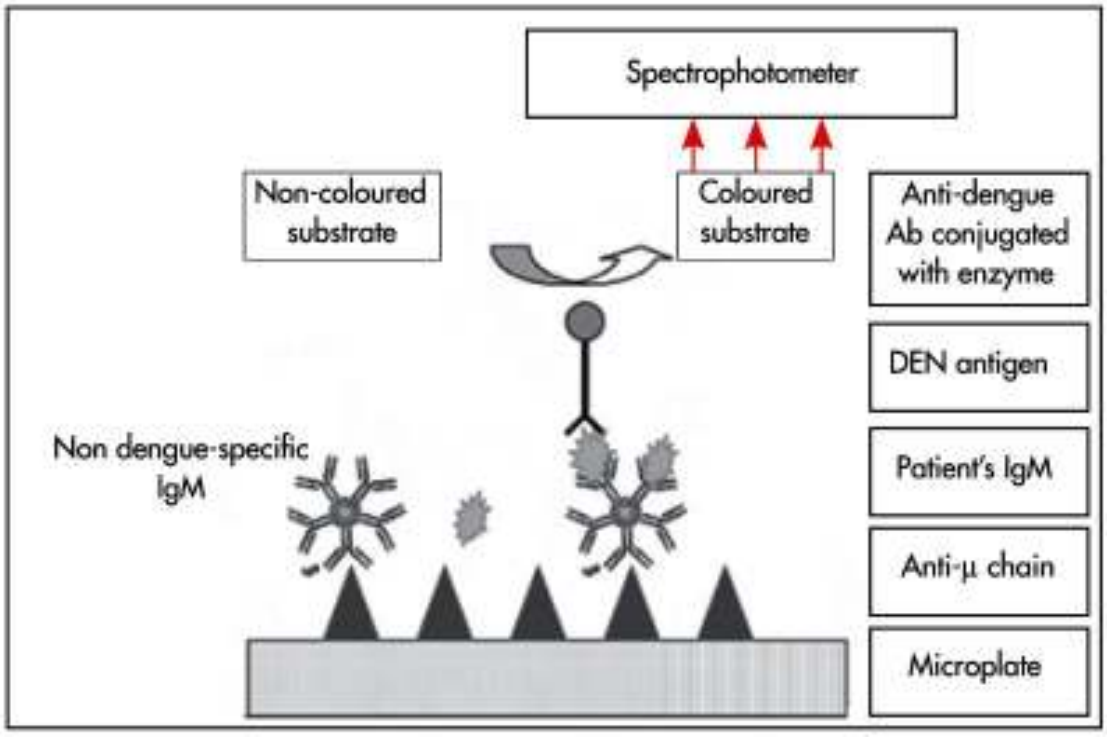
Source: Dengue guidelines 2009, WHO

Diagnosis

Serological diagnosis

MAC-ELISA: IgM antibody-capture enzyme-linked immunosorbent assay (MAC-ELISA) - in this test, patient's serum is neutralised by antibodies directed against μ chain, which is directed to human IgM coated onto a microplate. Directed antigen from 1-4 serotypes of DEN-1-4 bind to anti-dengue IgM antibodies which are showcased by monoclonal or polyclonal dengue antibodies conjugated with an enzyme that will transform a non-coloured product into coloured product directly or indirectly. Spectrophotometer is used to measure the optical density. MAC-ELISA has good sensitivity and specificity in detecting dengue after the onset of fever for ≥5 days[3]

Fig. 8: Principle of a MAC-ELISA test



Source: dengue guidelines 2009, WHO

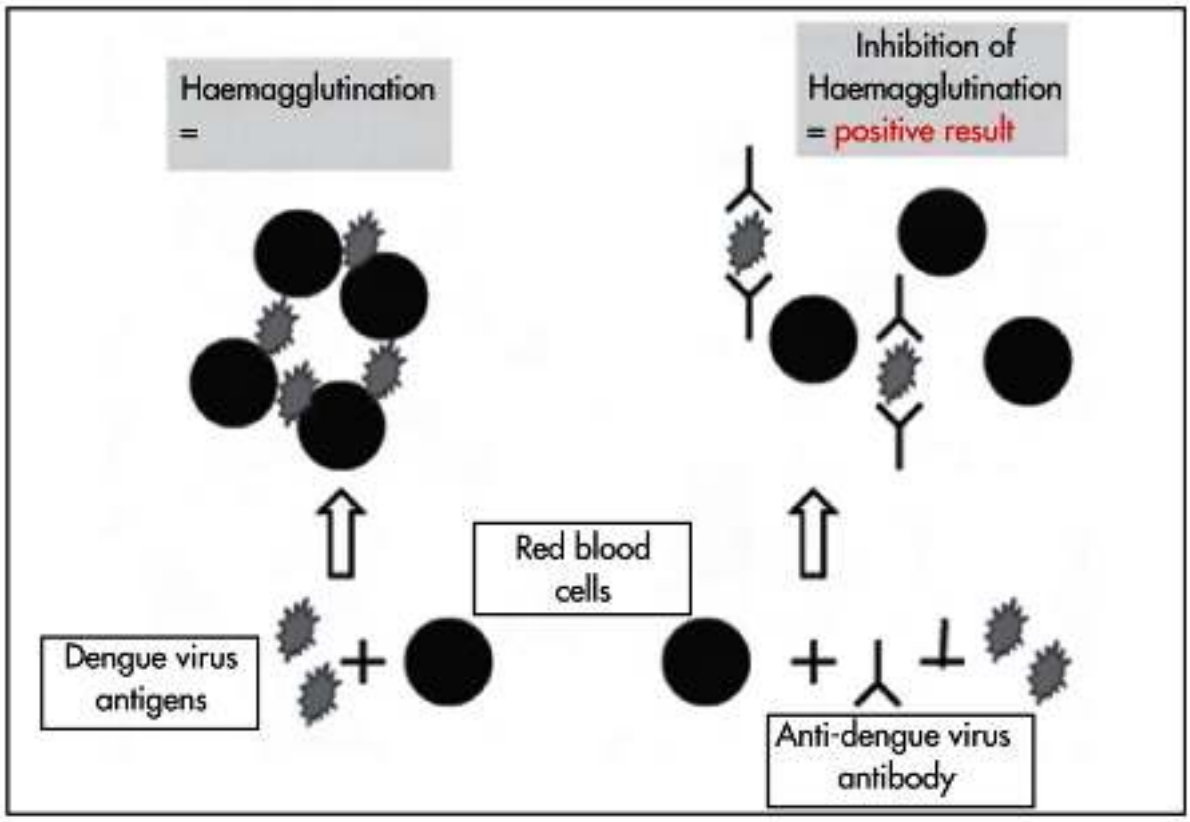
IgG ELISA: IgG ELISA can detect recent or past dengue infections if the aired sera are collected within the correct time frame. In a period of 10 months after the infection, E/M-specific capture IgG ELISA detects IgG Abs. A 4-fold rise in IgG antibodies in acute and convalescent phase may help in identifying infections which have occurred recently.

IgM/IgG ratio: IgM capture and IgG capture ELISAs are the most common assays used to differentiate primary from secondary infections. If the IgM/IgG 'OD ratio' is >1.2 in patient's sera at 1/100 dilution **OR** 1.4 upon using sera at 1/20 dilutions is primary infection

IgA: Serum anti-dengue IgA detection via capture ELISA, which detects anti-dengue virus IgA, is possible generally one day after that for IgM. After 8 days onset of fever, the IgA titre peaks and rapidly reduces, until it is undetectable by day 40. In serum and saliva, values of IgA are generally lower than IgM. However, the two techniques could be conducted simultaneously to interpret dengue serology.

Hemagglutination-inhibition test: The hemagglutination-inhibition (HI) is based on the dengue antigens' ability to agglutinate RBC of human O RBC which has been trypsinized. Agglutination in the sera is inhibited by anti-dengue antibodies. The extent of inhibition is measured via the HI test. Treatment is done with kaolin or acetone, which remove inhibitors of hemagglutination which are non-specific, and they are eventually adsorbed with trypsinized type O human RBC or gander to eliminate agglutinins which are non-specific. [3]

Fig. 9: Hemagglutination-inhibition assay



Source: Dengue guidelines 2009, WHO

Haematological tests

During the acute stages of dengue infection, platelets and haematocrit values are commonly measured. Drop in platelet is a characteristic feature of dengue haemorrhagic fever and platelet count <100,000 per µL may be seen in dengue fever. Between day 3 and day 8 post onset of illness, thrombocytopaenia is usually observed. Haemoconcentration, a rise in haematocrit of ≥20% compared to convalescent values, is indicative of plasma leakage due to vascular permeability causing hypovolaemia..

Virus isolation

During the phase of viremia, the specimen for virus isolation collected during the early course of the infection as the viral particle can be detected from serum, plasma and mononuclear cells in peripheral blood and even from tissues collected at autopsy. During specimen transportation to the laboratory due to its heat labile nature, specimen should be refrigerated or packed in wet ice. Cell lines of mosquito origin C6/36 or AP61 are the host cells of choice for routine isolation. Virus isolation followed by a confirmatory immunofluorescence assay may require 1-2 weeks.

Nucleic acid detection

RT-PCR: Several RT-PCR assays confer better sensitivity than virus isolation with a good rapid turnaround time for detecting dengue RNA in paraffin-embedded tissues. The steps comprise of extraction and purification of viral RNA from the specimens obtained by traditional liquid phase separation methods. However, it has been gradually substituted by reproducible and faster automated robotic system silica-based commercial kits. A nested RT-PCR assay employs universal dengue primers directing the C/prM region for an initial RTPCR. One-step multiplex RT-PCR can substitute the nested RT-PCR. Products are further separated using agarose gel electrophoresis, the ethidium bromide dye is used to amplify the products which are visualised as bands and titrated with standard molecular weight markers. In this, size of the bands assists in identifying dengue serotypes.

Real-time RT-PCR: This assay is for quantitating viral RNA uses primer pairs and probes that are directed to every dengue serotype. Detection of the reaction products in real time is enabled by fluorescent probe and a specialized PCR machine without electrophoresis. TaqMan or SYBR Green technologies are used for various real-time

RT-PCR assays. However, primers and probes cannot detect all the strains, as it may depend on their structure with the targeted viral gene sequence. Therefore, SYBR green real-time RT-PCR, which follows universal RTPCR protocols, has shown the advantage of easiness in primer design. However, theoretically it is less specific. Real-time RTPCR assays can be singleplex (detecting only 1 serotype at a time) or multiplex (detecting all 4 serotypes). The benefit is that a single process can identify all 4 serotypes in the absence of contamination risk. However, the sensitivity is comparatively lesser than nested RT-PCR assays.

Isothermal amplification methods

The nucleic acid sequence-based amplification (NASBA) assay is an 'isothermal RNA-specific amplification assay without the requirement of instrumentation of thermal cycling'. The primary phase is reverse transcription followed by the use of real-time fluorescent-labelled molecular beacon probes or electrochemiluminescence to detect amplified RNA. Nucleic acid sequence-based amplification can be a useful method for studying dengue, as it has sensitivity approximately that of viral particle isolation in cellular cultures for dengue virus detection.

Detection of antigens

Dengue antigens can be detected in acute-phase serum in patients secondarily infected with dengue, but it is rare due to the occurrence of virus-IgG antigen-antibody complexes. ELISA and dot blot assays are useful in detecting high levels of non-structural protein 1 (NS1) and envelop/membrane antigen in inpatients with dengue illness of primary and secondary type up to 9 days after disease initiation. Since all flaviviruses produce NS1 protein, the detection of NS1 helps as an early marker of dengue fever.

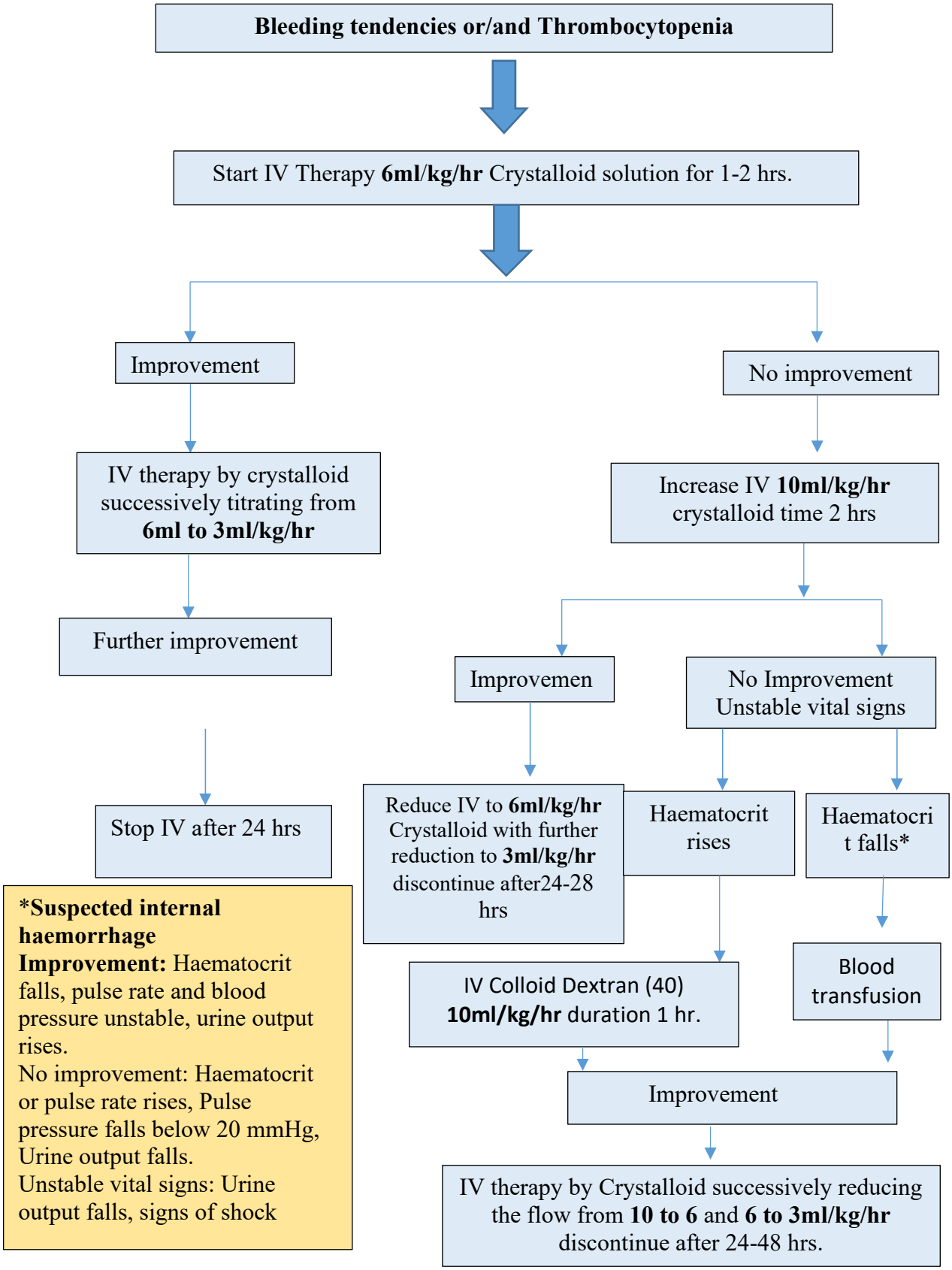
Treatment and management of dengue

In dengue management and treatment, it is imperative to classify the magnitude of dengue illness as given in below table 2 before starting the treatment.

