"CLINICAL AND ETIOLOGICAL PROFILE OF PATIENTS WITH ACUTE FEBRILE ILLNESS WITH THROMBOCYTOPENIA"

By

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DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA

In partial fulfillment of the requirement for the degree of

DOCTOR OF MEDICINE

IN

GENERAL MEDICINE

Under the guidance of

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MAY 2016

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Dr. SABARI GIRISH K

LIST OF ABBREVIATIONS

AMP	Adenosine Monophosphate
APP	Acute phase proteins
APR	Acute phase response
BBB	Blood brain barrier
CMV	Cytomegalovirus
CNTF	Ciliary Neuro Trophic Factor
CRP	C-reactive protein
CSF	Cerebrospinal Fluid
DF	Dengue Fever
DHF	Dengue Hemorrhagic Fever
DIC	Disseminated Intravascular Coagulation
DSS	Dengue Shock Sydrome
EDTA	Ethylenediamine tetraacetic acid
ELISA	Enzyme-linked immunosorbent assays
Gp	Glyco protein
HBV	Hepatitis B Virus
HIV	Human Immunodeficiency Virus
HSV	Herpes Simplex Virus
LPS	Lipopolysaccharide
ICAM	Inter cellular adhesion molecule
IgG	Immunoglobulin G
IFN	Interferons

IL	Interleukin
ITP	Idiopathic Thrombocytopenic Purpura
MAT	Microscopic agglutination test
NM	Not mentioned
PGE	Prostaglandins
POAH	Pre-optic/anterior Hypothalamus
RES	Reticuloendothelial System
RT PCR	Reverse Transcriptase Polymerase Chain Reaction
SAA	Serum amyloid A
TB	Tuberculosis
TTP	Thrombotic Thrombocytopenic Purpura
TNF	Tumour necrosis factor
vWF	von Willebrand factor

ABSTRACT

CLINICAL AND ETIOLOGICAL PROFILE OF PATIENTS WITH ACUTE FEBRILE ILLNESS WITH THROMBOCYTOPENIA

Background:

Fever is an easily noted and reliable marker of illness. Platelets play a central role in normal haemostasis and therefore also in thrombosis. Infections like dengue, leptospirosis, malaria, typhoid, miliary TB, HIV, septicemia are some of the common causes of fever with thrombocytopenia. Clinical manifestations commonly include petechiae, purpura, and gum bleed. Gastrointestinal bleed, intracranial bleed are rare complications. Early diagnosis and treatment of febrile illness with thrombocytopenia will prevent the complications like renal failure, hepatic dysfunction, acute respiratory distress syndrome, severe bleeding. Serial monitoring is said to have prognostic value. Hence this study.

Objectives:

To study clinical profile and etiological agents of the patients presenting with fever and thrombocytopenia.

To correlate thrombocytopenia grades with hemorrhagic manifestations.

Materials and Methods:

134 patients presenting with fever with thrombocytopenia are taken up for study. Inclusion criteria: 1) Age more than 18 years, 2) History of fever and 3) Oral temperature should be > 37.5^0 c. Exclusion criteria: 1)Patients who are on antiplatelet drugs. 2) Idiopathic thrombocytopenic purpura. The diagnostic work up of patients with fever and thrombocytopenia should include battery of investigations including biochemical tests; haemograms; peripheral smear. Platelet count was repeated serially on Day 1,Day 3,Day 5 and Day 7. The grading of the thrombocytopenia was done and correlated with presence of hemorrhagic manifestations.

Results:

32.8% were between age group 21-30 years. 51.5% were males and 48.5% were females. Mean duration of fever was 2.69± 1.7 days. All patients presented with fever, followed by vomiting(72.4%), myalgia (67.2%), headache(63.4%) and joint pains (12.7%). In our study 44.8% had bleeding manifestations. In that 27.6% presented with Conjunctival Hemorrhage, 17.9% with Bleeding Gums, 18.7% with Petechiae and 3% with Hematuria. In our study we observed that with increase in grade of platelet count there was increase in bleeding tendency. At presentation , In GRADE 1 no bleeding, in GRADE 2 4% had bleeding, in GRADE 3 62.8% had bleeding and in GRADE 4 86.5% had bleeding manifestations. This observation was statistically significant. In present study 64.9% were positive for Dengue, 19.4% were diagnosed to have Sepsis , 23.8% were positive for Malarial parasite, 6.7% had Mixed Infection and one case was positive for both sputum AFB samples. None were positive for Leptospira and Rickettsia. In subjects who had mortality had higher Blood urea, Serum creatinine, Total bilirubin, SGOT and SGPT.

Conclusion:

Our study shows that most common cause of fever with thrombocytopenia was Dengue followed by malaria and sepsis. Bleeding had a significant correlation in patients with GRADE 1 thrombocytopenia . Most common bleeding manifestation was conjunctival Hemorrhage followed by petechiae and gum bleed . Prognosis was good in 94% of subjects and were discharged and 6% had poor prognosis and died during the stay.

Key words – Fever ,Thrombocytopenia, Dengue, Malaria, Sepsis, Bleeding manifestations, Petechiae.

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INTRODUCTION

Fever has been recognized as a cardinal manifestation of disease since ancient times, as recorded by ancient scholars like Hippocrates.[1] Fever is an easily noted and reliable marker of illness.[2]

Normal body temperature displays a diurnal pattern with lower values in the early morning hours and higher values in the afternoon. Normal ranges are between 35.8°C (96.5°F) and 37.2°C (99°F). Fever is superimposed on this pattern and thus temperatures are usually greatest in the afternoon and evening.[2]

Fever is defined as an elevation of the body temperature above the normal circadian range as the result of a change in the thermoregulatory center located in the anterior hypothalamus.An AM temperature of >37.2°C (98.9°F) or a P.M. temperature of > 37.7°C (99.9°F) would define fever.3

Thrombocytopenia may result from impaired platelet production, accelerated platelet destruction and/or splenic sequestration. Infectious agents can also cause petechiea, purpura and diffuse bleeding manifestations through a variety of mechanisms including DIC, vasculitis, septic emboli , vascular toxins, direct vascular and endothelial invasion apart from thrombocytopenia.[3]

Thrombocytopenia is defined as platelet count <150,000/µl. At times the fever course is prolonged and fever with thrombocytopenia narrows the differential diagnosis of the clinical entity. Etiological agents include Malaria, Dengue, Chikungunya, Leptospirosis, Brucellosis, Enteric fever, HIV, miliary TB, Histoplasmosis, DIC, Gram negative and positive septicemia.[3]

Thrombocytopenia has an inverse relation to mortality and morbidity in various febrile illnesses, serial monitoring of platelet counts has prognostic value. This highlights the importance of thrombocytopenia in various febrile disorders. Early

diagnosis and treatment of febrile illness with thrombocytopenia will prevent the complications like renal failure, hepatic dysfunction, acute respiratory distress syndrome, severe bleeding.[4]

Hence this study.

OBJECTIVES

1) To study clinical profile and etiological agents of the patients presenting with fever and thrombocytopenia.

2) To correlate thrombocytopenia grades with hemorrhagic manifestations.

REVIEW OF LITERATURE

HISTORY OF FEVER

Sir William Osler stated humanity has three great enemies: fever, famine and war. Among these the most terrible is fever.

Carl Reinhold august Wunderlich defined the normal diurnal variation of the body temperature and gave the first quantitative definition of fever.[5] He described that fever can give more certainly than anything else information as to the grade of the disease. Because of his work, fever which was previously been viewed as a disease, came to be recognized more appropriately as a clinical sign.[5]

The concept of central set point temperature was introduced by Hammel HT who proposed an original neuronal model to explain regulation of set point temperature by preoptic nuclei. Heat production responses were shown to regulate near a Set-point of 37°C by the respective effector neurons. The term circadian was proposed by Franz Harberg in 1950's to denote daily cycles.[6]

In 1948, Kleitmann and Ramswaroop provided information concerning endogenous and exogenous influences on the diurnal rhythm of core temperature. In most of their subjects there was a 12 hr difference between the maximum and minimum observed temperatures.

The current concept of fever physiology is that, host cell derived molecules induce fever, which usually occurs in the context of an overall inflammatory response directed against pathogenic microbes. The host derived molecules responsible for fever used to be known as endogenous pyrogens as first demonstrated by Paul Beeson in 1948. He described temperature elevating effect of a substance obtained from polymorpho-nuclear leucocytes.[6]

Kluger and co-workers stated that endotoxin induced fever is mediated by interleukin -1b with induction of IL-6, suggesting that IL-6 might be the final common pathway for such fever.[7] Milton and Wendlandt proposed that E- series prostaglandins (PGE) might mediate the febrile response to pyrogens. This consensus of opinion still favors the proposition that PGE2 the endogenous isoform of PGE plays an essential role in fever production.[8]

Rotondo et al. proposed that PGE2 involved in fever might be generated peripherally, transported to pre-optic/anterior hypothalamus (POAH) by the blood stream and then being lipophilic, either cross the Blood Brain Barrier (BBB) at this site or diffuse to POAH through the organum vasculosum laminae terminalis to cause the induction of fever.[8]

PATHOPHYSIOLOGY OF FEVER

Body temperature is regulated around a set point of 36.8±0.4°C, and a circadian temperature rhythm exists in which the highest temperature of each day occurs around 6.00 pm. The variance between the highest and lowest core temperature in a given day is usually no more than 1^0C-1.5^0C.[9]

Fever is a physiological disorder in which temperature is elevated above the normal temperature. An elevated body temperature may accompany any condition in which endogenous or exogenous heat gain exceeds mechanisms of heat dissipation such as occurs with vigorous exercise, exposure to a warm ambient temperature, or the use of drugs that cause excess heat production or limit heat dissipation.

Fever is an elevation of body temperature that exceeds the normal daily variation and occurs in conjunction with an increase in the hypothalamic set point. Once the hypothalamic set point is raised neurons in the vasomotor centre are activated and vasoconstriction occurs. The individual first notices vasoconstriction in

the hands and feet. Shunting of blood away from the periphery to the internal organs decreases heat loss from the skin and the person feels cold. Shivering increases heat production from the muscles, however shivering is not required if heat conservation mechanisms raise blood temperature sufficiently.[10]

Process of heat conservation and heat production continue until the temperature of the blood bathing the hypothalamic neurons matches the new thermostat setting. Once that point is reached, the hypothalamus maintains the temperature at the febrile level by the same mechanisms of heat balance that functions in the afebrile state.

When the hypothalamic set point is again reset downward in response to either a reduction in the concentrations of pyrogens or the use of antipyretics, the process of heat loss through vasodilatation and sweating are initiated, loss of heat by sweating and vasodilatation continues until the blood temperature at the hypothalamic level matches the lower setting.

In order to maintain a relatively constant internal body temperature, fine balance between heat loss and heat production must be maintained so that any increase or decrease of one is promptly compensated by a similar increase or decrease of the other. Maintenance of body temperature with in a normal range is accomplished by a number of physiological process, involving both chemical and physical heat transfer. The operation of these mechanisms is integrated at various levels in the central nervous system.[11,12]

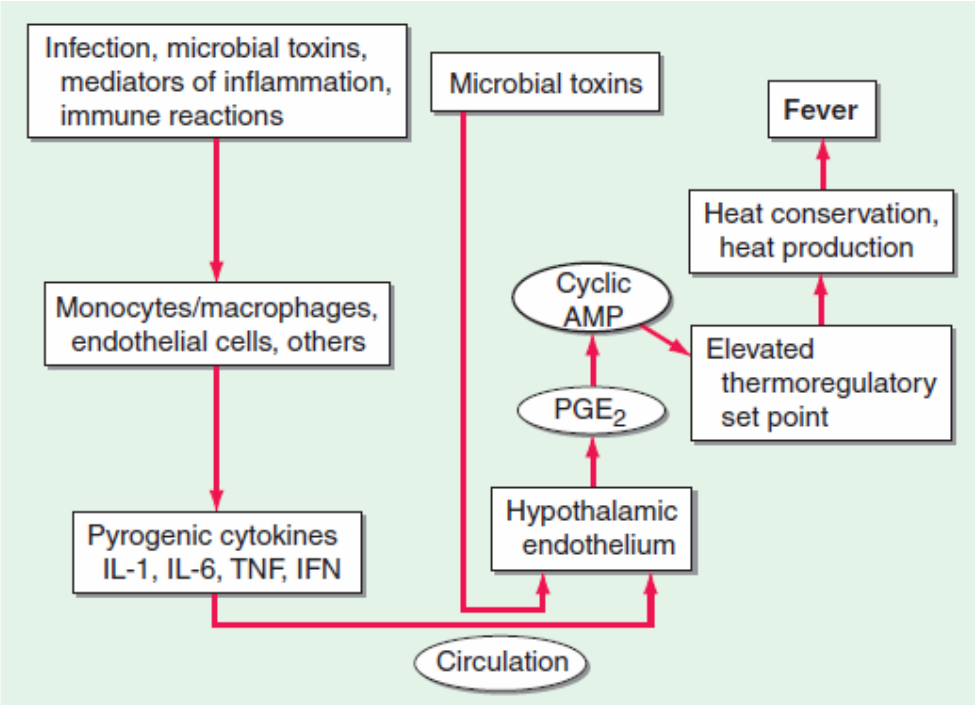
It is important to distinguish between fever and other causes of hyperthermia where, an elevation of body temperature above the hypothalamic set point due to insufficient heat dissipation.[11,12]

Heat production takes place through physiological oxidation of food materials in the body, combustion of carbohydrates, fats and proteins. The contribution of various organ systems to the total heat production varies according to circumstances.[11]

During physical work one generates much additional heat in the muscles. Heat production in the muscular systems has important role in temperature regulation because it is adopted to maintain uniform body temperature being readily increased or decreased according to the need.[11]

Heat is lost from the body by three channels. They are: 1. Skin 2. Lungs and 3. Excretions – mainly through conduction, radiation, evaporation and convection.[11,12]

IMAGE 1 : PATHOPHYSIOLOGY OF FEVER[9]



THERMOSTASIS :

Thermoregulation is controlled by a neutral structures and connections extending from the hypothalamus and limbic system to the lower brain stem and reticular formation, to the spinal cord and to the sympathetic ganglia. The preoptic region is sensitive to its own temperature and controls virtually all thermoregulatory responses, it is often described in terms of a negative feedback loop in a control system that regulates around a set-point temperature It integrates central and peripheral thermal information, apparently responding to such information by shifting the pre optic set point temperature.

Body temperature is mainly controlled by the hypothalamus. The hypothalamic thermoregulatory center balances the excess heat production derived from the metabolic activity in muscle and the liver with heat dissipation from the skin and lungs.

Heat regulating centre lies in the preoptic and the adjacent nuclei of the anterior hypothalamus in a small area called Thermostatic centre of the body.[9,11] Neurons in this centre becomes powerfully excited if the temperature of the hypothalamic tissue rises above normal. These neurons emit signals which increase heat loss, while at the same time decreasing heat production. As a result the body temperature falls towards normal. Conversely when the body temperature falls below normal, the thermosensitive cells becomes less excited which now elicits opposite signals decreasing the rate of heat loss and increasing the rate of heat production, thus increasing the body temperature towards normal. Lesions of the anterior hypothalamus abolishes these reactions and leads to loss of power to withstand high temperature.[9,13,14]

Spinal cord is the connecting path between heat regulating centers in the hypothalamus, peripheral thermoreceptors and effector organs, the cervical part of the sympathetic outflow which regulates peripheral circulation and heat regulation. Effect of section of spinal cord depends on the level. When the section of the cord is above or through the level of sympathetic outflow, gross disturbance of temperature regulation appears. Transection of spinal cord from the level of the upper thoracic segments downwards abolishes sweating and shivering below the level of transection.

EXOGENOUS PYROGENS

Cytokines IL-1, tumor neurosis factor and IL-6 account for endogenous pyrogen activity, exogenous pyrogens by themselves do not cause fever unless they elicit cytokine release. There are many different substances capable of causing fever in humans, micro organisms (primary cell wall components) microbial toxins, antigen antibody complexes, activated compliment components (c3a,c5a), pyrogenic steroids (etiocholanolone), drugs, polynucleic acids. Gram negative bacteria possess 2 known pyrogens – lipopolysaccharide [Lps] which is component of the bacterial outer membrane and peptidoglycan, which forms cross link lattice below the outer membrane.

Gram positive bacteria lack LPS, but contain peptidoglycan, lipotechoic acid and a group of rhamnose glucose polymers. The basic structure responsible for peptidoglycans pyrogenecity is muramyl peptide. Gram positive bacteria release exotoxins which can also cause fever. Exotoxins act by binding to major histocompatibility complex – class 1 molecules on antigen presenting cells, which is then able to bind to T-cell receptor, which then becomes activated and release TNF and 1L-1. The ability of exotoxins to activate large numbers of T-cells has led to its designation as superantigen.

ENDOGENOUS PYROGENS

Endotoxin is an example of a pyrogen that can act both directly on the hypothalamus to cause fever and induce endogenous pyrogens synthesis in various host cells which then induce fever.[7]

Cytokines are peptides released from connective tissue, inflammatory tissue, and immune system cells. They act by autocrine and paracrine mechanisms. Cytokines that are secreted from lymphocytes are called lymphokines. Those secreted by monocytes and macrophages are called monokines. Lymphokines are also known as interleukins, since they are not only secreted by leukocytes but also able to affect the cellular response of the leukocytes. Specifically interleukins are growth factor targeted to the cells of the hematopoietic origin.

L-1a, IL-1b, TNF-beta, 1FN-alpha, 1L-6 are known to be intrinsically pyrogenic they produce rapid onset of fever by acting directly on the hypothalamus. These now include a family of cytokines using the cell signaling apparatus gp-130. Antigen–antibody complexes, inflammatory bile acids and some lymphocyte products are endogenous molecules can also induce endogenous pyrogens not requiring an exogenous stimuli.

INTERLEUKIN - 1

Inducing gene expression for cycloxygenase is one of the most potent pro-inflammatory properties of IL-1 resulting in the synthesis of large amounts of prostaglandins. IL-1 activates cultured vascular endothelial cells at relatively at low concentrations by inducing expression of inter cellular adhesion molecule (ICAM-1) on the cell surface. This molecule interacts with the leukocyte glycoprotein complex designated leukocyte function antigens.[7]

PROSTAGLANDIN E2

PGE 2 the endogenous isoform of PGE plays an essential role in fever production. Induction of PGE2 is triggered by peripheral signals evoked by early, non cytokine factor elicited in response to infectious challenge.

During fever, in the hypothalamic tissue and in the third cerebral ventricle levels of PGE2 are elevated. The concentrations of PGE2 are highest near the circumventricular vascular organs (organum vasculosum of lamina terminalis) networks of enlarged capillaries surrounding the hypothalamic regulatory centers. Pyrogenic cytokines such as IL-1, IL-6 and TNF are released from the cells enter systemic circulation. The systemic effects of these circulating cytokines lead to fever by inducing synthesis of PGE2. They also induce PGE2 in peripheral tissues, the increase in PGE2 in the periphery accounts for the non-specific myalgia and arthralgia that often accompany fever. It is thought that some systemic PGE2 escapes destruction by lung and gain access to the hypothalamus via the internal carotid. It is the elevation of PGE2 in the brain that starts the process of raising the hypothalamic set point for core temperature.[8]

INTERFERONS

Interferons were the first cytokines administered to humans. Fever was a prominent effect of interferon therapy. In addition to antiviral activities IFN has several biological activities. These include important effects such as their capacity for increasing natural killer activity and enhancing expression of class I and II MHC antigens. Recombitant human IFN injected into humans at a dose of 10-100 u/kg causes chills and fever within 2 hrs.

Non-infectious diseases like vasculitis, rheumatoid arthritis, Lupus, trauma, haemorrhage, thrombophlebitis, drug fever and cancer will produce fever by concept

of cytokines inducing other cytokines in which both fever and acute phase response are common. Fever is also a prominent side effect of cancer chemotherapy.

Rejection with antibodies to CD3 is also associated with fever. It has been implicated that in all these diseases cytokines such as IL-1, TNF and IL-6 are involved in pathogenic process.

TUMOUR NECROSIS FACTOR (TNF)

TNF is a macrophage product that is directly cytotoxic for certain tumor cells. Human TNF has been cloned and has the same amino acid sequence as another macrophage product called cachectin. Recombinant IL-1 and recombinant TNF both stimulates synovial cell production of PGE and collagenases, endothelial cell procoagulant activity and release of platelet activating factor. Both molecules are cytotoxic for certain tumor cells and both induce hepatic acute phase response.

TNF also has the property of inducing the production of IL-1 in vivo. TNF increases PGE2 production within 30 min. This property is shared by 1L-1. The systemic response to LPS appears to be mediated by TNF. IL-6 production is stimulated by IL-1 and TNF. IL- 6 belongs to a family of cytokines that triggers cells via the glycoprotein (gp) 130 signaling apparatus. These receptors are present on nearly all cells. Pyrogenic cytokines such as IL-6, IL-11, oncostatin–m, CNTF, cardiotrofin-1 all use these receptors.[7]

ACUTE PHASE RESPONSE

Several inflammations are accompanied by a large number of systemic changes referred to collectively as acute phase response (APR). The APR consists of substitution of new set points for the homeostatic mechanisms that normally maintain

a constant internal environment during good health and is presumed to play a major role in adaptation and defense. APR may be transient, dissipating with recovery or can persist in chronic disease resulting in chronic APR.

Stimuli that commonly give rise to acute phase reactants include bacterial, viral infections, surgical or other trauma, neoplasms, tissue infection and various immunologically mediated inflammatory states.

Fever is only one of the changes in homeostatic settings that occur during APR. Anorexia, changes in plasma protein synthesis and altered synthesis of many endocrine hormones are other changes. In addition negative nitrogen balance, gluconeogenesis, decreased levels of zinc and iron and increased level of copper occurs.

There is leucocytosis and thrombocytosis, decreased erythropoesis resulting in what is commonly called anemia of chronic disease.

The c-reactive protein (CRP) and serum amyloid A (SAA) are two major human acute phase proteins (APP) whose levels are increased by greater than 1000 fold in the plasma following stimulation in infected individuals. Positive APP (levels increased) are Ceruloplasmin and the complement components C3, C4 and other negative APP (levels decreased/synthesis decreased) are albumin, trans thyretin, alpha2 – HS glycoprotein.

C-Reactive Protein (CRP)

The major function of CRP has been presumed to be related to its ability to bind specifically to phosphocholine and thus recognize some foreign pathogens as well as phospholipid constituents of damaged or necrotic cells. The CRP protein can then activate the complement system.

FEBRILE PATTERNS

Fever is a reliable clinical sign and with the fever pattern it is possible to suggest a diagnosis within the group of disease and this can lead to specific therapy and ultimate cure.