Table 2: Classification of severe dengue

Dengue fever/ dengue hemorrhage fever	Grade	Symptoms and clinical signs	Investigation
Dengue fever		Fever and 2 or more of following: 1. Headache 2. Retro-orbital pain 3. Myalgia 4. Arthralgia	Leucopenia, Thrombocytopenia
Dengue hemorrhage Fever	I	Above criteria for DF plus positive tourniquet test, evidence of plasma leakage	Thrombocytopenia platelet count <100,000/cumm Increase in haematocrit by ≥20%
Dengue hemorrhage fever	II	Aforementioned signs and symptoms and some evidence of spontaneous bleeding in skin or other organs (black tarry stools, epistaxis, more bleeding from gums, etc) and abdominal pain	Thrombocytopenia platelet count <100,000/cumm Increase in haematocrit by ≥20%
Dengue hemorrhage fever	III	Above signs and symptoms plus circulating failure (weak rapid pulse, pulse pressure	Thrombocytopenia: Platelet count <100,000/cumm. Increase in haematocrit by ≥20% Hypotension
Dengue hemorrhage Fever	IV	Profound shock with undetectable blood pressure or pulse. Haematocrit rise more than20%	Thrombocytopenia: platelet count <100,000/cumm Haemotocrit rise more than 20%

Fig. 10: Volume resuscitation flow diagram for inpatients with DHF grades 1 and 2



Dengue fever (DF)

In the acute phase of dengue fever, it is advised to take bed rest and use cold sponge if required to keep the temperature <39ºC. Antipyretics can be used for reducing the body temperature. However, aspirin/NSAIDs are not allowed to use, as it can cause emesis, acidosis, gastritis, and platelet dysfunction. Therefore, preferable drug is paracetamol in the following doses: 1-2 years: 60-120 mg/doses, 3-6 years: 120 mg/dose, 7-12 years: 240 mg/dose, adult: 500 mg/dose. Oral fluid and electrolyte therapy is recommended in case of excessive sweating or vomiting.

Management of dengue haemorrhagic fever (DHF) in febrile phase

To maintain the temperature <39ºC, paracetamol is recommended. According to patient tolerability, copious amount of fluid and oral hydration solution are preferable over plain water. In case, if the patient refuses to feed and vomiting continuously, IV fluid may be administered. This phase is critical, since it can transit from febrile to afebrile stage, hence it is necessary to closely monitor and examine the patients for initial signs of shock. Determination of haematocrit is essential for treatment, since it can explain of increased capillary permeability and need for IV fluids, and it should be evaluated every third day, until the temperature has remained normal for one or two days.

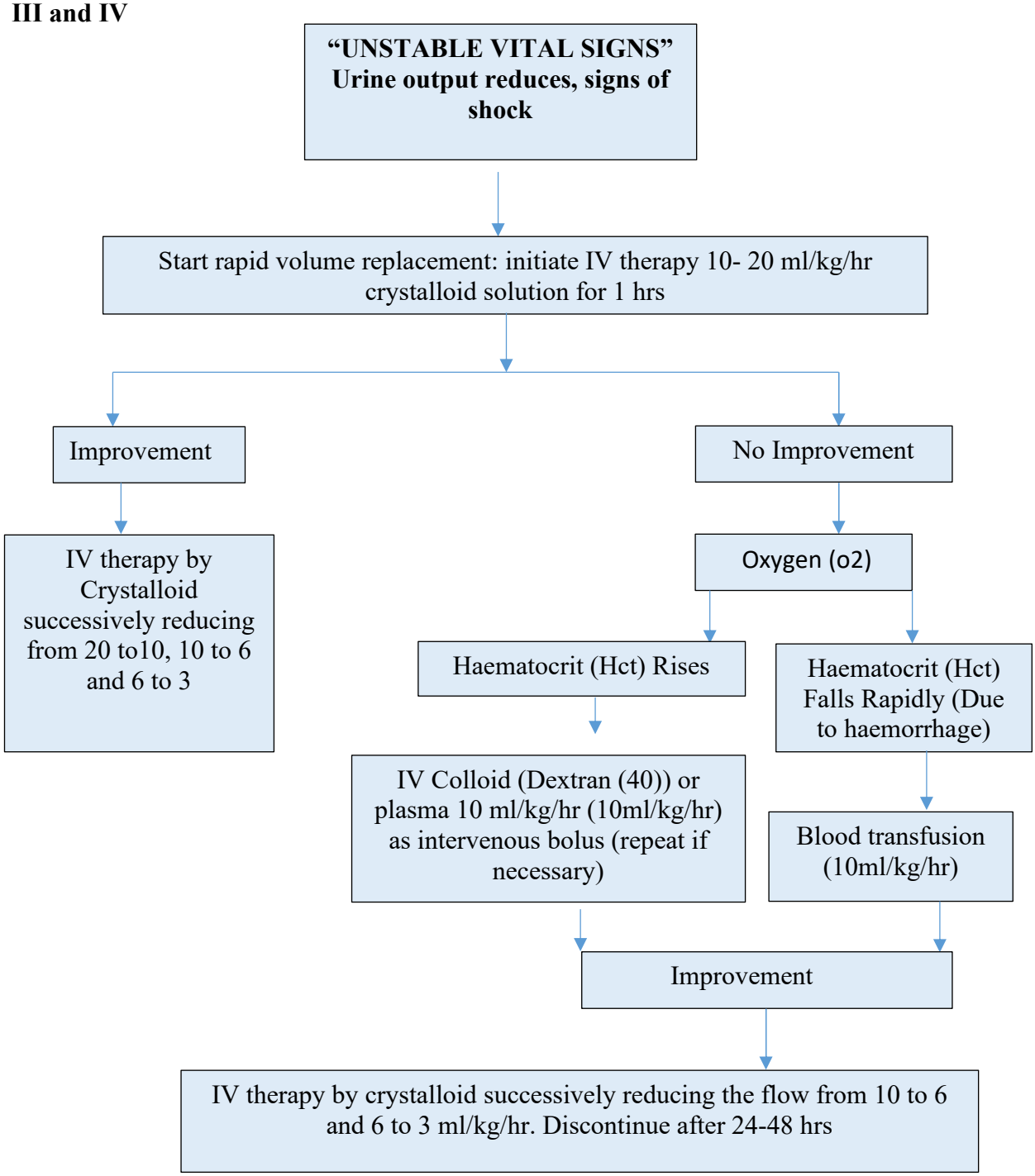
Management of dengue haemorrhagic fever grade I and II

In this phase, IV fluid therapy should be started in case of elevated hemoconcentration. Post treatment, if there is reduction in blood pressure or reduction in urine output or other shock features, the treatment for grade III/IV dengue hemorrhage fever /dengue shock syndrome should be instituted. Antipyretics like paracetamol along with oral rehydration and sponging are preferred.

Management of dengue haemorrhagic fever grade III and IV

Regular monitoring and intravenous fluid therapy should be initiated in necessary cases. If patient receive about 1000 ml of intravenous fluid, it should be changed to colloidal solution such as Haemaccel/Dextran 40 and in case of decreased hematocrit, patient should be given fresh whole blood transfusion 10ml/kg/dose. In case of persistent shock following early fluid replacement, internal bleeding should be suspected if there is persisting hematocrit decline. In the presence of haemoconcentration, it is difficult to assess the degree of internal loss. Hence, for all patients in shock, it is recommended to administer whole blood in small volumes of 10ml/kg/hour, as a precaution. All the patients in shock should be given oxygen.

Fig. 11: Volume resuscitation flow diagram for patients with DHF grades III and IV



- Reduction in platelet count and rise in haematocrit are essential for early diagnosis of DHF
- Cases of DHF should be observed every hour for vital signs and urinary output.

Biomarkers predicting severity of dengue

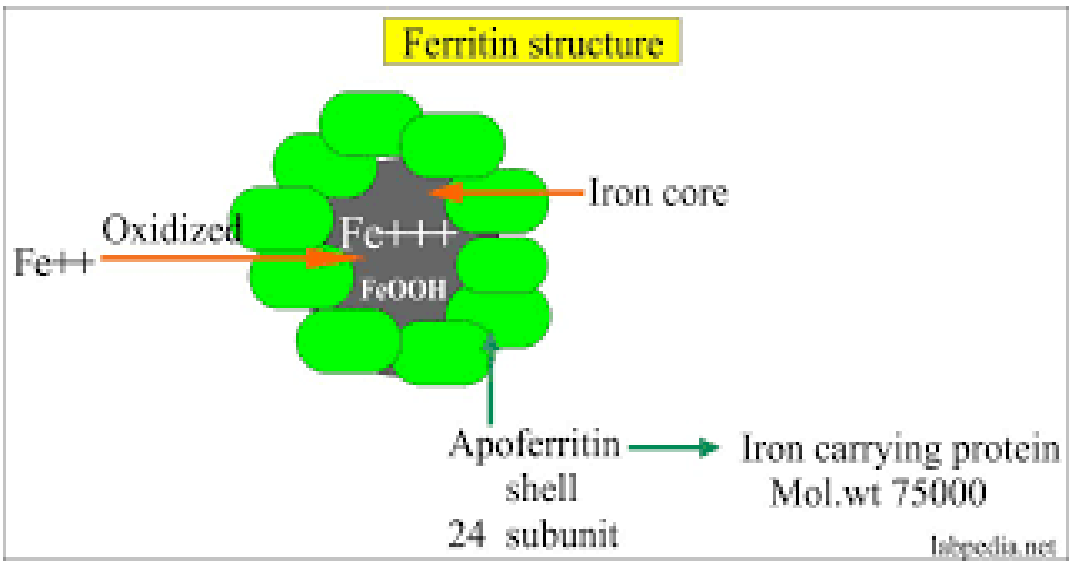
In serum plasma of patients with severe dengue, many biochemical compounds are either increasing or decreasing which makes them qualify to serve as biomarkers of severe dengue disease. The biomarkers such as total plasma cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) level were decreased in children with the severest disease compared with patients with mild DHF. Whereas, increased level of lipopolysaccharide is seen in dengue patients and associated with clinical disease severity. Similarly, serum aspartate aminotransferase and alanine aminotransferase high level found in severe disease which can be a predictor of severe disease. Inter-α Inhibitor Proteins concentrations were lower in pediatric patients suffering from severe dengue infection compared to mild dengue fever and healthy controls.[7] Several studies have proposed the potential of ferritin levels in early prediction of dengue severity. [9]

Serum ferritin

Ferritin molecule

Ferritin is a globular protein, which has the potential to store nearly 2250 iron (Fe3+) ions. It comprises of a proteinaceous capsule called Apoferritin comprising 24 light and heavy subunits, encircled by a crystalline core of phosphate and iron oxide.[47] It is an inflammatory marker formed by reticuloendothelial cells as a reciprocation to both inflammation and infection, with raised levels discovered in the bone marrow, liver, spleen and intestinal mucosa. It is produced in a substantial amount by phagocytic and hepatic cells, and its production induced by cytokines. The reticuoendothelial system plays a major role in iron metabolism by processing hemoglobin from senescent RBCs. Acute infection and inflammation trigger the inhibition of iron release and reduction of serum iron.[48]

Fig 12. : Structure of ferritin



The assessment of ferritin levels and corresponding cut-offs helps in monitoring the trends in iron deficiency and the impact on nutrition and health interventions. A direct correlation has been noted between serum ferritin levels and the total amount of stored iron. High serum ferritin level indicates iron excess and will be eliminated through stool. Serum ferritin has been recognized as the most sensitive marker for iron deficiency anemia. Whereas, the ferritin values are normal or elevated in anemia of chronic disease, lymphoid malignancies and acute and chronic liver diseases.[49]

Hyperferritinemia

Serum ferritin levels >500 µg/L is defined as hyperferritinemia. In dengue fever, it is correlate with immune activation and coagulation abnormalities. It has been identified as a trademark of illnesses, marked by hyperactivation of immunity, including macrophage activation syndrome (MAS) and hemophagocytic lymphohistiocytosis (HLH). Hyperferritinemia may serve as a invidious marker even in mild course of dengue from OFI. Since elevated cytokines levels have been found

in various infectious illnesses, this mechanism alone may not be sufficient to explain extremely elevated ferritin levels.[11]

Hyperferritinemia noted in dengue patients confer two contrasting functions. During the early stages of illness, raised serum ferritin values exert a shielding effect by chelating the toxic free iron radicals at the location of inflammatory action. In contrast, in cases which are severe, increased ferritin may undertake a pathogenic role by provoking immune mediated cells concluding in cytokine storm. [50]

Measurement of serum ferritin levels

Venous blood is used to measure the ferritin levels. Sometimes, the test is ordered with other tests, such as an iron level or a total iron-binding capacity (TIBC) test, to evaluate the body's iron stores. The normal range of ferritin noted in males and females is given below: [51]

Males	12 to 300 ng/mL
Females	12 to 150 ng/mL

2.4. Ferritin and iron

The maintenance of intracellular iron levels is mainly attained through the co-ordinated regulation of the iron-storage protein ferritin and the iron-uptake protein TfR1. The reticuloendothelial system plays a crucial role in regulating the iron metabolism in general and its handling within the immune cells. At different levels, the regulation of iron homeostasis is achieved through the co-ordinated action of cytokines, acute-phase proteins and immune-cell-derived radicals, and it ranges from transcriptional interference at the genomic level to regulation of iron transport potential of transmembrane iron channels. The development of hypo/

hyperferritinemia, as a part of chronic inflammatory conditions have also been reported to confer certain positive effects. This include restricting the availability of the essential nutrients and iron to invading pathogens and malignant cells, and enhancing the cell-mediated immune effector pathways directed against invading microbes.[52]

Correlation between serum ferritin and severity of dengue

A Kolkata- based study by Chaudhuri et al. has concluded that ferritin may serve as a marker for distinguishing dengue from infective or inflammatory etiology, in the absence of a positive NS1 antigen or a positive IgM antibody for dengue. CRP, platelet count, SGOT, SGPT, total count of WBC, and albumin. The study examined confirmed case of dengue fever (Clinically and serologically) (30) and cases of infective etiology (22). The study noted significantly elevated level of ferritin in dengue cohort, much higher than the OFI group. The study has identified 1291 prime cut-off for ferritin level to differentiate OFI from dengue. At this cut-off the sensitivity and specificity is 82.6% and 100%.respectively 1 A case study by Ray et al. has highlighted the need to conduct investigations for dengue-induced hemophagocytic lymphohistiocytosis (HLH).[52]

A study by Weg et al. evaluated ferritin concentrations in 148 dengue-infected patients from Aruba. The ferritin levels in the critical phase were found to be significantly elevated as opposed to those in the febrile phase. Whereas, comparing the febrile phase ferritin values across the three groups namely non-severe dengue without warning signs, non-severe dengue with warning signs, severe dengue, yielded no significant differences. The levels of ferritin in hospitalized patients in the febrile phase were significantly high compared to non-hospitalized patients (P= 0,0057) and

the findings were similar for hospitalized and non-hospitalized subjects in the critical phase (P <0001).[54]

A 2015 study by Soundravally et al. has concluded that ferritin may serve as an early biomarker for predicting disease severity. The study has noted a proportional raise in the serum ferritin levels throughout the disease progression and elevated ferritin level was found to be beneficial in predicting disease severity with corresponding sensitivity and specificity of 76.9 and 83.3 %, respectively, on the day of admission and the same was around 90 and 91.6 % at the time of defervescence.[9]

The study by Chaiyaratana et al (2008) included approximately 16000 patients in paediatric age group admitted with dengue illness during 2002-2005. Median duration of febrile period was found to be 5 days. The result revealed that both Dengue Fever and Dengue Haemorrhagic Fever subjects with raised ferritin values In the febrile, toxic and convalescent phases. Throughout the course of the infection, inpatients presenting with Dengue Haemorrhagic Fever had raised values of serum ferritin when compared with Dengue Fever.

A 2016 study by Nadeem et al. has noted the association of that serum ferritin levels with high magnitude of dengue illness. Average ferritin levels were significantly elevated in severe dengue inpatients versus dengue fever. In 70% of the subjects, serum ferritin level was >100 µg/dl, whereas 30% had ≤100 µg/dl. Out of 31 with normal ferritin concentration, development of severe dengue was noted only in 2 (6.45%). Among 73 subjects, 35 (47.94%) developed severe dengue with ferritin level >100 µg/dl (P <0.005). [12]

A study by Suresh et al. reported that ferritin biomarker assists in investigating the underlying pathogenic mechanism related to dengue and serves as an inexpensive and easily accessible biomarker. Evaluation of 100 dengue-positive cases on day 1 and day 4 demonstrated that the serum ferritin level is a good predictor of severe dengue, with an area under the curve (AUC) of 0.863 ($P < 0.05$) and 0.947 ($P < 0.05$) respectively.[5t]

Ahmed et al. investigated the diagnostic value of ferritin in predicting severity of dengue infection in paediatric cases. The prospective observational study evaluated 30 diagnosed cases of dengue with bicytopenia. The study has concluded that ,can predict the severity of dengue fever with the raised serum ferritin.[56]

A study by Valero et al. have noted increase expression of circulating ferritin and IL-18 in paediatric subjects infected by different serotypes of dengue virus. The researchers have noted increased ferritin and IL-18 levels ($P < 0.0001$) in dengue patients. However these levels were not associated with NS1 expression or type of infection. Elevated levels of both the molecules ($p < 0.001$) were noted in dengue with warning signs and severe dengue. [57]

A Thailand- based study by Chaiyaratana et al. has noted that high serum ferritin levels ≥1,200 ng/ml may be a predictor of dengue hemorrhagic fever. The study has noted that median serum ferritin levels (ng/ml) noted on day 2, 3, 4,5,6,7 and 8 in children with DHF were significantly higher than those with DF.[10] A cross-sectional study by Evalda et al. has reported that mean serum ferritin level in paediatric subjects with dengue shock (mean= 3628.8) was significantly more when compared to those without shock (mean= 717.8) $P <0.001$. The study has concluded on the statistically significant association between ferritin level and dengue shock and

has reported 2304.5 as the cut-off point of serum ferritin concentration for determining dengue shock with good sensitivity (0.92) and specificity (0.97).[58]

A study conducted among paediatric dengue patients in Kanchipuram, Tamil Nadu, India has reported the occurrence of hyperferritinemia in subjects with dengue fever and its association with dengue IgM status. The mean serum ferritin levels noted in the study population was 8762.224±3556.09 µg/m.l[59]

METHODOLOGY

Study design

The study was a hospital-based cross-sectional study.

Study period

1st January to 31st December 2020

Study population

The study was performed on consenting patients admitted in the wards at KLES Dr. Prabhakar Kore Hospital, Belgaum fulfilling the inclusion criteria during the study.

Inclusion criteria

Patients with dengue NS1 positive / dengue IgM positive of age ≥ 18 years.

Exclusion criteria

- Patients with
  - diabetes mellitus
  - HIV
  - known coagulation disorder
  - malignancy
  - alcoholic abuse
- Patients on immunosuppressive drugs
- Patients on steroids

Informed consent

Informed consent was obtained from all the study participants and only those participants who willingly signed the informed consent were included in the study. The risks and benefits involved in the study, and the voluntary nature of participation were explained to the participants before obtaining consent. Confidentiality of the study participants was maintained.

Sample size

Sample size was calculated by the following formula:

The minimum sample size formula based on prevalence rate is

$$n = \frac{z_\alpha{}^2 P(1-P)}{d^2}$$

where P is the percentage of prevalence and d is the percentage likely difference in the prevalence. zα is linked with the level of significance. For 5% level of the significance zα = 1.96.

With P = 50% and d = 25% of P = 12.5%, the sample size is 60

Data collection

All relevant parameters were written and entered in a structured Study Proforma.

Methodology

A detailed history was taken and clinical features were assessed. Basic laboratory tests were conducted such as complete blood counts, liver function tests, renal function tests, PT/INR, and USG Abdomen, serum ferritin.

Based on the clinical picture and test results, patients were divided into DF ,DHS, and DSS. The correlation between serum ferritin and the severity dengue was done.

Statistical analysis

All the data charted into Microsoft Excel and T-test was used for the evaluation of continuous data and chi-square for categorical data. Distribution of the variables after evaluation was graphically represented using histogram. Disease severity of patients categorized as DF, DHF, and DSS were graphically depicted using bargraph (excel 2103 16.0.13901.20400). Correlation of serum ferritin with different variables namely ascites, gall bladder wall edema, pleural effusion, bradycardia, tachycardia, normal sinus rhythm (NSR) and platelet count across different groups was carried out by running python code in Jupyter Notebook (6.2.0)

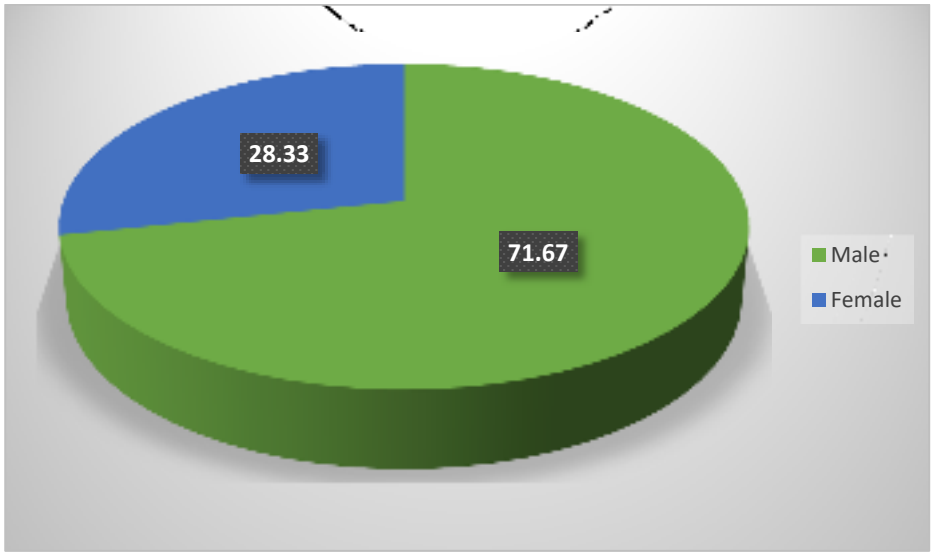
RESULTS

The present one-year cross sectional study titles 'A STUDY ON SERUM FERRITIN LEVELS IN DENGUE POSITIVE PATIENTS' was carried out in the Department of General Medicine, KLES Prabhakar Kore Hospital and Research Centre, Belagavi. During the study period from January 2020 to December 2020, included 60 patients with a mean age of 34.27±14.49. Among the recruited subjects 43 were males (72%) and 17 (28%) were females (Table 1, Fig.1).

Table1: Mean age and gender of recruited subjects (n=60).

Descriptive statistics n = 60	
Variables	**mean±SD**
Age	34.27±14.49
Gender (M/F)	43 /17

Fig. 1: **Gender distribution of study subjects (n=60)**

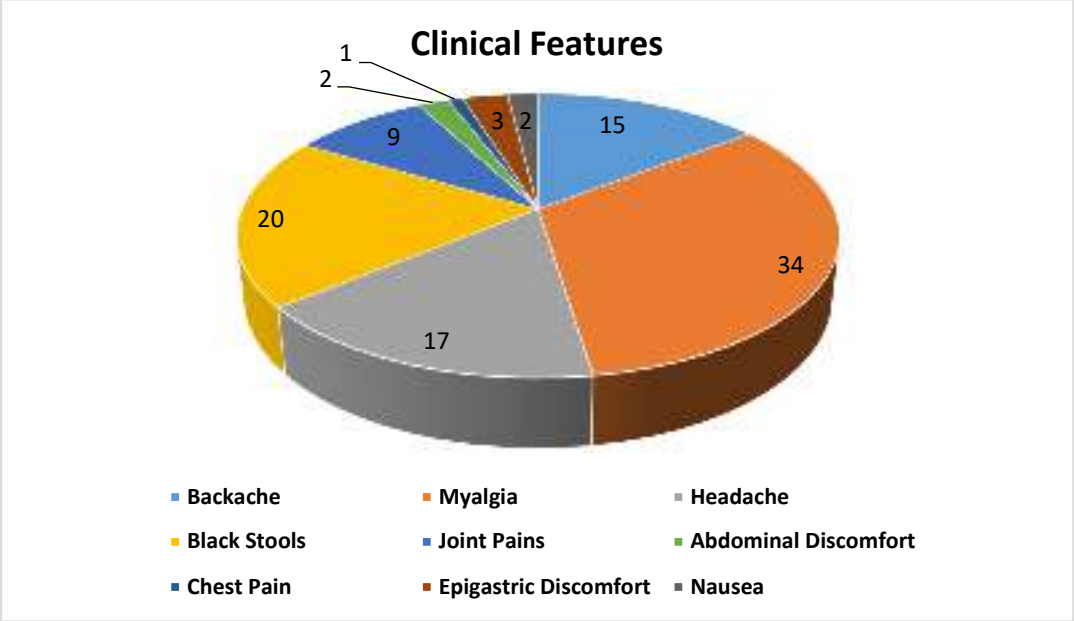


The incidence of clinical symptoms in selected subjects demonstrated that myalgia was the most prominent presentation (57%) followed by black stools (33%), headache (28%), body ache (25%), purpura (25%) and joint pain (9%) (Table 2, Fig. 2).

Table 2: Incidence of symptoms in dengue patients

Clinical presentation	n (%)
Myalgia	34 (56.67%)
Black stools	20 (33.33%)
Headache	17 (28.33%)
Purpura	15 (25.0%)
Body Ache	15 (25.0%]
Joint Pain	9 (15.0%)

Fig. 2: Pie chart illustrating the incidence of clinical symptoms in study participants

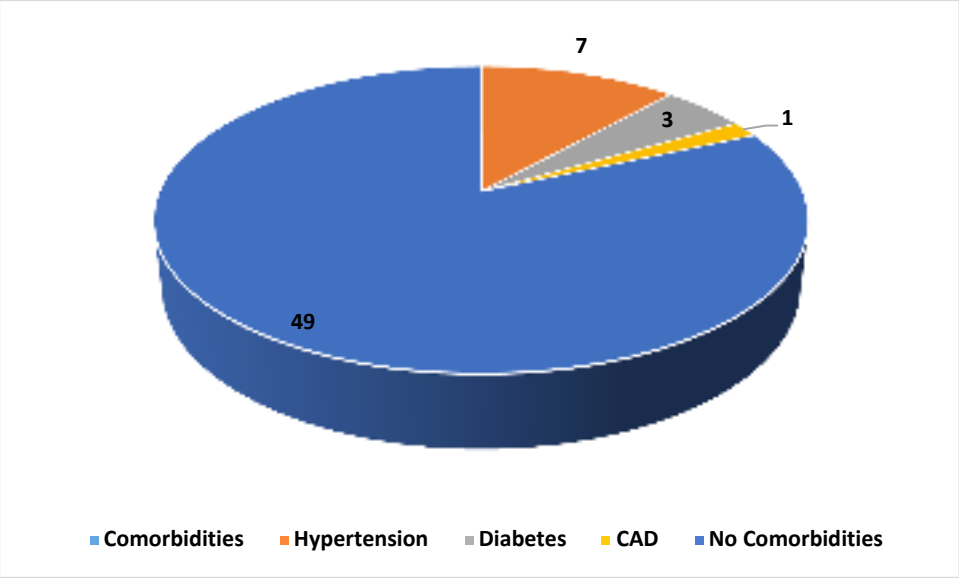


The distribution of comorbidities demonstrated that majority of the subjects did not have associated comorbidities (82%). Among the subjects with comorbidities, hypertension (12%) was most prominent, followed by diabetes (5%) and coronary arterial diseases (CAD, 2%) (Table 3, Fig. 3).

Table 3: Incidence of comorbidities among the study patients (n=60)

Comorbidities	n (%)
Hypertension	7 (11.67%)
Diabetes	3 (5.0%)
CAD	1 (1.67%)
No comorbidities	49 (81.67%)

Fig. 3: Pie chart illustrating comorbidities among study patients (n=60)

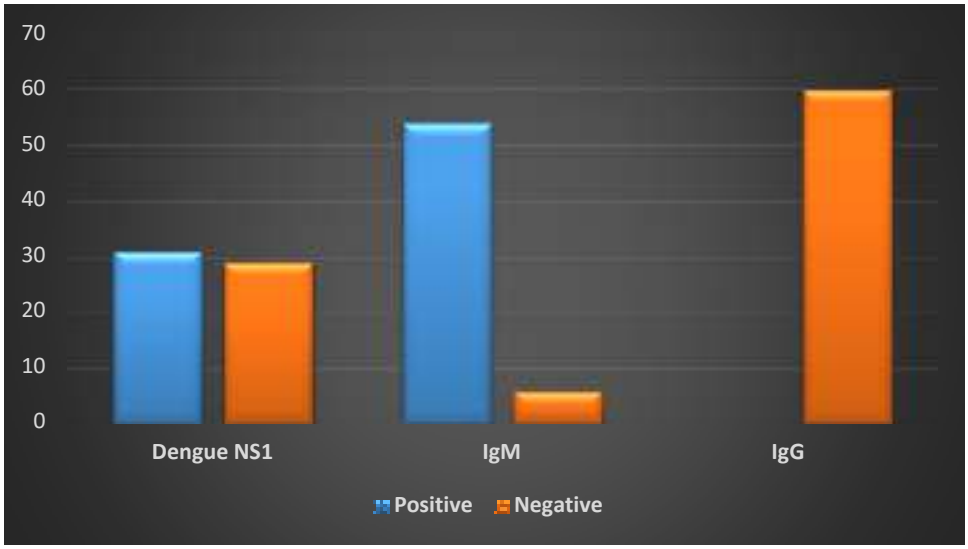


The assessment of different diagnostic tests demonstrated that 31 subjects were positive and 29 were negative for dengue NS1. IgM was found to be positive for 54 subjects, whereas, all subjects were found to be negative for IgG (Table 4, Fig. 4).

Table 4: Status of study subjects for different diagnostic tests

Tests	Positive	Negative
Dengue NS1	31	29
IgM	54	6
IgG	0	60

Fig. 4: Bar graph depicting the diagnostic status of subjects for NS1, IgM and IgG

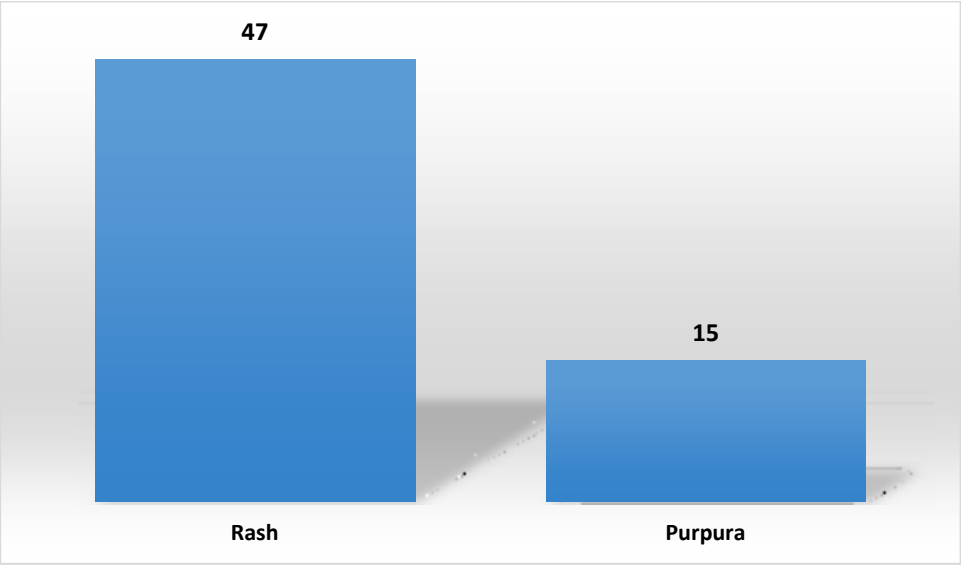


Evaluation of clinical symptoms demonstrated that the frequency of rash/blanching (n=47) was more common than purpura (n=15) among the study subjects.