1. Continous fever[3,15] – fever does not fluctuate more than about 1°C during 24 hrs but at no time touches the normal.
2. Remittent fever[3,15] – fever with daily fluctuation exceeding 2°C in 24 hrs but never touches the baseline.
3. Intermittent fever[3,15] – when fever is present only for several hours during the day. When a paroxysm of intermittent fever occurs daily, the fever is described as quotidian, when one day intervenes between consecutive attack it is tertian, when 2 days intervene between consecutive attacks it is quartan. Eg: malaria, localized pyogenic infection and bacterial endocarditis.
4. Saddle back fever[3,15] – with several days of fever, a gap of reduced fever of about 1 day and then several additional days of fever – seen in dengue and yellow fever.
5. Relapsing fever[3,15,16]– short febrile periods punctuating one or several days of normal temperature.

HIISTORY OF THROMBOCYTOPENIA

Since the time of Hippocrates, multiple cutaneous bleeding signs have been described as purpura. In Latin literature, the word purpura (from Greek porphyra) signifies the Precious purpledye, secreted by the purple snail, used as a status symbol during Antiquity in the middle Ages. Without knowledge of the different blood components and functions of course, no differentiation of bleeding signs was possible.

Krauss (1883) and Denys (1887) stated that platelets were diminished during the height of the purpura and increased when the haemorrhages ceased. These findings were confirmed by Hayem in (1895) who was able to perform more accurate platelet counts. Later, Henoch (1899), at that time Professor of Paediatrics in Berlin, differentiated purpura simplex with bleeding signs of the skin only (today known as dry purpura) from purpura haemorrhagica with mucosal bleeding (today known as wet purpura).

In 1557, Amatus Lusitanus mentioned a condition Morbus pulicaris absque febre (without fever). Lusitanus was born in Portugal, studied medicine at the University of Salamanca and had to flee from one country to another because of religious persecution. In his work Curationum medicinalum, he describes a boy with dark macules, resembling flea bites, had no fever and for several days had bloody discharges, eventually recovering.

Lusitanus further speculated whether the rash was due to nervous anxiety or an exudation of detrimental humors. What Lusitanus described could have been thrombocytopenic purpura.

In the early 17th century, Riverius attempted to distinguish purpura from pestilential fever or from a vitious quality of the blood or humors joined with malignity. In his Praxis medica, he described the spots arisen from the over thinness of the blood does sprout forth of the capillary veins into the skin where being retained, it loses its own color, and becomes either bluish or black, or light red, and causes great variety of spots.

In Jena, Hornung (1734) subdivided purpura into simplex, febrile and scorbutica, and 1 year later Paul Werlhof, poet, composer, linguist and physician,

described the disorder under the name of Morbus Maculosus Haemorrhagicus (Werlhof, 1735).

Werlhof described in a footnote a 16-year-old girl with cutaneous and mucosal bleeding which occurred after an infectious disease and recovered with citric acid.

The histogenesis of platelets from megakaryocytes was first described by John Wright in 1910. Adelson E described platelets as sponges in the year 1961. Behnke O described the electron microscope structure of platelet membrane in the year 1968.

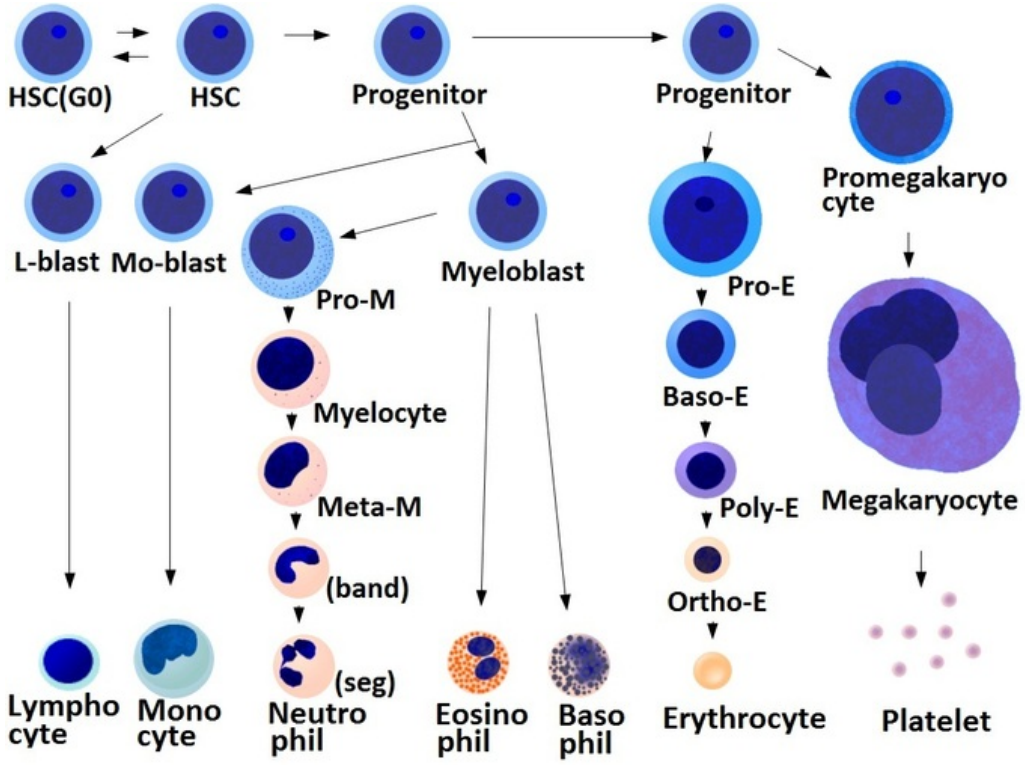
Penington DG ,Oslen TE, Fauser AA, Ebbe S, Yee T showed that thrombopoiesis is regulated by humoral mechanisms. Whenever there is a decrease in the platelet count either due to immune destruction on increased removal, megakaryocytes respond by an increase in number, size, ploidy and increase in the rate of maturation.

An estimated 15000000 megakaryocytes /kg body weight, averaging 12000 fl in volume, produce approximately 1000–1500 platelets each. Platelet counts normally range between 1.5 lakhs to 4.5 lakhs per microlitre and a count below 1.5 lakh is generally considered to constitute thrombocytopenia.

PLATELETS AND THROMBOPOISESIS

Platelets are the terminal stage of development of megakaryocyte series. Platelets are small, anucleate cells, they are formed in the bone marrow by megakaryocytes and released in to vascular compartment where they play an essential role in hemostasis.

IMAGE 2 : IMAGE OF HEMOPOIESIS



The most immature is the megakaryoblast which accounts for less than 8% of megakaryocyte population. The megakaryocyte population in total forms less than 1 % of Bone marrow cells.

Next stage is promegakaryocyte, they make up 25% of megakaryocyte population. These cells are nucleated and have basophilic cytoplasm. Next stage is the mature megakaryocytes which range from 30-90 μm in diameter and contain 4-16 nuclear lobes. Platelets appear to be formed by protrusion in to the bone marrow sinusoids of pseudopods of megakaryocyte cytoplasm. These pseudopods detach in the blood stream to yield small discoid platelets which play a role in hemostasis.

Each megakaryocyte can give rise hundred to thousand platelets .[17]

A mature platelet is 2-4 micrometer in diameter. Volume is 7.06± 4.85 micro m^3.

Thickness is 0.9 +_0.3 μm.

The normal life span is 8-12 days.

In the stored blood life span is 1-2 days.

Platelet turnover is 1.2-1.5 x 10^{11} /day

Once released from the marrow platelets are trapped in the marrow for 36 hours. 60-75% of the circulating platelets are in the blood. The remainder is in the spleen. Normal values for platelet numbers in peripheral blood vary with the method used for their estimation.

Normal range is 1.5 lakhs - 4.5 lakhs /cumm.

FUNCTIONS OF PLATELETS

1. Hemostasis :- Immediate reaction following vascular injury is vasospasm. Next reaction is formation of platelet plug.

   Following endothelial injury, platelets come is contact with subendothelial collagen, vWF and proteoglycans in the vessel wall. They exhibit 3 reactions

a) Adhesion

b) Secretion and activation. The activated platelets change shape, put out pseudopodia and discharge their granules.

c) Aggregation. The activated platelets stick to one another which is called aggregation.

   Aggregation is also fostered by platelet activating factor. Primary platelet plug gets formed which gets reinforced by fibrin to form stable platelet plug.

2. Growth factors that secreted by platelets cause vascular endothelial cells, vascular smooth muscle cells and fibroblasts to multiply and grow that helps repair damaged vascular walls.

3. They maintain the capillary integrity. This is evident by the fact that in thrombocytopenia due to any cause endothelium thins out with development of more fenestrations.

Under normal circumstances, hemostasis is regulated to promote blood flow; it is also prepared to clot blood rapidly to arrest blood flow and prevent exsanguination.

After bleeding is successfully halted, the system remodels the damaged vessel to restore normal blood flow.

The major components of the hemostatic system, which function in concert, are

1. Platelets and other formed elements of blood, such as monocytes and red cells
2. Plasma proteins (the coagulation and fibrinolytic factors and inhibitors) and
3. The vessel wall itself.

PLATELET PIUG FORMATION

Following vascular injury, platelets adhere to the site of injury, usually the denuded vascular intimal surface. Platelet adhesion is mediated primarily by von Willebrand factor (vWF), a large multimeric protein present in both plasma and in the extracellular matrix of the subendothelial vessel wall, providing sufficient strength to withstand the high levels of shear stress that would tend to detach them with the flow of blood. Platelet adhesion is also facilitated by direct binding to subendothelial collagen through specific platelet membrane collagen receptors.

Platelet adhesion results in subsequent platelet activation and aggregation. This process is enhanced by humoral mediators in plasma like epinephrine,thrombin; mediators released from activated platelets like adenosine diphosphate, serotonin; and vessel wall extracellular matrix constituents that come in contact with adherent platelets (e.g., collagen, vWF). Activated platelets undergo the release reaction,

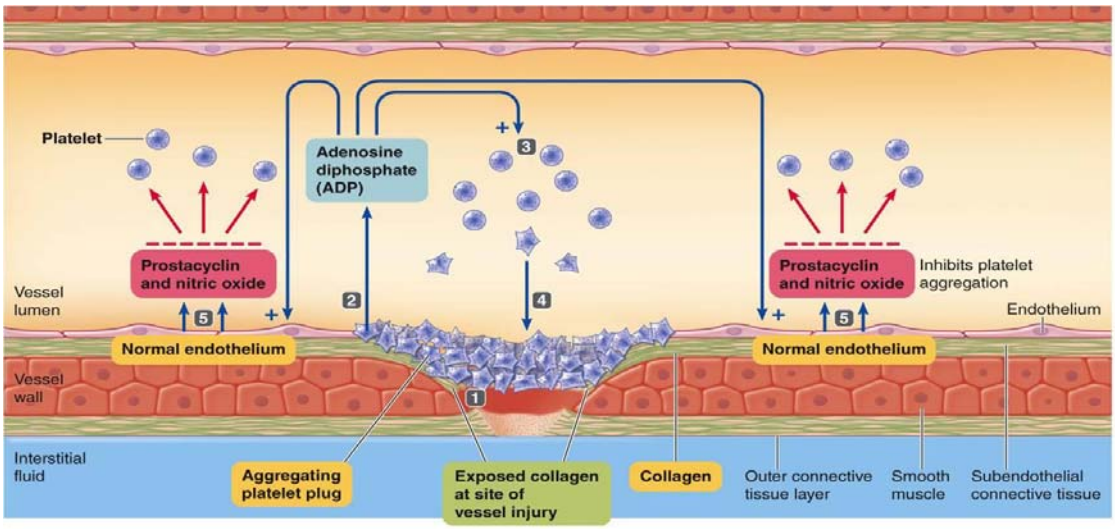
during which they secrete contents that further promote aggregation and inhibit the naturally anticoagulant endothelial cell factors. During platelet-platelet interaction additional platelets are recruited from the circulation to the site of vascular injury, leading to the formation of an occlusive platelet thrombus. The platelet plug is anchored and stabilized by the developing fibrin mesh. The platelet glycoprotein (Gp) IIb/IIIa complex is the most abundant receptor on the platelet surface. Platelet activation converts the normally inactive GpIIb/IIIa receptor into an active receptor, enabling binding to fibrinogen and vWF. Because the surface of each platelet has about 50,000 GpIIb/IIIa fibrinogen binding sites, numerous activated platelets recruited to the site of vascular injury can rapidly form an occlusive aggregate by means of a dense network of intercellular fibrinogen bridges. Since this receptor is the key mediator of platelet aggregation, it has become an effective target for antiplatelet therapy.