Table 5: frequency of clinical symptoms

Clinical Symptoms	Frequency
Rash/blanching	**47**
Purpura	**15**

Fig. 5: Bar graph depicting the frequency of rash and purpura

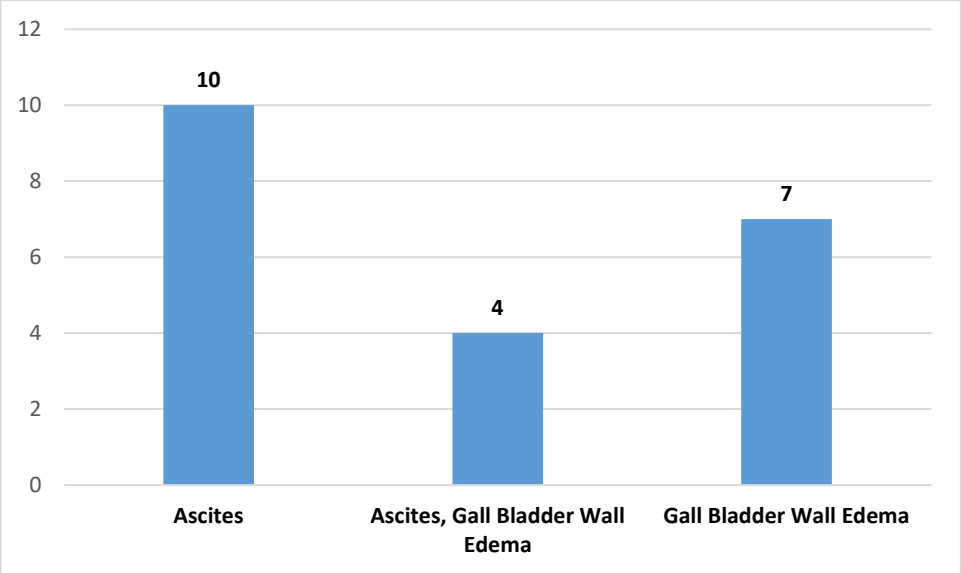


USG abdomen showed that the frequency of ascites was more common in study subjects (n=10) followed by gall bladder wall edema (n=7). The frequency of combined occurrence of ascites and gall bladder edema was 4.

Table 6: USG findings showing the frequency of ascites, and gall bladder wall edema

USG abdomen	Frequency
Ascites	10
Ascites, gall bladder wall edema	4
Gall bladder wall edema	7

Fig. 6: Graph showing USG findings on the frequency of ascites, and gall bladder wall edema



The mean distribution of routine serological parameters is represented in table 7. The findings showed that the mean platelet count was significantly low (0.33±0.256 10^9/L). Similarly, significantly elevated alkaline phosphatase (124.17±85.73 IU/L), SGOT (587.60±2109.57 IU/L) and SGPT (269.58±1050.64 IU/L) levels were noted. ESR and serum urea levels were also found to be elevated, and the corresponding values were 16.05±14.42 mm/hr and 32.65±27.39 mg/dL.

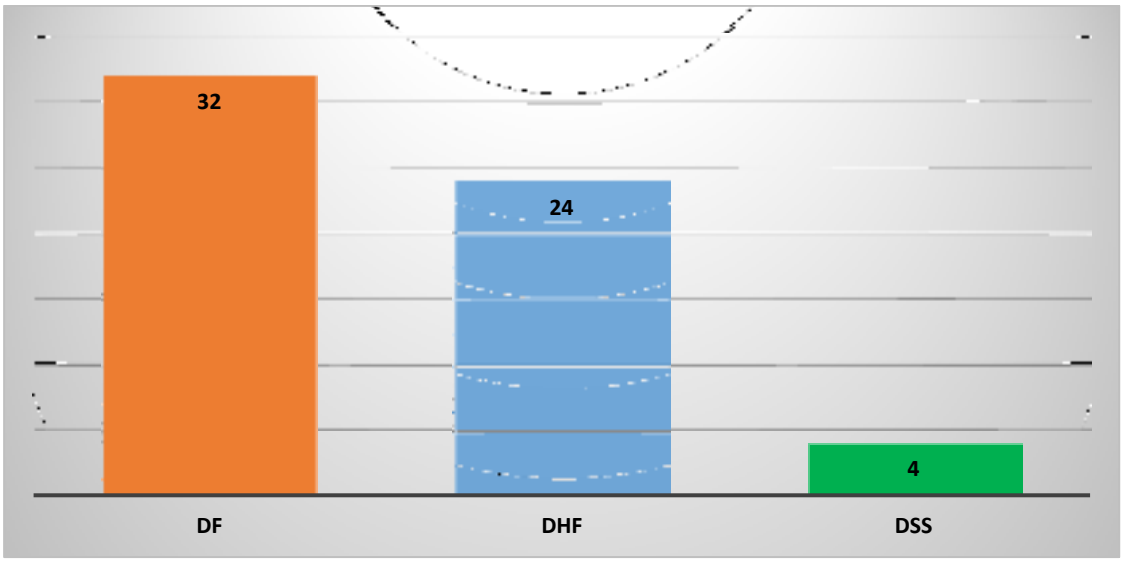
Table 7: Mean distribution of routine serum parameters

Routine evaluation	Mean±SD	Normal range male	Normal range female
HB (gm/dL)	14.38±2.66	14.0 and 17.5	12.3 and 15.3
PCV (%)	42.93±7.13	40-50	30-46
RBC (10^{12}/L)	5.09±1.54	4.5-6.5	3.8-5.8
WBC (10^9/L)	6.675±4.3	4-11	
Platelet (10^9/L)	0.33±0.256	150-450	
MCV (fl)	87.08±10.19	80-100	
MCHC (g/dL)	33.13±1.77	33.4–35.5	
MCH (pg)	29.04±3.62	27-32	
ESR (mm/hr)	16.05±14.42	1-10	
Neutrophil (%)	61.87±15.72	55-70	
Lymphocyte (%)	29.52±14.67	20-40	
NLR ratio	3.52±3.77	1-3	
Monocyte (%)	5.98±2.66	4-8	
Eosinophils (%)	1.23±1.70	1–4	
T. bilirubin (mg/dL)	1.13±1.16	0.2–1.2	
D. bilirubin (mg/dL)	0.72±1.09	0–0.3	
Albumin (g/dL)	3.48±0.6	3.4 to 5.4	
ALP (IU/L)	124.17±85.73	44 to 147	
SGOT (IU/L)	587.60±2109.57	5-40	
SGPT (IU/L)	269.58±1050.64	7-56	

A/G ratio	1.36±0.37	1.5-2.5
PT/INR	1.18±0.51	1.1
APTT ratio	1.27±0.63	27.0 – 41.0
Creatinine (mg/dL.)	1.11±0.78	0.8-1.3
Urea (mg/dL)	32.65±27.39	7 to 20
Sodium (mmol/L)	136.92±4.39	135-145
Potassium (mmol/L)	4.92±5.05	3.5-5
Chloride (mmol/L)	100.82±7.65	95-105

Categorization of the subjects into the three groups namely DF, DHF and DSS showed that 32 patients belonged to the DF group, followed by 24 patients in the DHF. The number of subjects with DSS was only 4 (Fig. 7).

Fig. 7: Categorization of the subjects into DS, DHF and DSS groups



Significance of different variables namely, age, gender, clinical presentations and serum parameters was evaluated across the 3 different groups. T-test is used for continuous data and chi-square for categorical data. The analysis demonstrated that rash/blanching (P=0.00), serum ferritin (P=0.00), T. bilirubin (P=0.00), D. bilirubin (P=0.00), albumin (P=0.01), SGOT (P=0.00), SGPT (P=0.00), PT/INR (P=0.00), APTT ratio (P=0.00) and RBC (P=0.05) were significant across the 3 dengue groups (Table 8, Fig. 8).

Table 8: Significance of different variables across the 3 groups

Variables n= 60	DF n = 32	DHF n = 24	DSS n = 4	P-value
Age	34.06±14.11	35.17±15.91	30.50±10.5	0.84
Gender	23 (9)	17 (7)	3 (1)	0.98
Body ache	24 (70.83%)	17 (70.83%)	4 (100%)	0.46
Myalgia	16 (50.0%)	9 (37.5%)	1 (25.0%)	0.48
Headache	24 (75.0%)	16 (66.67%)	3 (75.0%)	0.78
Black stools	24 (75.0%)	14 (58.33%)	2 (50.0%)	0.32
Joint pain	26 (81.25%)	21 (87.5%)	4 (100%)	0.56
Rash/blanching	27 (84.38%)	7 (29.17%)	3 (75.0%)	0.00
Purpura	8 (25.0%)	5 (20.83%)	2 (50.0%)	0.46
Dengue NS1	15 (46.88%)	12 (50.0%)	4 (100%)	0.13
Dengue IgM	28 (87.5%)	22 (91.67%)	4 (100%)	0.69
Sr. ferritin	5554.16±8839.04	15656.25±15629.29	34278.5±44391.04	0.00
HB	14.13±2.24	14.90±2.78	13.2±4.82	0.37
PCV	42.31±6.21	44.21±7.24	40.2±13.07	0.46
RBC	4.83±0.70	5.15±0.98	6.82±5.44	0.05
WBC	5.8±3.36	6.7±4.23	13.23±6.64	0.00
Platelet	0.398±0.262	0.253±0.225	0.258±0.308	0.09
MCV	87.72±9.27	86.29±11.68	86.68±9.97	0.88
MCHC	33.2±1.54	33.14±2.07	32.6±2.06	0.83
MCH	29.01±3.53	29.24±3.94	28.18±2.92	0.86

ESR	16.72±16.26	14.67±12.70	19.0±9.59	0.80
Neutrophil	61.44±17.10	61.92±14.24	65±16.51	0.92
Lymphocyte	29.63±16.02	30.08±13.46	25.25±12.89	0.83
NLR ratio	3.76±4.24	3.21±3.37	3.48±2.40	0.87
Monocyte	6.25±2.69	5.42±2.67	7.25±2.06	0.32
T. bilirubin	0.86±0.7	1.10±1.17	3.47±1.65	0.00
D. bilirubin	0.44±0.58	0.69±0.99	3.14±1.96	0.00
Albumin	3.56±0.5	3.49±0.64	2.65±0.61	0.01
ALP	121.53±96.65	123.33±68.35	150.25±105.93	0.82
SGOT	152.84±102.60	170.96±145.86	6565.50±6016.48	0.00
SGPT	85.63±57.18	82.75±66.72	2862.25±3469.64	0.00
A/G ratio	1.42±0.43	1.28±0.29	1.35±0.13	0.39
PT/INR	1.07±0.23	1.16±0.29	2.25±1.56	0.00
APTT ratio	1.14±0.2	1.24±0.3	2.43±2.13	0.00
Creatinine	1.01±0.73	1.16±0.82	1.66±0.89	0.29
Urea	27.34±21.06	35.21±33.66	59.75±12.34	0.07
Sodium	136.97±4.6	136.88±4.22	136.75±4.99	0.99
Potassium	5.44±6.89	4.17±0.52	5.28±0.62	0.65
Chloride	100.97±6.07	100.67±10.0	100.5±1.73	0.99

Variables checked for significance level (P-value<0.05)

Fig. 8: Distribution of rash blanching, RBC, PT/INR ratio, APTT ratio, and serum ferritin across the 3 dengue groups

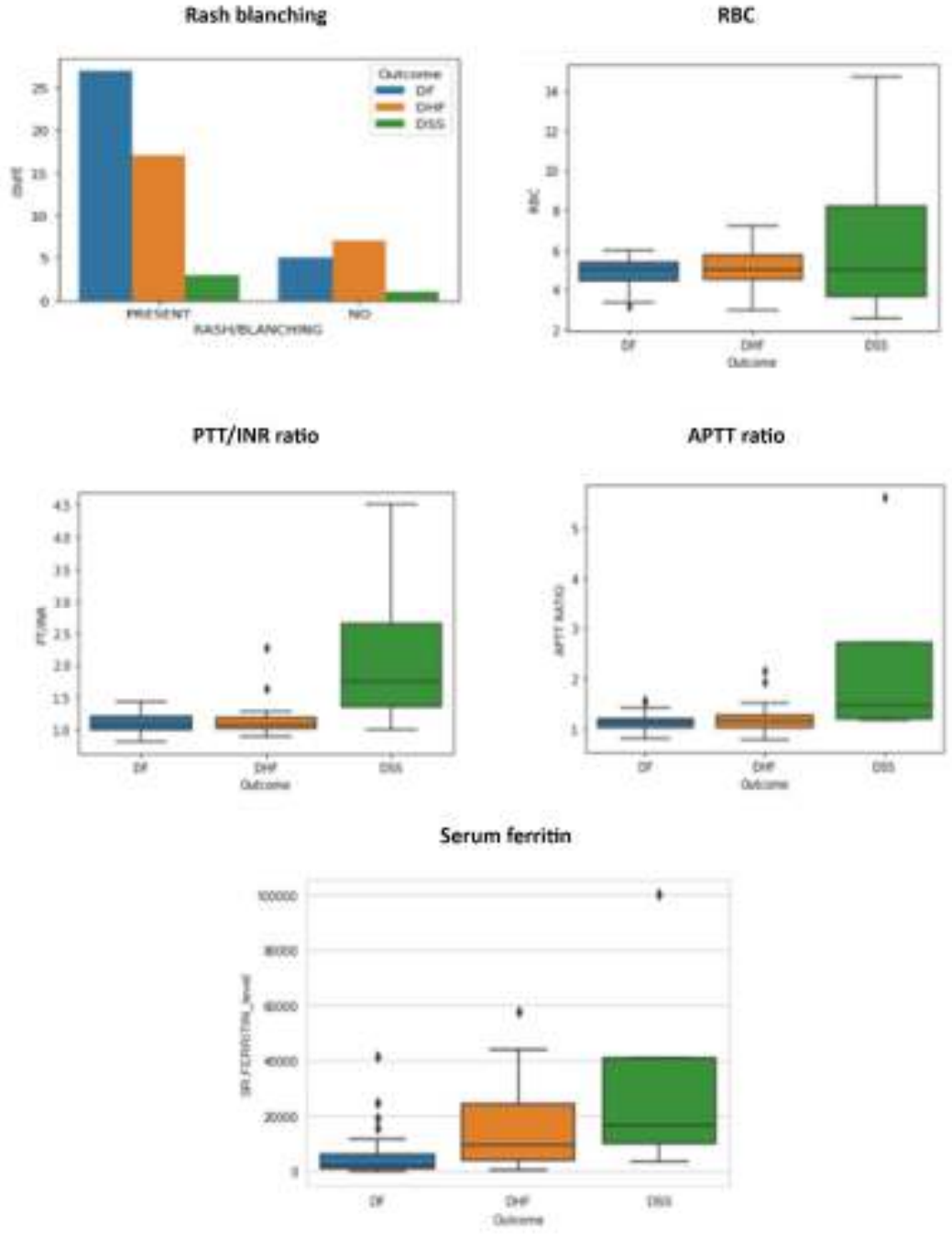
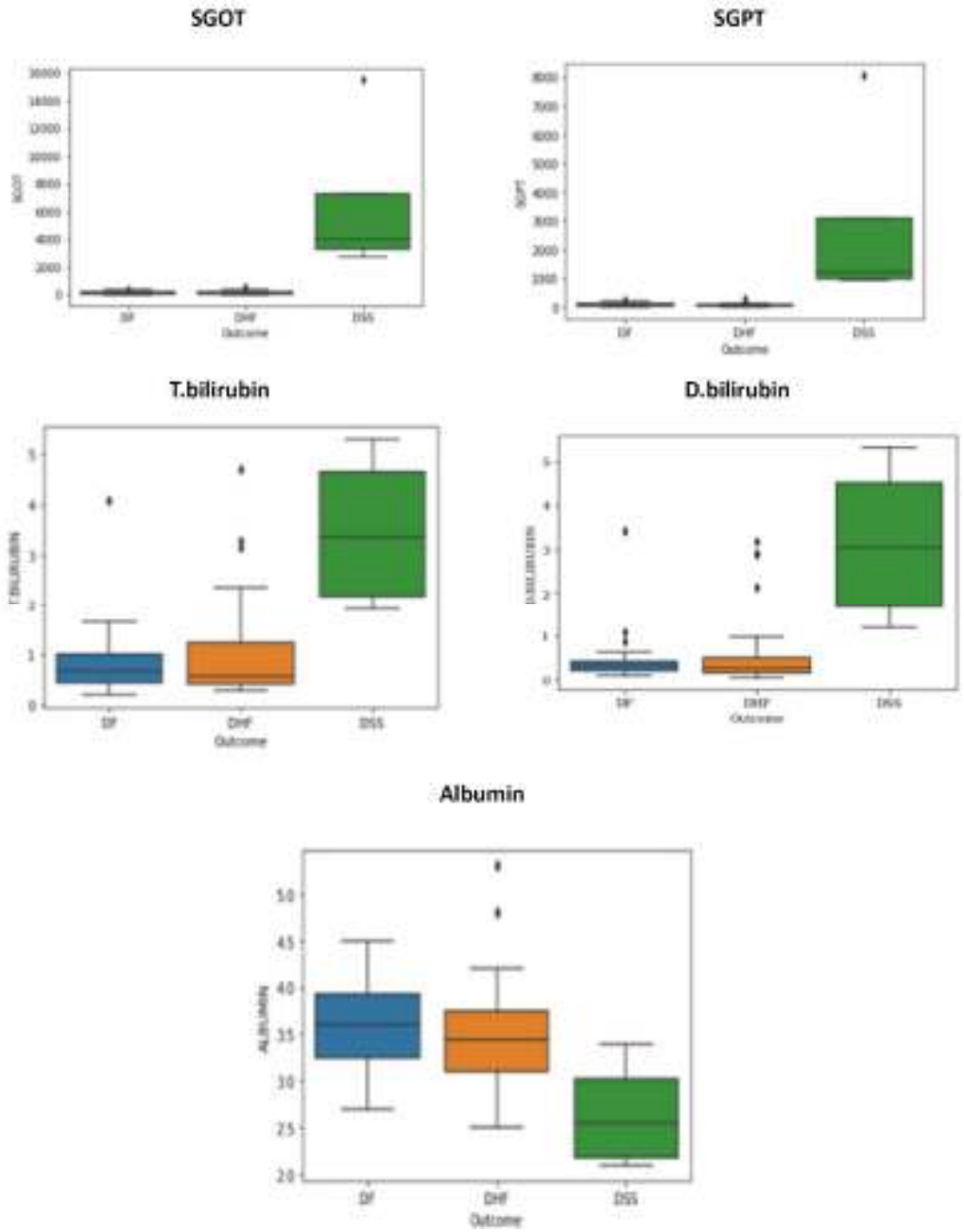


Fig. 9: Distribution of SGOT, SGPT, T. bilirubin, D. bilirubin and albumin across the 3 dengue groups



Correlation of serum ferritin with different variables namely ascites, gall bladder wall edema, pleural effusion, bradycardia, tachycardia, normal sinus rhythm (NSR) and platelet count across different groups was carried out by running python code in Jupyter Notebook (6.2.0). The analysis showed that the variables pleural effusion and platelet in DHF and DSS were significantly correlated with serum ferritin (Table 9).

Table 9: Correlation of serum ferritin with different variables

Variables	Sr. ferritin
Ascites	0.135123
Gall bladder wall edema	0.00835
Pleural effusion	0.449794
Bradycardia	0.025564
Tachycardia	-0.151738
Normal sinus rhythm (NSR)	-0.136033
Platelet (DF)	-0.254214
Platelet (DHF)	0.305173
Platelet (DSS)	0.990786

DISCUSSION

The current study included 60 patients with a mean age of 34.27±14.49, and the male-to-female ratio noted was 1:0.39. The present study findings corroborate the association of ferritin levels with the severity of dengue.

The study has noted myalgia as the prominent clinical symptom noted (57%) followed by black stools (33%), headache (28%), body ache (25%), purpura (25%) and joint pain (9%). In line with this finding, a Brazil-based prospective study has also reported myalgia and weakness as the two most common and persistent symptoms noted during the acute phase of dengue. The researchers have also noted that the persistence of symptoms was more predominant in patients with dengue warning signs.[60] A pilot study conducted at Hospital Serdang, Malaysia has also noted myalgia as the prominent symptom in dengue-infected subjects.[61]

Among the subjects with comorbidities, hypertension (12%) was most prominent, followed by diabetes (5%) and CAD. A systematic review and meta-analysis conducted by Badawi et al. involving 65 studies has noted obesity and overweight (i.e., BMI> 25 kg/m^2, 24.5%), hypertension (17.1%) and diabetes (13.3%) as the comorbidities linked to dengue infection.[62]

A retrospective analysis by Lee et al. emphasized on the association between co-existing comorbidities and dengue severity. The scientists have found that dengue patients with underlying diabetes was an independent risk factor for the development of dengue shock syndrome and severe dengue alike diseases. Evaluating the probability of co-existing comorbidity (ies) may help in triaging risky dengue patients. [63]

Assessment of various diagnostic tests demonstrated that 31 subjects were positive and 29 were negative for dengue NS1. Whereas, IgM was positive in 54 patients and IgG were negative in 60 patients respectively. A Southern India-based study conducted in a tertiary setting by Anand et al. evaluated the potential use of NS1 antigen assay as a substitute to RT-PCR for the early dengue diagnosis.

The corresponding positive detection rate noted for NS1, RT-PCR and IgM ELISA were 80.9%, 68.1% and 47.9%. The corresponding sensitivity, specificity, positive predictive value and negative predictive value noted for NS1 antigen ELISA were 96.8%, 53.3%, 81.6% and 88.9%. The study has concluded on the superiority of NS1 over RT-PCR with regard to cost, early dengue diagnosis, ease of performance and rapidity.[64]

Evaluation of clinical symptoms in the present study demonstrated that the frequency of rash (n=47) was more common than purpura (n=15) among the study subjects. Thomas et al. have evaluated the mucocutaneous manifestations of dengue fever and reported that >50% of infected subjects had rashes, which initially present as macular or maculopapular and later become diffusely erythematous.[65] A Tamil Nadu-based study by Mishra et al. has observed the occurrence of rash in 55 out of 387 patients with dengue fever. Development of worsening thrombocytopenia requiring platelet transfusion had also been noted in subjects with skin involvement.[66]

USG of abdomen indicated increased frequency of ascites in dengue patients (n=10) followed by gall bladder wall edema (n=7). The combined frequency of ascites and gall bladder edema was 4 as c possible complication in our study. Studies have reported ascites as a possible complication related to dengue, especially in severe cases like DHF. A 2016 study published in *BMC Infectious Diseases* has reported the development of a dengue score based on pleural effusion and/or ascites for stratifying

patients at risk for developing severe dengue.[67] A prospective observational study by Adil et al. has reported the strong correlation between gall bladder wall edema and DHF and highlighted its significance to assess dengue severity.[68] Similarly US-based study of severe dengue in Indonesian adults have concluded that US-based evaluation for subclinical plasma leakage and/or an edematous gallbladder wall may assist in monitoring the development of complications over conventional markers like hematocrit.[69]

The findings showed that the mean platelet count was significantly low (0.33 ± 0.256 10^9/L) in all dengue patients. Clinical evidence validates thrombocytopenia as a major clinical manifestation noted in both mild and severe dengue cases. The platelet count may reduce to 40000/µL within 3-7 days of dengue disease. The two major events linked to the development of thrombocytopenia in dengue patients are reduced production of platelets in the bone marrow and/or increased damage and clearance of platelets. Several studies have also suggested that platelet dysfunction is linked to prothrombotic complications noted in DSS and DHF.[70]

The analysis demonstrated that rash/blanching (P=0.00), serum ferritin (P=0.00), T. bilirubin (P=0.00), D. bilirubin (P=0.00), albumin (P=0.01), SGOT (P=0.00), SGPT (P=0.00), PT/INR (P=0.00), APTT ratio (P=0.00) and RBC (P=0.05) were significant across the DF, DHS, and DSS groups. Hepatic dysfunction marked by elevated levels of liver enzymes is often noted in severe and complicated dengue cases as opposed to classic dengue fever.[71] Joshi and Baid evaluated the biochemical profile of 57 patients admitted to a Mumbai-based tertiary care setting. The common laboratory findings noted by the researchers were thrombocytopenia (platelet $<100{,}000/mm^3$), elevated liver enzymes, hypoalbuminemia, hyponatremia, and

deranged PT/PTT.[72] A study by Srividhya et al. have found that the clinical course of a self-limiting dengue is prolonged by hepatic impairment and may serve as a predictor of morbidity and mortality. Hence liver enzymes may serve as an early marker for identifying high-risk cases.73 A systemic review and meta-analysis by Huy et al. concluded that the following factors are associated with DSS: age, female gender, abdominal pain, neurological signs, nausea/vomiting, , gastrointestinal bleeding, hemoconcentration, ascites, pleural effusion, hepatomegaly, hypoalbuminemia, hypoproteinemia, elevated liver enzymes, thrombocytopenia, PT, APTT, fibrinogen level, and dengue virus serotype-2 and primary/secondary infection. [74]

Another remarkable finding noted in the current study is the statistically significant difference in the levels of serum ferritin in DF, DHS, and DSS patients (P=0.00). In concurrence with this finding, the cross-sectional observational study by Nadeem et al. has concluded that serum ferritin may serve as indicator of disease severity if measurement is done on the day of admission . The researchers have noted that nearly 48% of the subjects with ferritin level >100 µg/dl (P <0.005) developed severe dengue.[12] An India-based cross-sectional study by Diwakar and Madhu has also demonstrated the significant association of elevated AST, ALT and serum ferritin with severity of dengue, thereby suggesting their potential use for early prediction of severe dengue . The corresponding sensitivity and specificity noted for AST (best cut-off of 380 IU/L) ALT and serum ferritin were 82.1% and 94.4%, 82.1% and 93.1%, and 85.7% and 87.5%.[75] Suresh et al. has carried out the measurement of serum ferritin level in 100 dengue-positive patients on day 1 (febrile phase) and day 4 (defervescence or convalescent phase) The study has declared that the serum ferritin may serve as an inexpensive and easily accessible tool for monitoring and

prognosticating dengue case. It may also help to investigate the underlying pathogenetic mechanism in severe dengue patients, which may assist in treatment customization.[55]

Variables such pleural effusion and platelet in DHF and DSS were found to be significantly correlated with serum ferritin. This could be considered as a remarkable and novel finding, as literature review shows that there are no studies evaluating such as association. Further studies are needed to identify such associations between the clinical signs, epidemiology, and biomarkers to better understand the pathogenesis linked to dengue severity.

CONCLUSION

The clinical spectrum of dengue ranges from mild ill health to severe life-threatening complications like Dengue shock syndrome/Dengue haemorrhagic fever. The present findings validate the role of serum ferritin as a important marker for differentiating mild non-severe dengue cases from severe dengue complications such as DSS/DHF. This would help clinician in triaging and closely monitoring the patient to avoid undue complication.

STRENGTHS

Early identification and treatment of DHF and DSS is paramount to prevent associated morbidity and mortality. The present study adds to the existing literature evidence recommending the use of serum ferritin as an adjunct marker for identifying dengue severity. The study also corroborate the occurrence of low platelet count in all dengue cases and the association between elevated liver enzymes and severe dengue disease. The current study holds significant relevance as very few studies have evaluated the difference in diverse biochemical parameters across the 3 dengue groups namely DF, DHS, and DSS.

LIMITATIONS

Limited sample size was the major limitation of the study. Although the present study has noted significant difference in elevated serum ferritin and hepatic enzyme levels, it has not investigated the cut-off values to be considered for triaging patients based on dengue severity. In addition, the study has not evaluated the derangements in the parameters at different phases of the disease i.e. febrile, critical, and convalescent.

SUMMARY

The study included 60 patients admitted in Department of General Medicine KLE Prabhakar Kore Hospital in the study period of January 2020 to December 2020 was undertaken to find A correlation between serum ferritin levels with severity of dengue. The study population had a mean age of 34.27±14.49, and the male-to-female ratio noted was 1:0.39. Myalgia was noted as the prominent clinical symptom noted (57%) followed by black stools (33%), headache (28%), body ache (25%), purpura (25%) and joint pain (9%). Hypertension (12%) was the most prominent comorbidity noted, followed by diabetes (5%) and CAD. The analysis demonstrated that rash/blanching (P=0.00), serum ferritin (P=0.00), T. bilirubin (P=0.00), D. bilirubin (P=0.00), albumin (P=0.01), SGOT (P=0.00), SGPT (P=0.00), PT/INR (P=0.00), APTT ratio (P=0.00) and RBC (P=0.05) were significantly correlated with DF, DHS, and DSS groups. Statistically significant difference in the levels of serum ferritin in DF, DHS, and DSS patients (P=0.00).

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ANNEXURE II. ETHICAL CLEARANCE.

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed-to-be-University)
Accredited 'A' Grade by NAAC (3rd Cycle) Given 'A' Category Status by MHRD (GoI)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http://www.jnmc.edu
E-Mail: dome@jnmc.edu
Phone: (0831-2058) Office: 2442359
Principal: 2451301
Fax No. +91 (0831) - 2420759

Ref: MDC/DOME/ 2216 Date: 24/12/2019

To,
REGISTRATION NO: BG0119015
PG student in Medicine,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled "A STUDY OF SERUM FERRITIN LEVELS IN DENGUE PATIENTS ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY", is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

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

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

ANNEXURE I

INFORMED CONSENT

Title Of Research Study:.

A STUDY ON SERUM FERRITIN LEVELS IN DENGUE POSITIVE PATIENTS -ONE YEAR HOSPITAL BASED CEROSS SECTIONAL STUDY

Principal Investigator:-
REGISTRATION NO: BG0119015
Post Graduate Student,
Department Of General Medicine,
JNMC, Belagavi.

Guide:-
Dr. _____
Professor
Department of General Medicine,
JNMC, Belagavi.

Introduction and Purpose:-

Dengue infection is a now a days a common out break in india.Dengue fever not only causes thrombocytopenia but has many complications. It's a need to know the severity of the disease while treating the patient and to follow up the improvement to the treatment given.