Fibrin Clot Formation

Plasma coagulation proteins (clotting factors) normally circulate in plasma in their inactive forms. The sequence of coagulation protein reactions that culminate in the formation of fibrin was originally described as a waterfall or a cascade. Two pathways of blood coagulation have been described : extrinsic or tissue factor pathway and the so called intrinsic or contact activation pathway.

Coagulation is normally initiated through tissue factor (TF) exposure and activation through the classic extrinsic pathway, but with critically important amplification through elements of the classic intrinsic pathway. These reactions take place on phospholipid surfaces, usually the activated platelet surface.

IMAGE 3: IMAGE OF PLUG FORMATION



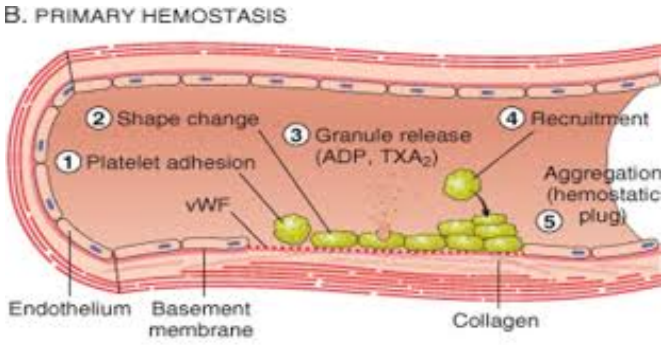
1 Platelets adhere to and are activated by exposed collagen at the site of vessel injury.

2 Activated platelets release ADP.

3 ADP activates other platelets passing by.

4 Newly activated platelets aggregate onto growing platelet plug and release even more platelet-attracting chemicals.

5 Normal (uninjured) endothelium releases prostacyclin and nitric oxide, which inhibit platelet aggregation, so platelet plug is confined to site of injury.



THROMBOCYTOPENIA

Thrombocytopenia defined as subnormal number of platelets in circulating blood, which are counts below the normal limits of 1.5lakhs.[18]

Thrombocytopenia can result from 4 processes.

1. Accelerated platelet destruction
2. Deficient platelet production
3. Abnormal distribution or pooling of platelets within the body.
4. Artifactual Thrombocytopenia

A single platelet count that is lower than normal should always be confirmed by a second count. Thrombocytopenia should also be confirmed by the examination of blood film. The electronic particle counters now widely employed gives accurate results.

Thrombocytopenia is characterized by bleeding most often form small vessels. This bleeding can manifest as petechiae over the skin, hemorrhages from mucosa of gastrointestinal or genitourinary tract. Intracranial haemorrhage is a dangerous consequence in thrombocytopenic patients.

CAUSES OF THROMBOCYTOPENIA

Decreased marrow Production

- Marrow infiltration with tumor, fibrosis
- Marrow failure- aplastic, hypoplastic anemias, drug effects
- Splenic sequestration of circulating Platelets
- Splenic enlargement due to tumor infiltration
- Splenic congestion due to portal hypertension

- Increased destruction of circulating Platelets

  Non-immune destruction

- Vascular prostheses, cardiac valves
- Disseminated intravascular coagulation
- Sepsis
- Vasculitis Immune destruction.
- Autoantibodies to platelet antigens
- Drug-associated antibodies
- Circulating immune complexes
- Systemic lupus erythematosus, viral agents, bacterial sepsis.

INCREASED PLATELET DESTRUCTION

The most common cause of thrombocytopenia is accelerated platelet destruction. It leads to stimulation of thrombopoiesis and consequently to an increase in the size, number and rate of maturation of precursor megakaryocytes.

When destruction exceeds the compensatory increase, thrombocytopenia results. Platelet destruction can occur both intracorpuscular and extracorpuscular. Intracorpuscular destruction is rare and is seen in some forms of hereditary thrombocytopenia such as Wiskott Aldrich syndrome. Platelet destruction is most often the result of extracorpuscular destruction and in this immunologic phenomena are most important.

Mechanisms of platelet destruction

1. Immune mediated

a) Autoantibody-mediated platelet destruction via reticuloendothelial system (RES) Example: ITP[19]Secondary - lymphoproliferative disease, collagen vascular disease, infections such as infectious mononucleosis, HIV

b) Alloantibody – mediated platelet destruction via RES Example: Neonatal alloimmune thrombocytopenia; post transfusion purpura.[20]

c) Antibodies against microbial antigens adsorbed onto platelets Example : Malaria-associated thrombocytopenia.[21]

d) Drug-dependent,antibody-mediated platelet destruction via RES Example : Drug-induced immune thrombocytopenic purpura (quinine, quinidine, sulfa drugs, vancomycin, etc).[22]

e) Platelet activation by binding of IgG Fc of drug-dependent IgG to platelet FcRIIa receptors Example: Heparin induced thrombocytopenia.[23]

2. Non-immune mediated

a) Platelet activation via thrombin or inflammatory cytokines Example: DIC,[24] septicemia and other systemic inflammatory response syndromes (adult respiratory distress syndrome, fat embolism, pancreatitis).

b) Platelet destruction via ingestion by macrophages (heamophagocytosis) Example : Infections, malignant lymphoproliferative disorders.[25]

c) Platelet destruction via platelet-activating proteinase

Example: Thrombotic thrombocytopenic purpura, haemolytic uraemic syndrome .[26,27]

DECREASED PLATELET PRODUCTION

Disorders that injure stem cells or prevent their proliferation frequently causes thrombocytopenia. Multiple cell lines get affected so that thrombocytopenia accompanied by varying degrees of anaemia and leucopenia, although thrombocytopenia may be the initial manifestation.

Most common cause of decrease production is marrow aplasia, marrow fibrosis or infiltration with malignant cells, ineffective thrombopoiesis, disorders of thrombopoietic control . Defect is readily established by Bone Marrow aspiration or Bone Marrow biopsy.[28]

ABNORMAL PLATELET POOLING

1. Disorders of spleen (Neoplasm, congestive, infiltrative)
2. Hypothermia.
3. Dilution of platelets with massive transfusions.

ARTIFACTUAL THROMBOCYTOPENIA

Falsely low platelet counts can sometimes result, this is called Artifactual thrombocytopenia. This should be considered in patients with low platelets but no petichiae or ecchymosis.

Causes of artifactual thrombocytopenia are:

- Platelet satellitism[29,30]
- Giant platelets

Platelet satellitism:

Platelet satellitism is a phenomenon of platelet rosetting around polymorphonuclear neutrophils, is observed in blood treated with EDTA as an anticoagulant at room temperature. Neither heparin nor citrate produces rosetting.

The proposed mechanisms include immunologic bonding through EDTA dependent antiplatelet and antineutrophil IgG autoantibodies directed against the glycoprotein IIb/IIIa complex and Fc γ receptors of platelets and neutrophils. Phagocytosis of platelets by polymorphonuclear leukocytes and monocytes is sometimes seen. Severe platelet satellitism is an important cause of spurious thrombocytopenia.

Giant platelet :

A platetet that is larger than usual, up to 10% of normal platelets are giant; when > 20% of platelets are giant, conditions considered are Bernard-Soulier syndrome–

BSS , ITP, lympho- and myeloproliferative disorders, reticulocytosis, DIC, SLE, gray platelet syndrome, May-Hegglin anomaly, Montreal platelet syndrome, TTP.

THROMBOCYTOPENIA ASSOCIATED WITH INFECTION :

Infection is a common cause of thrombocytopenia, occurring in approximately 50–75 % of patients with bacteremia or fungemia, and patients with septic shock or DIC.[31] Even when caused by bacteremia, the thrombocytopenia is generally mild to moderate in severity, and usually not accompanied by significant coagulation abnormalities or bleeding. chemokine-induced macrophage ingestion of platelets

(hemophagocytosis) and direct activation of platelets by endogenous mediators of inflammation (e.g., plateletactivating factor)[32]or certain microbial products[33] are mechanisms for thrombocytopenia in septicemia in the absence of DIC.

Prompt recognition and treatment of the infection is most important, as platelet count recovery tends to parallel the resolution of the infection. Prophylactic platelet transfusions are not required unless the plateletcount falls to <10 × 109/L, or unless comorbid clinical features increase the likelihood of serious bleeding (e.g., concomitant coagulopathy, an invasive procedure, uremic platelet dysfunction).

Immune platelet destruction, impaired platelet production secondary to HIV infection of megakaryocytes, drug- induced myelosuppression (commonly, zidovudine, ganciclovir, and trimethoprim / sulfamexthoxazole), HIV- associated thrombotic microangiopathy, hypersplenism, and marrow infiltration by tumor or opportunistic infections are potential causes of thrombocytopenia in HIV patients.[34]

Viral causes :

Dengue, HIV , CMV, HSV, Parvo-B19 , Hanta virus etc.[35] Viruses produce thrombocytopenia by impaired platelet production as a result of invasion of megakaryocytes by the virus, toxic effects of viral protein on progenitor cells, virus induced haemophagocytosis, destruction of circulating platelets by viruses – by viral antigen antibody complexes.[36]

Bacterial causes :

Gram positive and gram negative septicemia, leptospirosis, miliary tuberculosis, typhoid , mycoplasma pneumonia.[35,37]

Septicemia resulting from both gram negative and gram positive is the commonest cause of thrombocytopenia. It may be caused by disseminated intravascular

coagulation (DIC) and the diagnosis of DIC may be apparent when coagulation studies are performed.[38]

Disseminated intravascular coagulation (DIC) is a complex systemic thrombohemorrhagic disorder involving the generation of intravascular fibrin and the consumption of procoagulants and platelets. The resultant clinical condition is characterized by intravascular coagulation and hemorrhage.

DIC defined as an acquired syndrome characterized by the intravascular activation of coagulation with loss of localization arising from different causes. It can originate from and cause damage to the microvasculature, which if sufficiently severe, can produce organ dysfunction.[39]

DIC is a complication or an effect of progression of other illnesses and is estimated to be present in up to 1% of hospitalized patients.[40] DIC is associated with a number of clinical conditions and always secondary to an underlying disorder, generally involving activation of systemic inflammation. DIC has several consistent components including activation of depletion of clotting factors, intravascular coagulation, and end-organ damage. DIC is most commonly observed in severe sepsis and septic shock. Indeed the development and severity of DIC correlates with mortality in severe sepsis.[41,42]

Although bacteraemia, including both gram-positive and gram-negative organisms, is most commonly associated with DIC, other organisms including viruses, fungi, and parasites may cause DIC.

Platelets adherence to damaged vascular surfaces also accounts for thrombocytopenia in certain bacterial infections, such as meningococcemia. Endotoxin, exotoxin, platelet activating factor may damage platelets, resulting in increased clearance.

Protozoal causes :

Thrombocytopenia occurs in over 80% of patients with malaria and human platelets have been demonstrated to contain plasmodia species.[35] It was immune mediated destruction with elevated platelet activated immunoglobulin. It was demonstrated that ultra structural changes in platelets, and the level of parasitemia was the cause for thrombocytopenia. Antibodies against microbial antigens adsorbed onto platelets.

DENGUE

INTRODUCTION :

The first confirmed case report dates from 1789 and is by Benjamin Rush, who coined the term "breakbone fever" because of the symptoms of myalgia and arthralgia. The viral etiology and the transmission by mosquitoes were discovered in the 20th century by Sir John Burton Cleland.

Dengue infections caused by the four antigenically distinct dengue virus serotypes (DENV1, DENV2, DENV3, DENV4) of the family Flaviviridae. The infection is transmitted from person to person by Aedes mosquitoes. Dengue infections may be asymptomatic or may lead to an undifferentiated fever, dengue fever or dengue haemorrhagic fever (DHF).[43] Each year there are an estimated 50–100 million dengue infections, 500 000 cases of DHF and 20 000 deaths, mainly children.

Clinical features of classical dengue[44]

After an incubation period of 5–8 days following an infective mosquito bite, the disease in adults begins with a sudden onset of fever with severe headache, and any of the following: chills, pain behind the eyes – particularly on eye movement or eye pressure-photophobia, backache, and pain in the muscles, bone and joints of the extremities. The temperature is usually high (39–40°C); the fever may be sustained for 5–6 days and may occasionally have a biphasic course. Other common symptoms include sore throat, colicky pain, altered taste sensation, and abdominal tenderness, dragging pain in the inguinal region, constipation and general depression.

Symptoms vary in severity and usually persist for several days. Several types of skin rash have been described. Initially, diffuse flushing, mottling or fleeting pinpoint eruptions may be observed on the face, neck and chest. These are transient in nature. A second type of skin rash is a conspicuous rash that may be maculopapular or scarlatiniform and appears on approximately the third or fourth day. This rash starts on the chest and trunk and spreads to the extremities and face and may be associated with itching and dermal hyperaesthesia.A positive tourniquet test and petechiae on extremities are not uncommon.

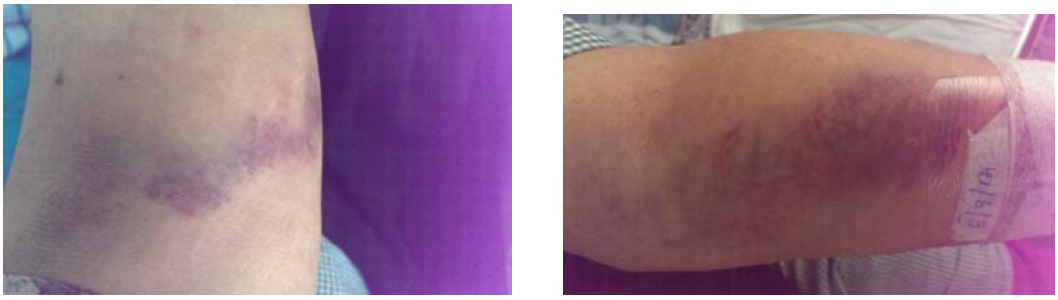
Epistaxis, gum bleeding, gastrointestinal haemorrhage, haematuria and hypermenorrhoea are common haemorrhagic complications have been reported in any epidemics of dengue fever, and on rare occasions severe bleeding has caused deaths in some epidemics.[45,46] Dengue fever with encephalitic signs but with normal cerebrospinal fluid has been reported in some epidemics.[46] Recently there has been an increase in reported cases of dengue encephalitis which was confirmed either by demonstration of virus, antigen or anti-dengue IgM antibody in cerebrospinal fluid.[47]

The most significant laboratory finding during the acute illness is leucopenia, which is usually noted 2–3 days after onset and lasts throughout the febrile phase. Mild to moderate thrombocytopenia is occasionally observed.[48]

COMPLICATIONS

- Hemorrhagic complications
- Liver failure- liver is involved in all types of dengue viral replication, DEN-3 or DEN-4 serotypes produce greater liver involvement. One-third of dengue infections experience liver derangements
- Encephalopathy- Dengue infections can cause headache, depressed sensorium, seizure, behavioral disorders, neck stiffness, paralysis, delirium, cranial nerve palsies, and coma. Encephalopathy in dengue infections has been ascribed to hepatic dysfunction, electrolyte imbalances, cerebral edema, hypoperfusion, cerebral anoxia, cerebral haemorrhage, microcapillary haemorrhage, release of toxic products, and dengue encephalitis.
- Myocarditis - Acute reversible myocardial dysfunction is the commonest cardiac complication. Alternation of tone, rhythm disorders, such as atrioventricular blocks and ventricular ectopic beats, ST segment and T wave changes, low ejection fractions, and global hypokinesia have been reported. Dengue myocarditis is generally reversible with favorable outcomes if diagnosed and treated early.

IMAGE 4 : Bleeding manifestations images in dengue fever



DENGUE HAEMORRHAGIC FEVER (DHF)

Pathophysiology:

The pathophysiological hallmarks of DHF are plasma leakage and abnormal haemostasis. Plasma leakage includes a rapid rise in haematocrit, pleural effusion and ascites, hypoproteinaemia and reduced plasma volume. Hypovolaemic shock and death due to loss of plasma.

A disorder in haemostasis involves all major components:[48]

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

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

(3) Coagulopathy, acute-type disseminated intravascular clotting (DIC) is documented in severe cases, often with prolonged shock and responsible for the severe bleeding.

(4) Bone marrow changes include depression of all marrow elements, with maturation arrest of megakaryocytes during the early phase of the illness.

Halstead proposed concept of sequential infection- Antibody dependent immune enhancement. Previous infection with a heterologous serotype results in production of nonprotective antiviral antibodies to other serotypes, these non protective antibodies bind to virion particles but are unable to neutralize them, these antibodies through interaction with Fc receptor ,focus secondary dengue virus on the target cell, which results in enhanced uptake and multiplication of virus in mononuclear phagocyte. The interval between sequential infections has been reported to be 1-5 years, but can be as long as 20 years. Sequence of infection DENV1----DENV2 is more virulent than DENV4--DENV 2.

The role of non-structural protein NS1 and complement in the pathogenesis of plasma leakage revealed that complement activation mediated by NS1 led to local and systemic generation of anaphylatoxin C5a and the terminal SC5b-9 complex.

The plasma levels of NS1 and SC5b-9 complexes correlated with disease severity and they were present in the pleural fluid from patients with dengue shock syndrome (DSS). The major role of NS1 as an important trigger for complete complement activation and the role of the terminal SC5b-9 complex in the pathogenesis of plasma leakage.[49] High circulating levels of NS1 that can be detected early in dengue illness are prone for development of DHF.[50]

CLINICAL FEATURES :

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

Febrile phase

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

Towards the end of febrile phase there is neutropenia, lymphocytosis with presence of atypical lymphocytes. Leucopenia usually reaches shortly before temperature and platelets drop.

Critical Phase

The critical phase, which is the period of plasma leakage, is reached near or by the time the fever subsides. In severe cases shock occurs. The skin is cold and clammy and the pulse pressure becomes narrow ≤20 mmHg with a slight elevation of diastolic level.

If no treatment is given the patient deteriorates rapidly into the stage of profound shock with an imperceptible pulse and blood pressure and dies within 12–24

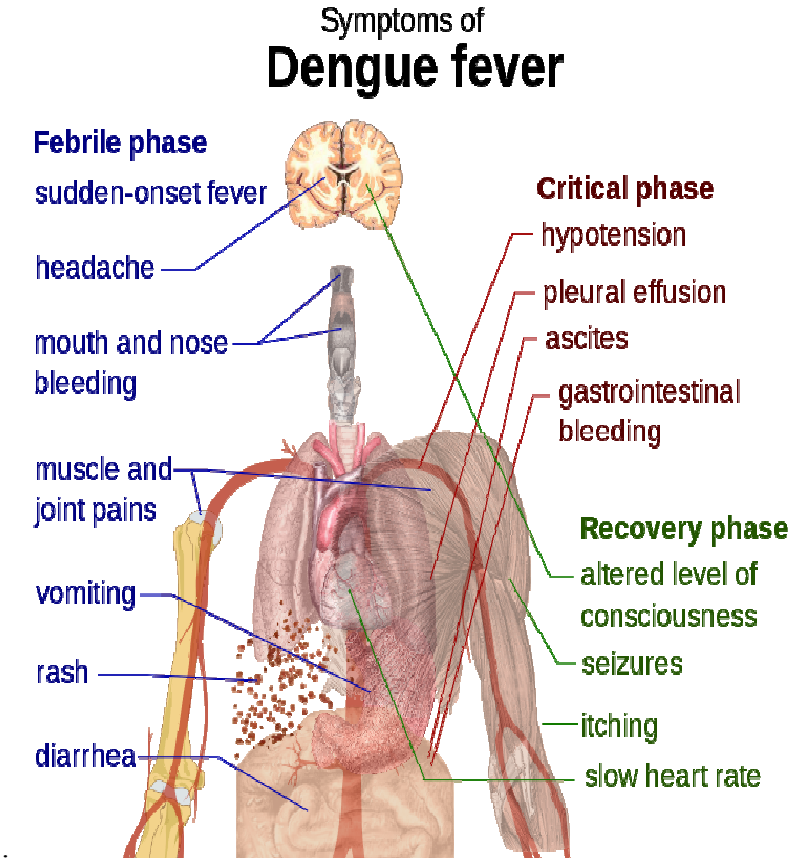


IMAGE 5 : SYMPTOMS OF DENGUE FEVER

Prolonged shock is often complicated by metabolic acidosis and severe bleeding, which indicates a poor prognosis. However, if the patient is properly treated before irreversible shock has developed, rapid, often dramatic recovery is the rule. Infrequently, encephalitic signs associated with metabolic or electrolyte disturbances, intracranial haemorrhage or hepatic failure occur and give rise to a more complicated course.[51] The critical phase usually lasts 24–48 h.

Haemoconcentration and thrombocytopenia are constant findings. The platelet count drops shortly before or simultaneously with the haematocrit rise (≥20%) and both changes occur before the subsidence of fever and before onset of shock. Clotting abnormalities are usually seen in severe cases with shock. Other changes include hypoproteinaemia, hypoalbuminaemia, hyponatraemia and mildly elevated alanine aminotransferase/aspartate aminotransferase levels.[52]

Bleeding tendencies should be closely watched for. When features of plasma leakage such as pedal edema, pleural effusion, ascites, are present, patient should be closely watched for and should be immediately managed. Dengue fever was a more common manifestation than DHF or DSS. During epidemic dengue should be strongly considered on the differential diagnosis of any patient with fever.[53]

SEROLOGICAL TESTING:

- Dengue IgM and IgG ELISA are sensitive (83.9-98.4%) and specific (100%), Dengue IgM antibodies appear in serum by the fifth day of infection and become undetectable by 30- 60 days of illness.
- ELISA FOR NS1(93.4% sensitive,100% specific) - FOR 1st 5 days

- IgM antibody capture ELISA- single sample alone is sufficient(80% sensitive in acute phase and 98% sensitive in convalescent phase)
- Diagnostic (four fold) increase in dengue antibody by heamagglutination test can be demonstrated from paired samples

Molecular diagnosis:

RT-PCR is a valuable diagnostic tool with high sensitivity and specificity even before dengue-specific antibodies are produced. RT-PCR is more sensitive (80-100%) when compared to virus isolation and also identifies the circulating serotype. It also avoids interference due to cross-reactivity of dengue serotypes with other flaviviruses. The disadvantage is its high cost and the expertise needed.

MALARIA

INTRODUCTION :

Malaria is a protozoan disease transmitted by the bite of infected Anopheles mosquitoes. Five species of the genus Plasmodium which are P. Falciparum, P. Vivax, Ovale, and P. Malariae , P.Knowlesi.