Procedure:

If you agree to be part of the research study, you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood and for the necessary investigations.

Risk and Benefits:

The only risk and possible discomfort you might get is while taking blood from your arm for the investigations. It may cause swelling, pain, redness (rarely happens) at the site from where the blood is drawn.

.You may not be benefitted by these investigations but you will be part of this study which is going to be useful to others in the future.

Alternatives:

Taking part in this study is voluntary. You may choose not to take part in this study.

If you decide to take part you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your participation in this study at any time. If you choose not to take part in the study, you will receive the standard treatment for patients with your condition.

Privacy and Confidentiality:

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution / Sponsor's policy:

Does not apply to this research

Financial incentives for participation:

You will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish the results:

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.

In case of the queries during study or in future you may contact following persons,

1. Dr. Roopa M. Bellad J.N.M.C Ethical Committee for Human Research 9480275601	2. Dr. _____ Professor Dept of General Medicine, JNMC, Belagavi.
3. **REG. NO: BG0119015** Investigator, PG in General Medicine, JNMC, Belagavi.	

CONSENT FORM

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read this consent form, or it has Been read to me, this consent form and have had all the questions answered

Signature / Left Thumb print of the Participant or legally authorized representative

Participant's name. :…….

Signature / Left thumb impression. :…….

of the participant

Name of the legally authorized. :…….

representative / guardian

Signature / Left thumb impression :…….

Witness' name :…….

Signature / Left thumb impression :…….

Investigator's name and signature. :…….

Date:

PLACE

ತಿಳುವಳಿಕೆಯ ಸಮ್ಮತಿ

ಸಂಶೋಧನಾ ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ: ಡೆಂಗ್ಯೂ ರೋಗಿಗಳಲ್ಲಿ ಸೀರಮ್ ಫೆರಿಟಿನ್ ಮಟ್ಟಗಳ ಅಧ್ಯಯನ -ಒಂದು ವರ್ಷದ ಆಸ್ಪತ್ರೆ ಆಧಾರಿತ ಅಡ್ಡ ವಿಭಾಗ ಅಧ್ಯಯನ

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ: -

REGISTRATION NO: BG0119015

ಸ್ನಾತಕೊತ್ತರ ವಿದ್ಯಾರ್ಥಿ,
ಜನರಲ್ ಮೆಡಿಸಿನ್ ಇಲಾಖೆ,
ಜೆಎನ್ಎಂಸಿ, ಬೆಳಗಾವಿ.

ಮಾರ್ಗದರ್ಶಿ: -

ಡಾ._____

ಪ್ರೊಫೆಸರ್
ಜನರಲ್ ಮೆಡಿಸಿನ್ ಇಲಾಖೆ,
ಜೆಎನ್ಎಂಸಿ, ಬೆಳಗಾವಿ.

ಪರಿಚಯ ಮತ್ತು ಉದ್ದೇಶ: -

ಡೆಂಗ್ಯೂ ಸೋಂಕು ಈಗ ಭಾರತದಲ್ಲಿ ಸಾಮಾನ್ಯ ವಿರಾಮ ಆಗಿದೆ. ಡೆಂಗ್ಯೂ ಜ್ವರವು ಥ್ರಂಬೋಸೈಟೋಪೆನಿಯಾಗೆ ಕಾರಣವಾಗುವುದಲ್ಲದೆ ಅನೇಕ ತೊಡಕುಗಳನ್ನು ಹೊಂದಿದೆ. ರೋಗಿಗೆ ಚಿಕಿತ್ಸೆ ನೀಡುವಾಗ ರೋಗದ ತೀವ್ರತೆಯನ್ನು ತಿಳಿದುಕೊಳ್ಳುವುದು ಮತ್ತು ನೀಡಿದ ಚಿಕಿತ್ಸೆಯ ಸುಧಾರಣೆಯನ್ನು ಅನುಸರಿಸುವುದು ಅಗತ್ಯವಾಗಿದೆ.
ಸೀರಮ್ ಫೆರಿಟಿನ್ ಮಟ್ಟವು ರೋಗದ ತೀವ್ರತೆಯನ್ನು ನಿರ್ಣಯಿಸಲು ಸಹಾಯ ಮಾಡುತ್ತದೆ.

ವಿಧಾನ:

ಸಂಶೋಧನಾ ಅಧ್ಯಯನದ ಭಾಗವಾಗಲು ನೀವು ಒಪ್ಪಿದರೆ, ನಿಮಗೆ ಸಂಬಂಧಿತ ಇತಿಹಾಸವನ್ನು ಕೇಳಲಾಗುತ್ತದೆ ಮತ್ತು ಸಂಬಂಧಿತ ಕ್ಲಿನಿಕಲ್ ಪರೀಕ್ಷೆ ಮತ್ತು ತನಿಖೆಗೆ ಒಳಪಡಿಸಲಾಗುತ್ತದೆ. ಅಗತ್ಯ ತನಿಖೆಗಾಗಿ ನೀವು ರಕ್ತವನ್ನು ಸಹ ನೀಡಬೇಕಾಗುತ್ತದೆ.

ಅಪಾಯ ಮತ್ತು ಪ್ರಯೋಜನಗಳು:

ತನಿಖೆಗಾಗಿ ನಿಮ್ಮ ತೋಳಿನಿಂದ ರಕ್ತವನ್ನು ತೆಗೆದುಕೊಳ್ಳುವಾಗ ನೀವು ಪಡೆಯುವ ಏಕೈಕ ಅಪಾಯ ಮತ್ತು ಸಂಭವನೀಯ ಅಸ್ವಸ್ಥತೆ. ಇದು ರಕ್ತವನ್ನು ಎಳೆಯುವ ಸ್ಥಳದಲ್ಲಿ ಬೆವರುವಿಕೆ, ನೋವು, ಕೆಂಪು (ವಿರಳವಾಗಿ ಸಂಭವಿಸುತ್ತದೆ) ಗೆ ಕಾರಣವಾಗಬಹುದು.
ಈ ತನಿಖೆಯಿಂದ ನಿಮಗೆ ಯಾವುದೇ ಪ್ರಯೋಜನವಾಗದಿರಬಹುದು ಆದರೆ ಭವಿಷ್ಯದಲ್ಲಿ ಇತರರಿಗೆ ಉಪಯುಕ್ತವಾಗಲಿರುವ ಈ ಅಧ್ಯಯನದ ಭಾಗವಾಗುತ್ತೀರಿ.

ಪರ್ಯಾಯಗಳು:

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವುದು ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸದಿರಲು ನೀವು ಆಯ್ಕೆ ಮಾಡಬಹುದು.

ನೀವು ಭಾಗವಹಿಸಲು ನಿರ್ಧರಿಸಿದರೆ ಮತ್ತು ನಂತರ ಅಧ್ಯಯನದಿಂದ ಹಿಂದೆ ಸರಿಯಲು ನಿಮ್ಮ ಮನಸ್ಸನ್ನು ಬದಲಾಯಿಸಿದರೆ. ನಿಮ್ಮ ನಿರ್ಧಾರವು ಪ್ರಸ್ತುತ ಅಥವಾ ಭವಿಷ್ಯದ ಆರೋಗ್ಯ ರಕ್ಷಣೆ ಅಥವಾ ನೀವು ಸ್ವೀಕರಿಸುವ ಇತರ ಸೇವೆಗಳನ್ನು ಬದಲಾಯಿಸುವುದಿಲ್ಲ. ಅಧ್ಯಯನ ವೈದ್ಯರು ಅಥವಾ ಪ್ರಾಯೋಜಕರು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆಯನ್ನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನಿಲ್ಲಿಸಬಹುದು. ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸದಿರಲು ನೀವು ಆರಿಸಿದರೆ, ನಿಮ್ಮ ಸ್ಥಿತಿಗೆ ರೋಗಿಗಳಿಗೆ ಪ್ರಮಾಣಿತ ಚಿಕಿತ್ಸೆಯನ್ನು ನೀವು ಸ್ವೀಕರಿಸುತ್ತೀರಿ.

ಗೌಪ್ಯತೆ ಮತ್ತು ಗೌಪ್ಯತೆ:

ಈ ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ನಿಮ್ಮ ಬಗ್ಗೆ ಸಂಗ್ರಹಿಸಲಾದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಕಾನೂನಿನಿಂದ ಅನುಮತಿಸುವ ಮಟ್ಟಿಗೆ ಗೌಪ್ಯವಾಗಿಡಲಾಗುತ್ತದೆ. ಈ ಸಂಶೋಧನಾ ದಾಖಲೆಯಲ್ಲಿ ಕೋಡ್ ಸಂಖ್ಯೆಗಳು ನಿಮ್ಮನ್ನು ಗುರುತಿಸುತ್ತವೆ. ಈ ಅಧ್ಯಯನದ ಮಾಹಿತಿಯನ್ನು ಪ್ರಕಟಿಸಬಹುದು ಆದರೆ ಯಾವುದೇ ಪ್ರಕಟಣೆಯಲ್ಲಿ ನಿಮ್ಮ ಗುರುತು ಗೌಪ್ಯವಾಗಿರುತ್ತದೆ.

ಸಂಸ್ಥೆ / ಪ್ರಾಯೋಜಕರ ನೀತಿ: ಈ ಸಂಶೋಧನೆಗೆ ಅನ್ವಯಿಸುವುದಿಲ್ಲ

ಭಾಗವಹಿಸುವಿಕೆಗೆ ಆರ್ಥಿಕ ಪ್ರೋತ್ಸಾಹ:

ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನಿಮಗೆ ಯಾವುದೇ ಉಡುಗೊರೆಗಳನ್ನು / ಪ್ರೋತ್ಸಾಹಕಗಳನ್ನು ನೀಡಲಾಗುವುದಿಲ್ಲ / ನೀಡಲಾಗುವುದಿಲ್ಲ.

ಫಲಿತಾಂಶಗಳನ್ನು ಪ್ರಕಟಿಸಲು ಅಧಿಕಾರ:

ಅಧ್ಯಯನದ ಫಲಿತಾಂಶಗಳನ್ನು ಎಂಡಿ ಪದವಿ, ವಿಮರ್ಶೆ ಮತ್ತು ಪ್ರಕಟಣೆ ಪೂರ್ಣಗೊಳಿಸುವ ಅಗತ್ಯತೆಯ ಭಾಗವಾಗಿ ಬೆಳಗಾವಿಯ ಕೆಎಲ್ಇ ವಿಶ್ವವಿದ್ಯಾಲಯಕ್ಕೆ ರವಾನಿಸಲಾಗುತ್ತದೆ.

ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಅಥವಾ ಭವಿಷ್ಯದಲ್ಲಿ ನೀವು ಈ ಕೆಳಗಿನ ವ್ಯಕ್ತಿಗಳನ್ನು ಸಂಪರ್ಕಿಸಬಹುದು,

REGISTRATION NO: BG0119015

ತನಿಖಾಧಿಕಾರಿ,
ಜನರಲ್ ಮೆಡಿಸಿನ್‌ನಲ್ಲಿ ಪಿಜಿ,
ಜೆಎನ್‌ಎಂಸಿ, ಬೆಳಗಾವಿ.

ಡಾ. _____

ಪ್ರೊಫೆಸರ್
ಜನರಲ್ ಮೆಡಿಸಿನ್ ಇಲಾಖೆ,
ಜೆಎನ್‌ಎಂಸಿ, ಬೆಳಗಾವಿ.

ಯಾವುದೇ ನೈತಿಕ ಸಮಸ್ಯೆಗಳು ಮತ್ತು ಪ್ರಶ್ನೆಗಳ ಸಂಪರ್ಕದ ಸಂದರ್ಭದಲ್ಲಿ

ಡಾ.ರೂಪಾ ಎಂ ಬೆಲ್ಲಾದ, ಎಂಡಿ
ನೈತಿಕ ಸಮಿತಿಯ ಮುಖ್ಯಸ್ಥ
ಮಾನವ ಸಂಶೋಧನೆ
ಜೆಎನ್‌ಎಂಸಿ, ಬೆಳಗಾವಿ.

ಒಪ್ಪಿಗೆ ಪತ್ರ

ಕೆಳಗೆ ಸಹಿ ಮಾಡುವ ಮೂಲಕ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನಾನು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪುತ್ತೇನೆ. ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಹಿಂತೆಗೆದುಕೊಳ್ಳಬಹುದು. ಈ ಫಾರ್ಮ್‌ಗೆ ಸಹಿ ಮಾಡುವ ಮೂಲಕ ನಾನು ನನ್ನ ಯಾವುದೇ ಕಾನೂನು

ಹಕ್ಕುಗಳನ್ನು ಬಿಟ್ಟುಕೊಡುತ್ತಿಲ್ಲ. ಕೆಳಗಿನ ನನ್ನ ಸಹಿ ನಾನು ಈ ಒಪ್ಪಿಗೆಯ ಫಾರ್ಮ್ ಅನ್ನು ಓದಿದ್ದೇನೆ ಅಥವಾ ಈ ಸಮ್ಮತಿಯ ಫಾರ್ಮ್ ಅನ್ನು ನನಗೆ ಓದಿದ್ದೇನೆ ಮತ್ತು ಎಲ್ಲಾ ಪ್ರಶ್ನೆಗಳಿಗೆ ಉತ್ತರಿಸಿದೆ ಎಂದು ಸೂಚಿಸುತ್ತದೆ

ಭಾಗವಹಿಸುವವರ ಅಥವಾ ಕಾನೂನುಬದ್ಧವಾಗಿ ಅಧಿಕೃತ ಪ್ರತಿನಿಧಿಯ ಸಹಿ / ಎಡ ಹೆಬ್ಬೆರಳು ಮುದ್ರಣ
ಭಾಗವಹಿಸುವವರ ಹೆಸರು: .....

ಭಾಗವಹಿಸುವವರ ಸಹಿ / ಎಡ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ: .....

ಕಾನೂನುಬದ್ಧವಾಗಿ ಅಧಿಕೃತ ಪ್ರತಿನಿಧಿ / ರಕ್ಷಕರ ಹೆಸರು: ....

ಸಹಿ / ಎಡ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ: ....

ಸಾಕ್ಷಿಯ ಹೆಸರು: ....

ಸಹಿ / ಎಡ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ: ....

ದಿನಾಂಕ:

ಸ್ಥಳ

माहितीपूर्ण संमती

संशोधन अभ्यासाचे शीर्षकः डेंग्यूच्या रुग्णांमध्ये सीरम फेरेटिन पातळीचा अभ्यास-एका वर्षाच्या रुग्णालयात आधारित क्रॉस विभागीय अभ्यास.

प्रधान अन्वेषक: -
REGISTRATION NO: BG0119015
पदव्युत्तर विद्यार्थी,
सामान्य औषध विभाग,
जेएनएमसी, बेळगावी.

मार्गदर्शनः-
डॉ. _____
प्राध्यापक
सामान्य औषध विभाग,
जेएनएमसी, बेळगावी.

परिचय आणि उद्देश: –

डेंग्यूचा संसर्ग आता एक दिवस झाला आहे. डेंग्यू तापामुळे केवळ थ्रोम्बोसाइटोपेनियाच उद्भवत नाही तर त्यामध्ये बरीच गुंतागुंत आहे. रुग्णावर उपचार करताना रोगाची तीव्रता जाणून घेणे आणि दिलेल्या उपचारांमध्ये सुधारणा करण्याचा प्रयत्न करणे आवश्यक आहे.
सीरम फेरीटिन पातळीमुळे रोगाच्या तीव्रतेचे मूल्यांकन करण्यात मदत होऊ शकते.