THROMBOCYTOPENIA IN MALARIA :

Thrombocytopenia is seen in both complicated and uncomplicated malaria. In the study by Sharma. K. et al Thrombocytopenia was present in as high as 90% of patients, Horstman et al found thrombocytopenia in 85% of P.falciparum and 72% of P.vivax patients respectively. Thrombocytopenia is generally unrelated to clinical severity but the degree of thrombocytopenia co-related with the size of the spleen .

Thrombocytopenia usually resolves spontaneously once the infection subsides. The pathogenesis of thrombocytopenia is thought to be similar to that of anaemia and they often co-exists .Various studies have shown that anaemia and thrombocytopenia occur simultaneously and subside gradually with therapy and clearance of parasitemia. The factors involved in pathogenesis of thrombocytopenia include

1) Hypersplasia of reticuloendothelial cells and increased phagocyte destruction.
2) Hypersplenism and splenic pooling of parasites.
3) Destruction of platelets bound by immune complexes by the reticuloendothelial system.
4) And rarely disseminated intra vascular coagulation.

Immunological basis for thrombocytopenia

The low platelet count emerged as the strongest predictor of malaria.[54] Platelet count of less than 1,50,000 increases the likelihood of malaria by 12-15 times.[55]Anti-Platelet IgG has also been implicated in the pathogenesis of thrombocytopenia.[56] Thrombocytopenic malaria, in contrast to the non-thrombocytopenic variety correlates with a higher degree of parasitemia and increased cytokine production.[57] The mechanism of thrombocytopenia in malaria could be due to peripheral destruction and consumption by DIC.

Immune mediated lysis, sequestration in the spleen and a dyspoietic process in the marrow with diminished platelet production have all been postulated. Abnormalities in platelet structure and function have been described as a consequence of malaria, and platelet can be invaded by malarial parasites themselves.

Two types of changes in platelet dysfunction are seen in malaria. Initially there is platelet hyperactivity, this is followed by platelet hypoactivity. Aggregating

agents like immune complexes, surface contact of platelet membrane to malarial red cells and damage to endothelial cells will result platelet hyperactivity . The injured platelets undergo lysis intravascularly. The release of platelet contents can activate the coagulation cascade and contributes to DIC. Transient platelet hypoactivity is seen following this phase and returns to normal in 1 to 2 weeks.

Thrombocytopenia an indicator of acute vivax malaria and a finding that is frequent and present even before anemia and splenomegaly set in. The possible mechanisms leading to thrombocytopenia in malaria includes immune mechanisms, oxidative stress, alterations in splenic functions and a direct interaction between plasmodium and platelets.[58]

Thrombocytopenia has an excellent sensitivity and very good specificity for vivax malaria. Normal platelet count provides very strong evidence against malaria as the etiology of fever without a focus.[59] Thrombocytopenia has an excellent sensitivity and a very good specificity for vivax malaria. Thrombocytopenia is an important marker in the diagnosis of malaria . In endemic regions patients with thrombocytopenia should be screened for possible malaria.[60]

LEPTOSPIROSIS

INTRODUCTION :

Leptospirosis is a zoonosis that occurs in many parts of the world but most frequently in tropical and subtropical regions. The major maintenance hosts are rodents and the organism is passed in their urine for long periods of time, even for the lifetime of the animal. Humans are infected through direct or indirect contact with the urine, blood, or tissue of infected animals. Most cases are mild or asymptomatic but the most severe illness, often referred to as Weil's disease, characterized by a severe

febrile illness with bleeding, jaundice and renal failure, may be associated with death through renal failure or pulmonary haemorrhage.[61,62,63,64,65]

The causative agents belong to the genus Leptospira, fine spiral bacteria of 0.1μm in diameter and 6–20μm in length.[66] Under dark ground microscopy, the organism appears straight with one or both ends hooked. Spinning motility around their long axis may disguise the spiral nature of the organisms.[67]

CLINICAL PRESENTATION

Bacteraemic phase

First phase does not involve much inflammation, direct hepatocellular damage leads to jaundice, and tubular damage. Haemorrhage may be present in any internal organ, and reflects endothelial damage and increased capillary fragility.[68] Cell damage may occur by interference by glycolipoprotein fractions with Na-K ATPase.

Incubation period is usually 7–12 days, there follows an acute febrile, influenza-like illness with chills, sore throat, headache, myalgia, back pain, anorexia, nausea and vomiting and, sometimes, herpes labialis. Sometimes the acute phase is severe, the patient is prostrate and has a persistently high fever (39–40°C) with exquisitely tender muscles, some cough and perhaps even haemoptysis, with dyspnoea and persistent vomiting. Abdominal pain is common and the patient tends to be constipated. There may be moderate hepatomegaly but splenomegaly is less common. The platelet count may fall and thrombocytopenic purpura and frank bleeding ensue. Urinalysis shows proteinuria but creatinine clearance usually remains normal until tubular necrosis or glomerulonephritis occurs.

Immune phase

The second phase of the illness is characterized by the host immune response and includes immune complex glomerulonephritis and vasculitis with endothelial injury.

Second phase begins after the initial illness, characteristically the patient having developed antibodies to the infecting organism. The antibody response is predominantly in the IgM class, which has strong agglutinating properties and may persist for many months. In mild cases, the second phase may be associated with minimal symptoms and signs but in a proportion of more severe infections, meningeal or hepatorenal manifestations predominate. In the severe form of the disease, the first and second phases merge imperceptibly; with persistent high fever the patient deteriorates, becoming jaundiced and starting to bleed into the skin, mucous membranes and lungs.

The liver enlargement is now more prominent. As the sclerae become icteric, the suffused vessels glow orange. Purpura and ecchymoses are seen. High mortality rate associated with oliguric renal failure, shock and myocarditis. The patient develops pulmonary oedema and subpleural pulmonary haemorrhages with haemoptysis. Acute adult respiratory distress syndrome occurs occasionally and, in these cases, smoking may be an important risk factor.[69] The patient will deteriorate rapidly if significant gastrointestinal haemorrhage occurs, but pulmonary haemorrhage is an important cause of death.[70,71] The electrocardiogram is often abnormal, reflecting myopericarditis. Renal dialysis requires in patients who develop oliguria, then anuria with rising plasma creatinine concentrations. The bilirubin concentration is high, but often without marked enzyme abnormalities, and the combination of high bilirubin and creatinine levels should immediately raise the

suspicious of leptospirosis. Renal failure is the usual cause of death but myocarditis, renal failure, haemorrhage and cerebral artery thrombosis may also be contributory. In those who survive without renal support, the creatinine concentration begins to fall at the end of the second week of the illness, indicating rapid resolution of the tubular necrosis. All renal function parameters will have returned to normal by 6 months except urinary concentrating ability.[72]

DIAGNOSIS:

- A definite diagnosis of leptospirosis is based either on isolation of the organism from patient or on seroconversion or a rise in antibody titer in microscopic agglutination test (MAT).
- In cases with strong clinical evidence of infection, a single antibody titer of 1:200–1:800 in the MAT is required. A fourfold or greater rise in titer is detected between acute- and convalescent-phase serum specimens.
- Antibodies generally do not reach detectable levels until the second week of illness. The antibody response can be affected by early treatment
- Leptospires can be isolated from blood and CSF during first 10 days of illness and from urine for several weeks beginning at ~1 week.
- Dark-field examination of blood or urine frequently results in misdiagnosis and should not be used.

MECHANISMSOF THROMBOCYTOPENIA	INFECTIONS
Haemophagocytosis	Septicemia [73], Epstein Barr virus[74]
Increased platelet destruction	Meningococcemia [75], Dengue
Platelet reactive auto antibodies	
Hemolytic uremic syndrome	Verocytotoxin producing E.coli[76] HIV [77]
Antibodies against platelet absorbed microbial antigens	Malaria [78]
Hypersplenism	Hepatitis, Malaria
Decreased platelet production	Ehrlichiosis [79], Tuberculosis
Infection of megakaryocytes	HIV [80]
Platelet destruction+ hypersplenism	Malaria

CLINICAL FEATURES OF THROMBOCYTOPENIA:

Manifestations of thrombocytopenia include epistaxis, purpura, gingival bleeding, sub conjunctival hemorrhage, haematemesis, malena, hematuria, intracranial hemorrhage, menorrhagia, postpartum hemorrhage.

Bleeding that requires blood transfusion is unusual unless the platelet count is less than 10,000 per microlitre.[81] Petechiae are small capillary haemorrhages the size of pinhead to much larger.

Patients who appear to increased risk include

1) Older patients
2) Chronic, refractory patients with history of haemorrhage

3) Patients with concomittent bleeding diathesis such as uraemia and hemophilia.[82]

Major danger is bleeding in to the brain. Retinal haemorrhages are unusual. Marrow aplasia, fibrosis or infiltration with malignant cells, drugs, vasculitis,transient immunologic thrombocytopenia which complicates infection are the most common causes for thrombocytopenia. Low platelet counts may be the initial manifestation of HIV, SLE and myelodysplastic syndromes.[83]

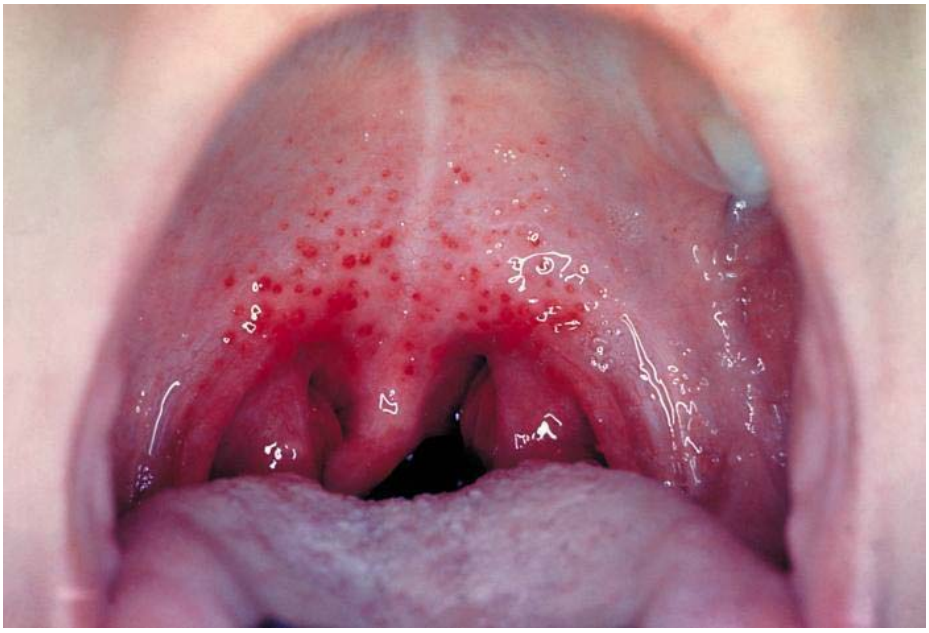
Counts more than 50000/μL there may be bleeding only following trauma. Between 10000 and 50000/μL spontaneous bleeding can occur.

Mortality can occur with counts less than 10,000 although the incidence is very low. Spontaneous bleeding in to the skin the form of petechiae appear as minute red to purple haemorrhages that range in size from pinpoint to pin head. They are flat and do not blanch on pressure. The presence of petechiae on the face is unusual except while coughing. Ecchymosis can develop on skin surface but they seldom dissect in to deeper tissue planes.

Gingival bleeding and epistaxis are common. The genitourinary tract can also be a source of bleeding. Intracranial bleed occurs in less than 1% with severe thrombocytopenia. These haemorrhages are usually subarachnoid.[5] Spontaneous gingival bleeding in an otherwise asymptomatic patient should make us consider thrombocytopenia as one of the differential diagnosis. Gastrointestinal bleed can manifest as malena or less commonly as haematemesis.

In Gandhii AA study they concluded that common bleeding manifestations are petechiae, purpura and gum bleeding.[84,85]

IMAGE 6 : IMAGES OF BLEEDING MANIFESTATIONS



CLINICAL IMPLICATIONS OF THROMBOCYTOPENIA :

- The normal blood platelet count is 1,50,000–4,50,000/L
- Platelet count of >1 lakh, are usually asymptomatic and bleeding time (BT) remains normal.[80]
- Platelet count of 50,000 – 1,00,000 cause mild prolongation of the BT, bleeding occurs only after severe trauma. [86]
- Bleeding rarely occurs in isolated thrombocytopenia at counts <50,000/L and usually not until <10,000– 20,000/L.
- Majority of bleeding manifestations occur in patients with less than 10,000/cumm.[87]
- Coexisting coagulopathies, as seen in liver failure or disseminated coagulation; infection; platelet-inhibitory drugs; and underlying medical conditions can all increase the risk of bleeding in thrombocytopenic patient.
- Platelet count of <50,000/µl have easy bruising, manifested by skin purpura after minor trauma.[35,86]
- Platelet count of <20,000/µl have spontaneous bleeding, they usually have petechiae, and may have intracranial or spontaneous internal bleeding.[35,86]
- Most procedures can be performed in patients with a platelet count of 50,000/L. The level needed for major surgery will depend on type of surgery and the patients' underlying medical state, although a count of approximately 80,000/L is likely sufficient.
- Mucosal bleeding symptoms are more suggestive of underlying platelet disorders or von Willebrand disease (vWD), termed disorders of primary hemostasis or platelet plug formation.[88]

- Treating the causative agent will improve the platelet count.[89]Grading of thrombocytopenia is carried out according to National Cancer Institute (NCI) Common Terminology Criteria.[90]

Grade 0: Within normal limit, platelet count 150,000 or above.

Grade I: Platelet count between 75,000 and 150,000.

Grade II: Platelet count between 50,000 and 75,000.

Grade III: Platelet count between 25,000 and 50,000.

Grade IV: Platelet count less than 25,000.

INVESTIGATIONS

A. Complete haemogram :

1) ESR : > 30 mm/hr suggests – TB; malignancy.
2) Leucopenia – in early dengue before the IgM ELISA dengue is positive.
3) Leucocytosis – predominantly neutrophils indicates septicemia.
4) Blood smear – Dohle bodies; toxic granules suggests septicemia also should be examined for malarial parasites.

B. Rapid spot test:

For plasmodium vivax and plasmodium falciparum species. It is very sensitive for detection of malaria.

C. WIDAL : tube method for identification of enteric fever.

D. IgM ELISA dengue – will be positive after 5th day of fever and rising titres are indicative of dengue.

E. IgM ELISA leptospiral antibodies: In very acute, toxic presentation with conjunctival suffusion with renal and liver parameters being abnormal. In patients with fever and

thrombocytopenia with renal and liver parameters being abnormal, it is very important to consider.

i. Malarial infections
ii. Leptospiral
iii. Dengue infections
iv. Septicaemia with multiorgan dysfunction syndrome

Platelet counts should also be repeated and observed for bleeding manifestations.

Diagnosis of Thrombocytopenia

Thrombocytopenia is said to be present when the platelet count is <1.5 lakhs/microlitre. A single platelet count that is lower than normal should always be confirmed by a second count.[91]

Platelet enumeration is more difficult in view of small size, their ability to adhere to foreign substances and aggregate when activated. Thrombocytopenia should also be confirmed by examination of the blood film as well. The electronic counters give the most reliable results.

Errors in counting can arise both because of clumping of platelets in some individuals in whom the platelet clump in the presence of EDTA anticoagulant and also some small extraneous particles may be mistaken for platelets. Others include giant platelets, lipaemia and previous contact with foreign substances. Automated methods provide the best method of counting large number of cells and in minimizing statistical errors. Autoanalysers are better than manual counting. The degree of reproducibility is very high, which is not seen with the manual counters.

Automated instruments provide data with increased reliability, precision,accuracy and reproducibility.

Advantages of automated counters are decreased lab cost, decreased turn around time and increased accuracy.

Types of automated instrument

1) Aperture impedance counters
2) Optical method counters.

Principles of platelet transfusion therapy

Johns Hopkins in 1910 physician; W.W. Duke, demonstrated the relation of blood platelets to hemorrhagic disease, described a method for determining the bleeding time, and for the first time showed that hemorrhagic disease caused by thrombocytopenia could be relieved by transfusion. However, reliable methods for platelet preparation were not developed until 1950.[92]

Platelet preparations

Platelet Concentrates and Apheresis Platelets

Platelet transfusions are available as platelet concentrates or as apheresis units. The former are prepared from units of whole blood by centrifugation and the latter are collected by pheresis devices. Various arguments have been proposed for the superiority of apheresis platelets, including reduced rates of alloimmunization and transfusion reactions.[93,94]

Cryopreserved Platelets

Cryopreserved platelets have been developed for long-term platelet storage using dimethylsulfoxide (DMSO) or glycerol. The average post-transfusion recovery of cryopreserved platelets is about 50%. Hemostasis seems to be maintained with DMSO preserved platelets.

Lyophilized Platelets

In 1995 Read and co-workers reported that lyophilized platelets may support hemostasis in an animal model.[95] They reported that they could correct the bleeding time in thrombocytopenic animals, and also that transfused reconstituted lyophilized platelets participated in carotid arterial thrombus formation in a canine model. This form of platelet is currently undergoing human clinical trials and is not yet approved for routine use.

RECENT REVIEW OF LITERATURE

Gandhi AA, Akholkar PJ. Clinical and laboratory evaluation of patients with febrile thrombocytopenia. NJMR, Vol 5 (1), Jan- Mar 2015:43-46

In their study they concluded that fever with thrombocytopenia reveals infections like dengue and malaria are common causes because of seasonal and regional variations. Common Bleeding manifestations are petechiae /purpura and gum bleeding.

Lakum N, Makwana H, Shah R. A study pf laboratory profile of fever with thrombocytopenia in adult patients at C.U.Shah Medical College, Surendranagar.

SEAJCRR, Jan- Feb 2014;3(1):556-561.

In their study they concluded that Infection is the most common cause of patient presenting with fever with thrombocytopenia. Among infection malaria was the commonest followed by dengue hemorrhagic fever. In bleeding manifestation petechiae was the commonest cause At presentation majority of patient having platelet count in range of 50,000 to 1,00,000/cumm

Bhalara SK, Shah S, Goswami H, Gonsai RN. Clinical and etiological profile of thrombocytopenia in adults: A tertiary care hospital based cross sectional study. International Journal of Medical Science and Public Health 2015:4;7-10

In their study they concluded that Dengue fever was the most common cause of thrombocytopenia and the most common etiology found in patients who had bleeding secondary to thrombocytopenia with gum bleed as a common manifestation.

Putta suresh, C.Ramesh Kumar, C. Yamini Devi, K.Deva Priyanka. Incidence of Bleeding Manifestations in Fever with Thrombocytopenia Cases. J of Evidence Based Med & Hlth care, vol 2,issue : 15; April 2015; 2154-2156.

In their study they conclude that Fever with thrombocytopenia is the commonest problem in the medical wards. Malaria fever was the commonest cause of fever with thrombocytopenia followed by dengue fever. Bleeding is not attributable to thrombocytopenia if platelet count is >1,00,000. Bleeding is usually due to thrombocytopenia if platelet count is <50,000/µl. Bleeding manifestations commonly seen in dengue fever with thrombocytopenia.

Fazal F, Biradar S. Clinical and laboratory profile of dengue fever. Journal of Evidence Based Medicine and Healthcare 2015:2;1136-1147

In their study they concluded that dengue fever was a more common manifestation than DHF or DSS. During epidemic dengue should be strongly considered on the differential diagnosis of any patient with fever.

Arshad AR. Thrombocytopenia in Malaria: Can platelet counts differentiate Malaria from other Infections. Journal of the College of Physicians and Surgeons Pakistan 2015:25;31-34

concluded that thrombocytopenia has an excellent sensitivity and very good specificity for vivax malaria. Normal platelet count provide very strong evidence against malaria as the etiology of fever without a focus.

concluded that thrombocytopenia is an important marker in the diagnosis of malaria. In endemic regions patients with thrombocytopenia should be screened for possible malaria.

METHODOLOGY

METHOD OF STUDY:

This study was done on 134 patients, who were admitted to Sri Devraj Urs Medical College and Research Hospital, Tamaka , kolar during a period of December 2013 to December 2014.

We prospectively randomly collected a series of 134 patients with fever and thrombocytopenia.

METHOD OF COLLECTION OF DATA :

Once the patients admitted with fever and those who had thrombocytopenia, a careful history was recorded, general physical examination was done. Detailed examination of various systems was done. Routine investigations were done, the specific and special investigations were done as and when indicated. In whom a final definite diagnosis was reached, were treated for the disease.

Platelet count was repeated serially on Day 1,Day 3,Day 5 and Day 7

The grading of the thrombocytopenia was do and correlated with presence of hemorrhagic manifestations.

Informed written consent was obtained from all the patients participating in the study after clearly explaining the study procedure.

The study was approved by the Ethical committee, Sri Devaraj Urs Medical College , Kolar.

INCLUSION CRITERIA:

1) Age more than 18 years
2) History of fever.
3) Oral temperature should be > 37.5^0 c

EXCLUSION CRITERIA:

1) Patients who are on antiplatelet drugs.
2) Idiopathic thrombocytopenic purpura.

SAMPLE SIZE :

The required sample size for this study is estimated based on the prevalance of thrombocytopenia of 45.2% in a study. [96] so taking prevalence (p)= 45.2%

$$N=z_\alpha^2\, pq/d^2$$

where z_α= 95% confident interval which is equal to 1.96

d= absolute error 10%

q= (100-p)=(100-45.2)= 54.8

STUDY DESIGN :

Observational hospital based study.

STUDY PERIOD:

DEC 2013 TO DEC 2014.

STATISTICAL METHODS:

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square was used as test of significance. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two groups. and ANOVA (Analysis of Variance) was the test of significance to identify the mean difference between more than two groups. p value <0.05 was considered as statistically significant.

INVESTIGATIONS

a) Complete haemogram

1) ESR – It is a non specific test, it is raised in most conditions.

2) Leucopenia – seen in viral fever.

3) Leucocytosis – predominantly neutrophils indicates septicemia.

4) Blood smear – Dohle bodies; toxic granules suggests septicemia also should beexamined for malarial parasites.

b) Rapid spot test : For plasmodium vivax and plasmodium falciparum species. It is very sensitive for detection of malaria.

c) WIDAL – tube method for identification of enteric fever.

d) IgM ELISA dengue – will be positive after 5th day of fever and rising titres are indicative of dengue.

e) IgM ELISA leptospiral antibodies – In very acute, toxic presentation with conjunctival suffusion with renal and liver parameters being abnormal.