प्रक्रियाः

आपण संशोधन अभ्यासाचा भाग होण्यास सहमत असल्यास, आपणास संबंधित इतिहास विचारला जाईल आणि संबंधित क्लिनिकल परीक्षा आणि तपासणीस पात्र केले जाईल. आवश्यक तपासणीसाठी आपल्याला रक्त द्यावे लागेल.

जोखीम आणि फायदे:

तपासणीसाठी आपल्या बाहेरून रक्त घेत असताना आपल्याला फक्त धोका आणि संभाव्य असुविधाची समस्या उद्भवू शकते. ज्या स्थानावरून रक्त ओढले आहे त्या जागेवर सूज, वेदना, लालसरपणा (क्वचितच घडते) होऊ शकते.
या तपासणीमुळे आपल्याला फायदा होणार नाही परंतु आपण या अभ्यासाचा भाग व्हाल जे भविष्यात इतरांना उपयुक्त ठरेल.

विकल्पः

या अभ्यासामध्ये भाग घेणे ऐच्छिक आहे. आपण या अभ्यासामध्ये भाग न घेणे निवडू शकता.
आपण भाग घेण्याचा निर्णय घेतला आणि नंतर अभ्यासापासून दूर जाण्यासाठी आपले मत बदलल्यास. आपल्या निर्णयामुळे आपल्याला प्राप्त झालेल्या वर्तमान किंवा भविष्यातील आरोग्य

सेवा किंवा इतर सेवा बदलणार नाहीत. अभ्यास डॉक्टर किंवा प्रायोजक या अभ्यासात आपला सहभाग कधीही थांबवू शकतात. आपण अभ्यासामध्ये भाग न घेण्याचे निवडल्यास आपल्या स्थितीबद्दल आपल्याला रूग्णांसाठी प्रमाणित उपचार मिळेल.

गोपनीयता आणि गोपनीयता :

या अभ्यासाच्या दरम्यान आपल्याबद्दल संकलित केलेली सर्व माहिती कायद्याद्वारे परवानगी असलेल्या मर्यादेपर्यंत गोपनीय ठेवली जाईल. कोड नंबर आपल्याला या संशोधन रेकॉर्डमध्ये ओळखतील. या अभ्यासाची माहिती प्रकाशित केली जाऊ शकते परंतु आपली ओळख कोणत्याही प्रकाशनात गोपनीय असेल.

संस्था / प्रायोजक यांचे धोरणः

या संशोधनास लागू होत नाही

सहभागासाठी आर्थिक प्रोत्साहनः

अभ्यासामध्ये भाग घेण्यासाठी आपल्याला कोणत्याही भेटवस्तू / प्रोत्साहन दिले जाणार नाहीत.

परिणाम प्रकाशित करण्यासाठी अधिकृतताः

अभ्यासाचे निकाल एमडी पदवी, आढावा आणि प्रकाशन पूर्ण करण्याच्या आवश्यकतेनुसार केएलई विद्यापीठ, बेळगाव येथे पाठविले जातील.

अभ्यासाच्या वेळी किंवा भविष्यातील प्रश्नांच्या बाबतीत आपण खालील व्यक्तींशी संपर्क साधू शकता,

REGISTRATION NO: BG0119015

अन्वेषक,
जनरल मेडिसीन मधील पीजी,
जेएनएमसी, बेळगावी.

डॉ. _____

प्राध्यापक
सामान्य औषध विभाग,
जेएनएमसी, बेळगावी.

कोणत्याही नैतिक समस्या आणि क्वेरीच्या संपर्कात असल्यास

डॉ. रूपा बेलाड, अध्यक्ष,
नैतिक समिती मानव संशोधन
जे.एन.एम.सी, बेळगावी.

संमती फॉर्म

मी खाली स्वाक्षरी करून या अभ्यासात भाग घेण्यास स्वेच्छेने सहमत आहे. मी कधीही माघार घेऊ शकतो. या फॉर्मवर सही करून मी माझा कोणताही कायदेशीर हक्क सोडत नाही. खाली माझी स्वाक्षरी सूचित करते की मी हा संमती फॉर्म वाचला आहे किंवा हा संमती फॉर्म मला वाचला आहे आणि मला सर्व प्रश्नांची उत्तरे दिली आहेत

सहभागी किंवा कायदेशीररित्या अधिकृत प्रतिनिधीची सही / डावा अंगठा प्रिंट

सहभागीचे नाव: .....

स्वाक्षरी / डावा अंगठा ठसा: ....
सहभागीचा

कायदेशीररीत्या अधिकृत नाव: .....
प्रतिनिधी / पालक

स्वाक्षरी / डावा अंगठा ठसा: .....

साक्षीचे नाव: ....

स्वाक्षरी / डावा अंगठा ठसा: ....

अन्वेषकांचे नाव आणि स्वाक्षरीः .....

तारीख:

ठिकाणः

ANNEXURE III

CASE NO:

NAME:

AGE/SEX:

IP NO.:

ADDRESS:

OCCUPATION

COMPLAINTS AT PRESENTATION:

PAST HISTORY -

FAMILY HISTORY -

PERSONAL HISTORY -

TREATMENT HISTORY -

PHYSICAL EXAMINATION:

GENERAL CONDITION:

PALLOR- YES/NO

ICTERUS-YES/NO

LYMPHADENOPATHY-YES/NO

CYANOSIS- YES/NO

CLUBBING-YES/NO

EDEMA-YES/NO

VITALS:

TEMPERATURE

PULSE

RESPIRATORY RATE

BLOOD PRESSURE

RASH

PURPURA

SYSTEMIC EXAMINATION:

RESPIRATORY SYSTEM –

CARDIOVASCULAR SYSTEM –

PER ABDOMEN –

CENTRAL NERVOUS SYSTEM -

INVESTIGATIONS

Hb	**TOTAL BILIRUBIN**
PCV	**DIRECT BILIRUBIN**
RBC	**ALBUMIN**
WBC	**ALKALINR PHOSPHATASE**
PLATELET	**SGOT**
MCV	**SGPT**
MCHC	**A/G RATIO**
ESR	**PT /INR**
NEUTROPHIL	**CREATININE**
LYMPHOCYTES	**UREA**
MONOCYTES	**CREATININE**
ESINOPHILS	**SODIUM**
BASOPHILS	**POTASSIUM**
DENGUE NS1	**CHLORIDE**
DENGUE IgM	
SERRUM FERRITN	
USG ABDOMEN AND THORAX	
CHEST X RAY	
ECG	

IP NO	AGE	SEX	FEVER	BACKACHE	MAYALGIA	HEADACHE	BLACK STOOLS	JOINT PAINS	OTHERS	HYPERTENSIVE	DIABETIC	CAD	CVD	COPD	RASH/BLANCHING	PURPURA	DENGUE NS1	DENGUE IGM	DENGUE IGG	SR.FERRITIN	HB	PCV	RBC	WBC	PLATELET	MCV	MCHC	MCH
1023567	37	MALE	PRESENT	PRESENT	PRESENT	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	POSITIVE	POSITIVE	NEGATIVE	41249	15.6	45.1	4.45	6400	17000	101.4	35	34.5
1017270	40	MALE	PRESENT	NO	NO	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	POSITIVE	POSITIVE	NEGATIVE	2585	15.4	44	5.07	4100	19000	86.7	35.1	30.5
1029551	24	FEMALE	PRESENT	NO	NO	NO	NO	NO	EPIGASTRIC DISCOMFORT	NO	NO	NO	NO	NO	NO	NO	NO	NEGATIVE	POSITIVE	NEGATIVE	11433	15.5	46.9	5.25	6000	36000	89.4	33	29.5
1027902	39	MALE	PRESENT	PRESENT	NO	NO	PRESENT	NO	EPIGASTRIC DISCOMFORT	NO	NO	NO	NO	NO	PRESENT	PRESENT	NEGATIVE	POSITIVE	NEGATIVE	1561	16	46.1	5.41	8500	6000	85.2	34.7	29.6
1023418	50	FEMALE	PRESENT	NO	PRESENT	PRESENT	PRESENT	NO	NO	NO	YES	NO	NO	NO	PRESENT	PRESENT	POSITIVE	POSITIVE	NEGATIVE	816	11.6	35.3	4.2	3000	29000	84	33	27.7
1022910	19	MALE	PRESENT	PRESENT	NO	NO	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	POSITIVE	POSITIVE	NEGATIVE	4356	17.5	53.5	4.56	9700	15000	117.3	32.7	38.3
1021061	20	FEMALE	PRESENT	NO	NO	NO	NO	PRESENT	NO	NO	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	894	10.6	32.5	4.54	8700	67000	71.6	32.5	23.3
5706492	25	MALE	PRESENT	NO	NO	NO	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	POSITIVE	POSITIVE	NEGATIVE	3089	17.2	45.2	4.52	6200	17000	83.5	33.6	23.4
1019877	62	FEMALE	PRESENT	NO	PRESENT	NO	NO	PRESENT	ABDOMINAL DISCOMFORT	YES	YES	NO	NO	NO	PRESENT	PRESENT	POSITIVE	NEGATIVE	NEGATIVE	33307	12.8	39.4	4.39	8600	10000	89.7	32.4	29.1
1012170	50	MALE	PRESENT	NO	PRESENT	NO	NO	NO	LOSS OF APPITITTE	NO	NO	NO	NO	NO	PRESENT	NO	POSITIVE	POSITIVE	NEGATIVE	834	12.7	38.9	4.38	2600	66000	88.6	33.6	28.4
1018679	59	MALE	PRESENT	NO	PRESENT	PRESENT	NO	NO	NO	YES	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	2088	13.6	40.7	4.57	8300	32000	89	33.4	29.7
1031827	45	FEMALE	PRESENT	PRESENT	NO	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	POSITIVE	POSITIVE	NEGATIVE	6383	13.1	39.3	4.7	1900	34000	83.5	33.4	27.9
1021053	27	FEMALE	PRESENT	NO	PRESENT	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	POSITIVE	POSITIVE	NEGATIVE	1788	11.3	32.6	4.16	3600	14000	78.5	34.5	27
1021005	20	FEMALE	PRESENT	NO	NO	NO	NO	PRESENT	NO	NO	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	894	10.6	32.5	4.54	8700	67000	71.6	32.5	23.3
1021776	28	FEMALE	PRESENT	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NEGATIVE	POSITIVE	NEGATIVE	4289	13.9	39.4	4.7	8600	20000	83.8	35.3	29.5
1020100	27	MALE	PRESENT	PRESENT	PRESENT	NO	NO	PRESENT	NO	NO	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	3197	19	50.2	7.24	4400	18000	69.2	33.4	26.2
5930456	20	MALE	PRESENT	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	281	13.9	41.5	5.09	5760	10000	80.5	32.4	26.2
1030291	42	MALE	PRESENT	NO	NO	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	P0SITIVE	POSITIVE	NEGATIVE	22865	16.5	45	5.75	3800	37000	79.8	36.3	29
1022660	20	MALE	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	PRESENT	POSITIVE	POSITIVE	NEGATIVE	44232	15.6	47	5.45	17800	10000	86.2	33.3	28.7
1026738	41	MALE	PRESENT	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	25852	15.5	47	5.14	7900	17000	91.6	32.9	30.1
1026916	24	MALE	PRESENT	NO	PRESENT	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	1057	17.4	52.4	5.97	7600	18000	87.9	33.3	29.2
1028095	18	MALE	PRESENT	NO	NO	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	NEGATIVE	POSITIVE	NEGATIVE	14066	17.7	50.8	6.54	4400	11000	77.7	34.9	27.1
1028758	24	MALE	PRESENT	NO	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	POSITIVE	POSITIVE	NEGATIVE	36902	16.7	49.4	6.18	5400	21000	79.9	33.8	27
1024514	26	MALE	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	POSITIVE	POSITIVE	NEGATIVE	6286	15.5	51.4	5.9	2100	16000	87.1	30	28.8
1030627	42	MALE	PRESENT	NO	PRESENT	NO	NO	NO	NO	NO	YES	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	579	15.1	44.2	5.36	4800	22000	82.3	34.2	28.2
1016382	27	FEMALE	PRESENT	NO	NO	NO	NO	NO	ABDOMINAL DISCOMFORT	NO	NO	NO	NO	NO	NO	NO	NO	NEGATIVE	POSITIVE	NEGATIVE	158	11	32.9	3.77	14000	69000	87.3	33.5	29.2
1025284	24	MALE	PRESENT	NO	PRESENT	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	POSITIVE	POSITIVE	NEGATIVE	30339	14.5	42.9	4.64	4900	7000	92.4	33.8	37.2
1031946	42	MALE	PRESENT	NO	NO	NO	NO	NO	PAIN ABDOMEN	YES	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	984	17.4	50.6	5.17	18.1	19000	84.5	26.5	32.6
1024514	26	MALE	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	POSITIVE	POSITIVE	NEGATIVE	6286	15.5	47	5.4	2100	16000	87.1	33	28.8
1028073	18	MALE	PRESENT	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	14066	17.7	50.8	6.54	4400	11000	77.7	34.9	27.1
1021170	86	MALE	PRESENT	NO	NO	NO	NO	NO	CHEST PAIN	YES	NO	YES	NO	NO	NO	NO	NEGATIVE	POSITIVE	NEGATIVE	587	9.1	30.4	2.98	9200	96000	102	29.9	30.5
999998	25	FEMALE	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	POSITIVE	NEGATIVE	NEGATIVE	10862	14.1	42.1	4.48	3000	60000	94.1	33.3	31.4
1028665	35	MALE	PRESENT	NO	PRESENT	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	57775	14.6	46.9	5.8	8000	64000	77.4	32.6	23.2
1027403	23	MALE	PRESENT	NO	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	PRESENT	NEGATIVE	POSITIVE	NEGATIVE	24678	17.5	50.8	5.6	4000	18000	89.4	34.4	30.7
1029225	24	MALE	PRESENT	NO	NO	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	POSITIVE	NEGATIVE	NEGATIVE	1797	18.6	55.4	4.91	3400	10000	112.8	33.6	37.9
1028745	50	FEMALE	PRESENT	NO	PRESENT	PRESENT	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NEGATIVE	POSITIVE	NEGATIVE	10826	12.1	37.8	4.88	9500	30000	78.4	32.1	25.1
1030096	26	MALE	PRESENT	NO	NO	NO	PRESENT	NO	PAIN ABDOMEN	NO	NO	NO	NO	NO	PRESENT	NO	POSITIVE	POSITIVE	NEGATIVE	15825	18.1	54	5.46	4800	13000	110	33.5	37
1042038	25	FEMALE	PRESENT	NO	PRESENT	NO	PRESENT	NO	PAIN ABDOMEN	NO	NO	NO	NO	NO	PRESENT	PRESENT	POSITIVE	POSITIVE	NEGATIVE	12314	7.9	24.2	2.54	7440	11000	98.8	32.6	32.2
1051717	29	MALE	PRESENT	NO	PRESENT	NO	NO	NO	NAUSEA	NO	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	743	14	43.4	5.02	2600	53000	86.6	32.2	27.9
1052263	49	MALE	PRESENT	NO	PRESENT	NO	NO	NO	PAIN ABDOMEN	NO	NO	NO	NO	NO	PRESENT	PRESENT	P0SITIVE	POSITIVE	NEGATIVE	3140	17.1	51.4	5.48	2220	15000	94.5	33	31.2
1042841	38	FEMALE	PRESENT	PRESENT	PRESENT	NO	PRESENT	NO	EPIGASTRIC DISCOMFORT	NO	NO	NO	NO	NO	PRESENT	NO	P0SITIVE	POSITIVE	NEGATIVE	4548	12.9	39.8	4.29	7200	8000	92.8	32.6	30.2
1043959	45	MALE	PRESENT	NO	NO	NO	NO	NO	NAUSEA	NO	NO	NO	NO	NO	PRESENT	NO	P0SITIVE	POSITIVE	NEGATIVE	3665	15.3	45.3	5.99	11700	9000	75.6	33.8	25.5
6022347	36	FEMALE	PRESENT	NO	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	4009	15.4	47.7	5.31	6400	26000	89.8	32.3	29
1048529	31	MALE	PRESENT	NO	PRESENT	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	POSITIVE	POSITIVE	NEGATIVE	1E+05	10.8	36.4	4.05	22800	72000	89.9	29.7	26.7
1050560	21	MALE	PRESENT	NO	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	POSITIVE	POSITIVE	NEGATIVE	21135	18.8	54.9	14.7	11000	11000	82.4	34.3	28.3
1050741	68	MALE	PRESENT	NO	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	P0SITIVE	POSITIVE	NEGATIVE	1869	15.1	39.9	5.19	4900	12000	76.9	37.8	29.1
1050471	32	FEMALE	FEVER	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	PRESENT	NEGATIVE	POSITIVE	NEGATIVE	44	10.4	34.2	5.01	5300	53000	68.2	30.5	20.8
1049033	30	FEMALE	PRESENT	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	PRESENT	P0SITIVE	NEGATIVE	NEGATIVE	19382	11	35	3.95	6280	23000	88.6	31.4	27.8
1049005	50	MALE	PRESENT	PRESENT	NO	NO	NO	PRESENT	NO	NO	NO	NO	NO	NO	PRESENT	PRESENT	P0SITIVE	POSITIVE	NEGATIVE	475	14.9	47.6	5.33	5.95	30000	89.3	31.3	28
1048432	42	MALE	PRESENT	NO	PRESENT	NO	PRESENT	NO	NO	YES	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	1003	15.1	46	5.27	9040	20000	87.3	32.8	28.7
1041838	26	MALE	PRESENT	NO	PRESENT	NO	NO	PRESENT	NO	NO	NO	NO	NO	NO	PRESENT	NO	P0SITIVE	POSITIVE	NEGATIVE	2647	14.4	42.5	4.79	2400	64000	88.7	33.9	30.1
1041593	34	MALE	PRESENT	PRESENT	PRESENT	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	PRESENT	PRESENT	NEGATIVE	POSITIVE	NEGATIVE	23470	17.2	47.4	6.43	15500	6000	73.7	36.3	26.7
1052529	25	FEMALE	PRESENT	NO	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	POSITIVE	NEGATIVE	NEGATIVE	1656	10.5	32.8	3.13	10800	91000	104	30.5	31.9
1046010	19	MALE	PRESENT	NO	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	POSITIVE	NEGATIVE	NEGATIVE	1838	14.6	43.2	4.75	5410	71000	90.9	33.8	30.7
1031093	20	MALE	PRESENT	NO	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	8297	10.9	31.8	4.2	11300	70000	75.9	34.1	25.9
1029978	28	MALE	PRESENT	NO	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	7568	11.5	33.5	3.31	7200	53000	101.2	34.3	34.7
1033065	55	MALE	PRESENT	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	3472	14	40.7	4.03	12000	87000	101	34.4	34.7
1034894	35	MALE	PRESENT	NO	PRESENT	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	PRESENT	PRESENT	POSITIVE	POSITIVE	NEGATIVE	18675	10.6	34.5	4.21	2250	40000	81.9	30.7	25.2
1047772	18	MALE	PRESENT	PRESENT	PRESENT	NO	NO	NO	NO	NO	NO	NO	NO	NO	PRESENT	PRESENT	NEGATIVE	POSITIVE	NEGATIVE	145	16	48.4	5.29	10600	30000	91.5	33.1	30.2
1046553	65	MALE	PRESENT	NO	PRESENT	NO	NO	YES	NO	YES	NO	NO	NO	NO	PRESENT	NO	NEGATIVE	POSITIVE	NEGATIVE	5436	13.7	43.1	5.67	10.6	89000	76	31.8	24.2

ESR	NEUTROPHIL	LYMPHOCYTE	MONOCYTE	ESINOPHIL	IP NO	BASOPHIL	T.BILIRUBIN	D.BILIRUBIN	ALBUMIN	ALP	SGOT	SGPT	A/G RATIO	PT/INR	APTT RATIO	CREATININE	UREA	SODIUM	POTASSIUM	CHLORIDE	CHEST X RAY	ECG	DF	DHF	DSS
5	80	15	4	1	1023567	0	0.64	0.32	3.5	73	242	136	1.4	1.2	1.19	1.09	15	143	3.38	101	MILD PLEURAL EFFUSION	NSR	YES	NO	NO
5	80	12	8	0	1017270	0	1.26	0.61	3.6	144	128	38	1.7	1.24	1.19	0.95	27	138	2.48	99	NORMAL	NSR	YES	NO	NO
12	62	31	5	2	1029551	0	0.6	0.09	2.9	130	437	207	1.5	0.96	0.81	1.1	38	131	5.85	95	NORMAL	NSR	YES	NO	NO
25	64	31	5	0	1027902	0	1.55	0.87	3.6	83	282	186	1.1	1.03	1.15	0.72	19	138	3.91	103	B/L PLEURAL EFFUSION	BRADYCARDIA	YES	NO	NO
52	46	48	6	0	1023418	0	0.36	0.22	3.4	391	174	77	1.1	0.91	1.56	0.91	18	136	4.82	102	NORMAL	NSR	YES	NO	NO
22	66	32	0	2	1022910	1	0.42	0.15	3.5	200	99	68	1.3	1.02	1.53	3.71	84	138	5.45	101	B/L PLEURAL EFFUSION	TACHYCARDIA	NO	YES	NO
56	66	17	8	3	1021061	0	0.56	0.22	2.8	71	96	60	0.8	1.09	1.07	0.68	58	140	3.61	104	NORMAL	NSR	YES	NO	NO
10	68	22	5	5	5706492	0	0.9	0.4	4	193	120	19	2.4	1.04	1.12	0.9	24	137	3.8	105	NORMAL	NSR	YES	NO	NO
35	78	20	8	2	1019877	0	0.51	0.19	4	88	85	43	1.1	1.21	1.94	1.39	37	132	4.2	91	PLEURAL EFFUSION	NSR	NO	YES	NO
5	62	28	10	0	1012170	0	0.4	0.2	4	47	112	74	1.2	1.29	1.41	0.92	28	142	3.8	101	NORMAL	NSR	YES	NO	NO
49	91	7	2	0	1018679	0	4.09	3.43	2.8	176	79	70	1.1	1.16	1.12	4.75	111	131	4.74	88	NORMAL	NSR	YES	NO	NO
41	55	40	5	0	1031827	0	0.75	0.35	3.3	87	106	24	1.2	0.9	1.4	0.8	16	136	3.83	101	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
10	60	30	9	1	1021053	0	0.29	0.04	4.2	59	24	12	2.2	1.16	1.13	0.71	10	139	3.68	104	B/L PLEURAL EFFUSION	BRADYCARDIA	NO	YES	NO
56	66	17	8	3	1021005	0	0.56	0.22	2.8	71	96	60	0.8	1.09	1.12	0.68	58	140	3.61	104	NORMAL	NSR	YES	NO	NO
19	49	43	3	5	1021776	0	0.75	0.26	3.1	117	116	45	1.2	0.96	1.19	0.52	12	139	4.48	98	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
18	60	34	5	1	1020100	0	0.41	0.05	4	89	152	82	1.5	1.02	1.16	0.95	29	135	3.93	96	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
5	58	34	6	2	5930456	0	0.8	0.4	3.7	419	93	35	1.5	1.08	1.2	0.7	21	137	43	108	NORMAL	NSR	YES	NO	NO
6	68	16	6	0	1030291	0	0.6	0.29	4.8	60	51	36	1.5	1.03	1.02	1.25	26	131	4.23	86	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
3	60	20	2	1	1022660	0	4.7	3.17	3.2	159	519	195	1.3	1.29	2.15	1.87	79	139	4.97	99	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
50	70	23	7	0	1026738	0	0.46	0.26	3.5	134	123	89	1.3	1.14	1.18	0.72	28	136	4.32	96	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
3	61	28	6	5	1026916	0	0.78	0.35	3.6	59	74	45	1.3	1.17	1.07	0.84	13	141	3.89	99	NORMAL	NSR	YES	NO	NO
4	59	35	6	0	1028095	0	0.41	0.14	3.1	131	230	70	1.1	1.04	1.25	0.73	20	135	4.36	98	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
5	60	34	5	1	1028758	0	1.35	0.43	3.1	54	577	224	1.1	0.91	1.05	0.98	22	135	4.29	98	B/L PLEURAL EFFUSION	BRADYCARDIA	NO	YES	NO
4	56	34	10	0	1024514	0	0.89	0.4	4.5	46	118	84	1.9	1.08	1.29	0.98	29	134	5.02	95	NORMAL	NSR	YES	NO	NO
15	41	40	8	1	1030627	0	0.49	0.18	3.9	101	63	46	1.6	1.02	0.97	1.08	16	137	4.25	101	NORMAL	NSR	YES	NO	NO
14	75	13	2	0	1016382	0	0.33	0.25	2.8	143	251	134	1	0.82	0.99	0.39	10	143	4.07	109	NORMAL	NSR	YES	NO	NO
5	72	12	10	0	1025284	0	3.29	2.89	3.9	43	325	141	1.4	1.29	1.53	1.11	17	141	4.28	97	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
21	43	44	3	0	1031946	0	3.17	2.9	3.4	247	65	45	1.2	1.14	1.16	0.78	35	144	4.48	111	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
4	56	34	10	0	1024514	0	0.89	0.4	4.5	46	118	84	1.4	1.08	1.29	0.98	29	134	5.02	95	NORMAL	NSR	YES	NO	NO
4	59	35	6	0	1028073	0	0.41	0.14	3.1	131	230	70	1.1	1.04	1.25	0.73	20	135	4.36	98	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
10	76	18	4	2	1021170	0	0.42	0.12	2.8	131	235	70	1.1	2.27	1.01	3.59	156	147	3.98	107	NORMAL	TACHYCARDIA	NO	YES	NO
20	39	52	8	1	999998	0	0.45	0.27	3.8	50	336	245	1.3	1.22	1.02	0.53	10	135	4.26	93	NORMAL	NSR	YES	NO	NO
2	34	57	6	3	1028665	0	0.37	0.15	3.5	97	175	98	1.2	1.01	1.16	0.97	13	140	3.43	100	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
3	64	30	4	2	1027403	0	0.99	0.34	3.8	66	107	43	1.9	1.116	1.04	1.31	36	146	4.67	106	NORMAL	NSR	YES	NO	NO
3	78	14	8	0	1029225	0	0.52	0.15	3.7	71	107	88	1.1	1.19	01-Jan	0.98	21	130	3.27	90	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
27	86	9	5	0	1028745	0	2.37	2.14	2.7	332	90	55	0.9	1.18	0.94	0.87	79	141	4.36	103	NORMAL	NSR	N	YES	NO
5	79	13	2	1	1030096	0	1.65	1.07	3.6	76	390	185	1.6	0.94	0.95	0.9	24	133	3.11	90	NORMAL	NSR	YES	NO	NO
28	45	40	5	0	1042038	0	5.28	5.3	2.2	105	4541	946	1.2	1.48	1.18	1.09	58	140	4.81	102	B/L PLEURAL EFFUSION	SINUS TACHYCARDIA	NO	NO	YES
34	53	37	10	0	1051717	0	0.62	0.31	4	48	147	68	1.8	1.06	1.05	0.91	26	136	4.12	101	NORMAL	NSR	YES	NO	NO
8	55	35	8	2	1052263	0	0.6	0.3	3.4	210	106	39	1.4	1.1	1.02	1.4	51	133	3.1	104	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
14	48	42	7	3	1042841	0	0.3	0.25	3.5	157	363	275	1.5	1.28	0.98	0.6	15	136	3.87	139	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
18	80	13	7	0	1043959	0	4.44	4.26	2.9	120	3471	1444	1.4	2.03	1.74	1.29	68	132	6.06	99	NORMAL	TACHYCARDIA	NO	NO	YES
10	42	49	9	0	6022347	0	0.3	0.2	2.8	69	86	32	1.2	1.02	1.23	0.8	15	139	4.7	108	NORMAL	TACHYCARDIA	YES	YES	NO
24	77	16	7	0	1048529	0	1.9	1.18	2.1	306	15521	8056	1.3	4.5	5.6	2.99	70	142	5.48	102	B/L PLEURAL EFFUSION	SINUS TACHYCARDIA	NO	NO	YES
6	58	32	10	0	1050560	0	2.26	1.83	3.4	70	2729	1003	1.5	1	1.21	1.26	43	133	4.76	99	NORMAL	NSR	NO	NO	YES
10	70	20	10	0	1050741	0	0.65	0.33	3.8	93	110	83	1.4	1	1.21	1.95	73	123	3.76	85	NORMAL	TACHYCARDIA	YES	NO	NO
29	29	52	10	9	1050471	0	0.38	0.18	3.1	92	59	26	1	0.98	0.86	0.94	13	140	3.7	104	NORMAL	NSR	YES	NO	NO
8	63	30	4	3	1049033	0	1	0.5	2.7	91	62	39	0.9	1.43	1.1	0.7	23	132	6	103	NORMAL	NSR	YES	NO	NO
8	52	40	6	2	1049005	0	0.8	0.3	3.3	130	190	107	0.9	0.85	1.14	0.6	17	137	5.1	108	NORMAL	NSR	YES	NO	NO
10	37	55	7	1	1048432	0	1.3	0.4	3.3	152	215	122	1.3	1.25	1.32	0.8	13	140	4.3	103	NORMAL	NSR	YES	NO	NO
10	60	33	6	1	1041838	0	0.27	0.16	4.1	53	60	46	2	0.96	1.19	1.03	15	137	3.96	104	NORMAL	NSR	YES	NO	NO
10	94	6	0	0	1041593	0	0.59	0.25	5.3	97	26	29	1.8	0.95	1.17	0.84	14	135	4.51	97	B/L PLEURAL EFFUSION	SINUS TACHYCARDIA	NO	YES	NO
10	89	5	6	0	1052529	0	0.21	0.16	3.1	176	245	74	1.7	1.15	1.09	0.74	12	131	4.52	101	NORMAL	NSR	YES	NO	NO
30	39	56	3	2	1046010	0	0.4	0.2	3.4	100	206	109	1	1.42	0.82	0.9	18	140	3.9	110	NORMAL	NSR	YES	NO	NO
15	52	43	5	0	1031093	0	1.2	0.96	2.5	121	179	129	0.8	1.02	1.33	0.7	28	130	3.9	92	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
5	66	29	4	1	1029978	0	1.3	0.4	4	351	78	123	1.4	1.01	1.54	1	22	137	4.4	102	NORMAL	NSR	YES	NO	NO
18	92	6	2	0	1033065	0	0.7	0.2	3.6	102	34	31	2.3	1.28	0.85	0.7	26	134	4.2	100	NORMAL	SINUS TACHYCARDIA	YES	NO	NO
10	62	31	3	2	1034894	0	2.1	0.7	3.5	76	34	27	1.2	1.63	0.79	0.8	18	139	4	102	B/L PLEURAL EFFUSION	NSR	NO	YES	NO
5	77	12	10	1	1047772	0	1.44	0.41	4.3	41	13	10	2	1.24	1.14	0.86	15	143	4.39	110	NORMAL	NSR	YES	NO	NO
10	25	67	5	3	1046553	0	0.4	0.2	3.7	75	156	74	1	1 .10	1.56	0.9	18	137	4.5	102	NORMAL	NSR	YES	NO	NO