IMAGE 7 : CBC MACHINE - Alere h 560

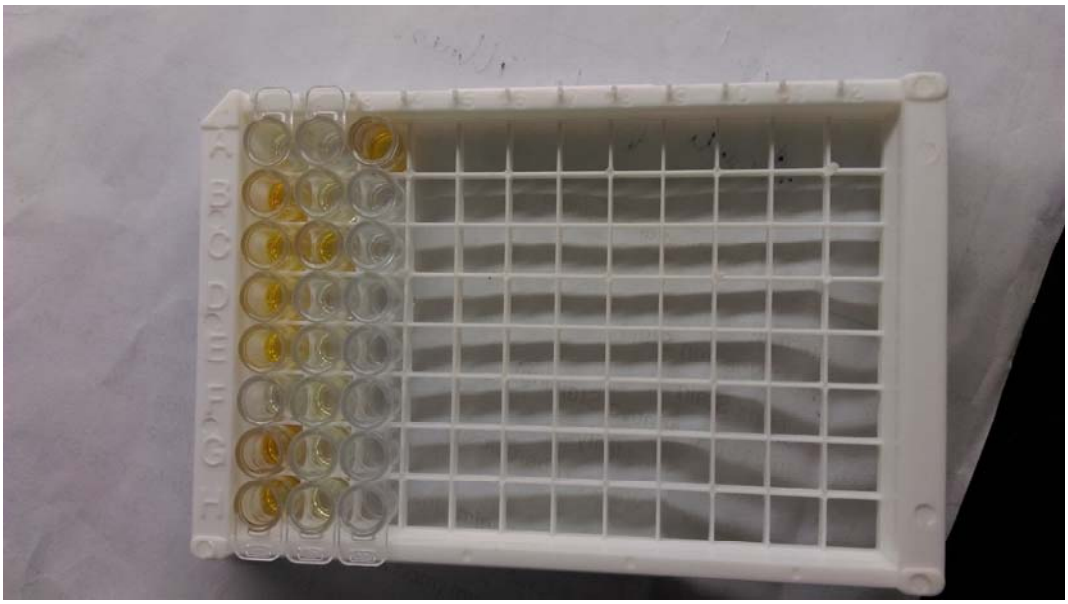


IMAGE 8: MALARIA CARD TEST

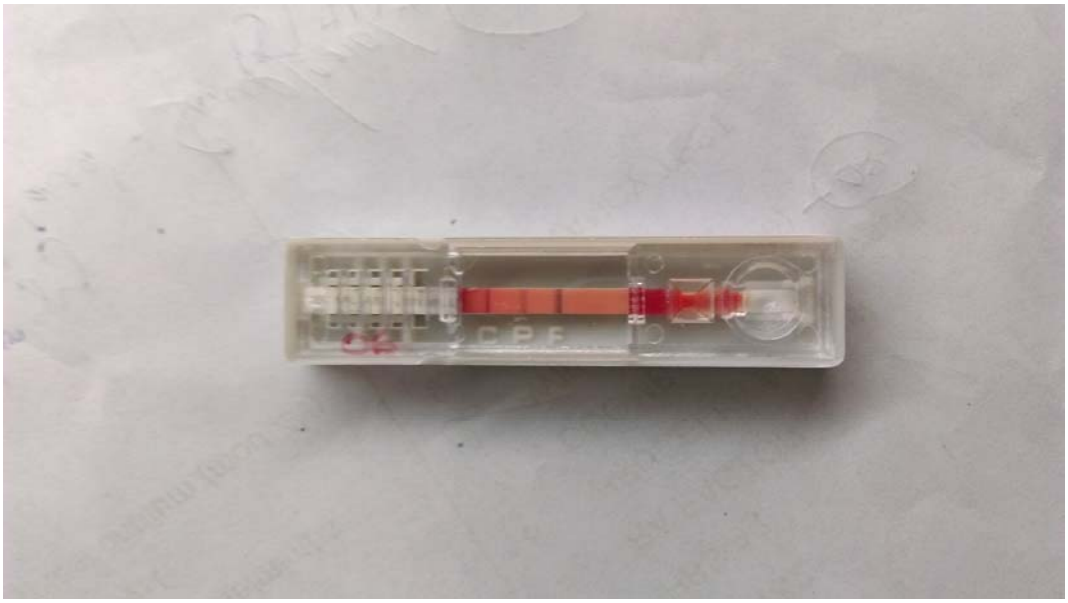


IMAGE 9 : ELISA

RESULTS

Table 1: Age distribution of subjects

		Frequency	Percent
Age	< 20 years	14	10.4
	21 to 30 years	44	32.8
	31 to 40 years	37	27.6
	41 to 50 years	25	18.7
	> 50 years	14	10.4
	Total	134	100.0

In this study majority 32.8% of subjects are in the age group 21 to 30 years followed by 27.6% in 31 to 40 years. Least no of cases are seen in < 20 years and > 50 years (10.4% respectively).

Mean age of subjects is 35.49 ± 12.94 years.

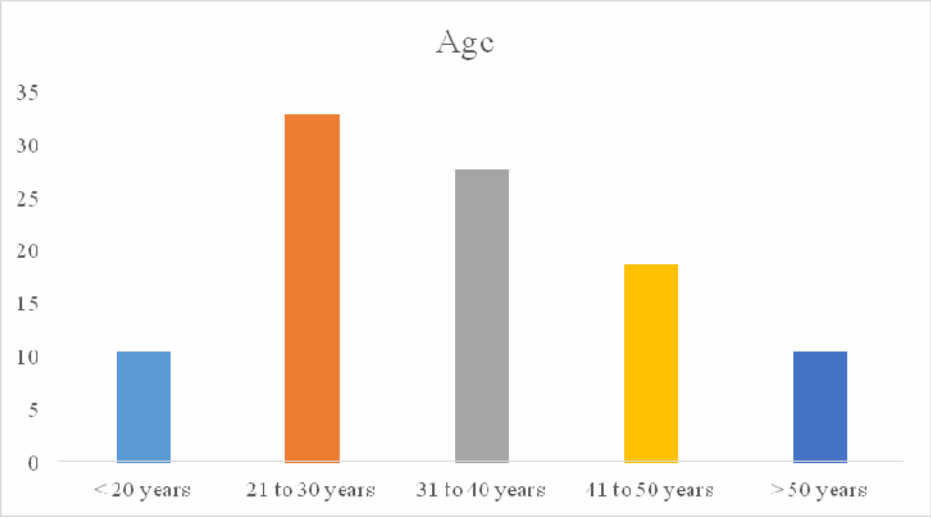


Figure 1: Bar diagram showing Age distribution of subjects

Table 2: Gender distribution of subjects

		Frequency	Percent
Gender	Female	65	48.5
	Male	69	51.5
	Total	134	100.0

Majority of the patients are males (51.5%) and 48.5% are females.

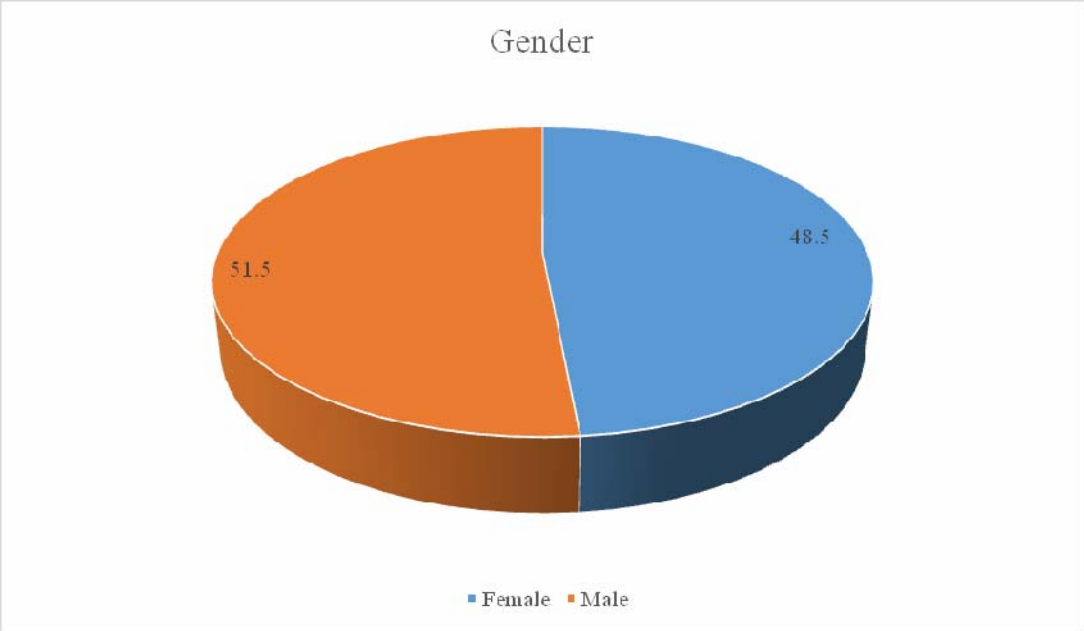


Figure 2: Pie diagram showing gender distribution of subjects

Table 3: Clinical Features at presentation in subjects

	Yes		No	
	Frequency	**Percent**	**Frequency**	**Percent**
Fever	134	100.0	0	0
Headache	85	63.4	49	36.6
Joint pains	17	12.7	117	87.3
Vomiting	97	72.4	37	27.6
Myalgia	90	67.2	44	32.8
Abdominal pain	36	26.9	98	73.1
Dyspnea	14	10.4	120	89.6
Rashes	36	26.9	98	73.1
Bleeding manifestations	60	44.8	74	55.2

All the cases had fever, mean duration of fever is 2.69 ± 1.71 days. 63.4% had headache, 12.7% had joint pains, 72.4% had vomiting, 67.2% had myalgia, 26.9% had abdominal pain & rashes respectively, 10.4% had dyspnea and 44.8% had bleeding manifestations.

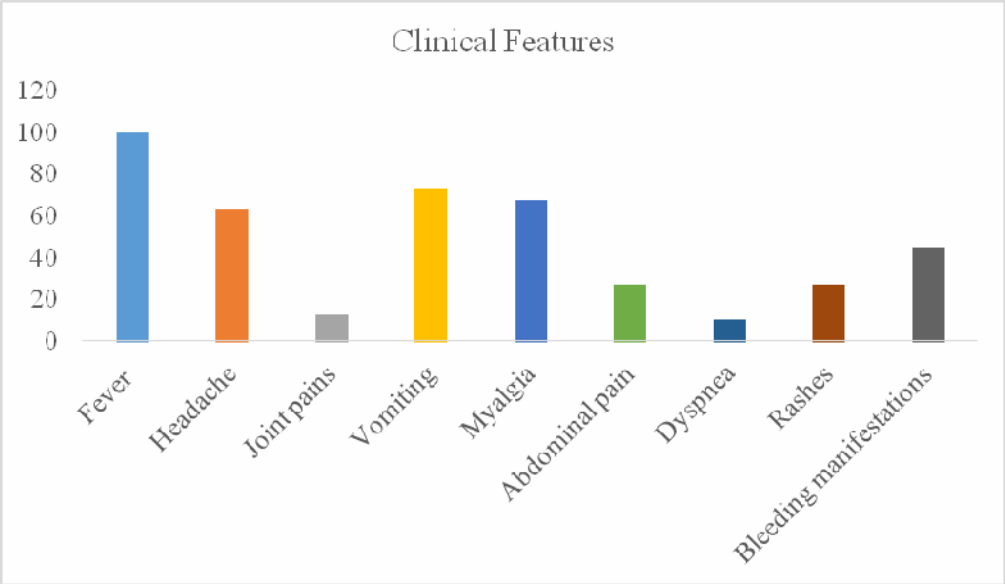


Figure 3: Bar diagram showing Clinical Features of subjects

Table 4: Duration of Fever at Presentation in Subjects

		Frequency	Percent
Duration of Fever Grouped	**1 to 3 days**	102	76.1
	4 to 6 days	30	22.4
	> 6 days	2	1.5
	Total	134	100.0

Majority of the patients presented within 3 days of fever (76.1%), 22.4% in 4 to 6 days and 1.5% presented after one week.

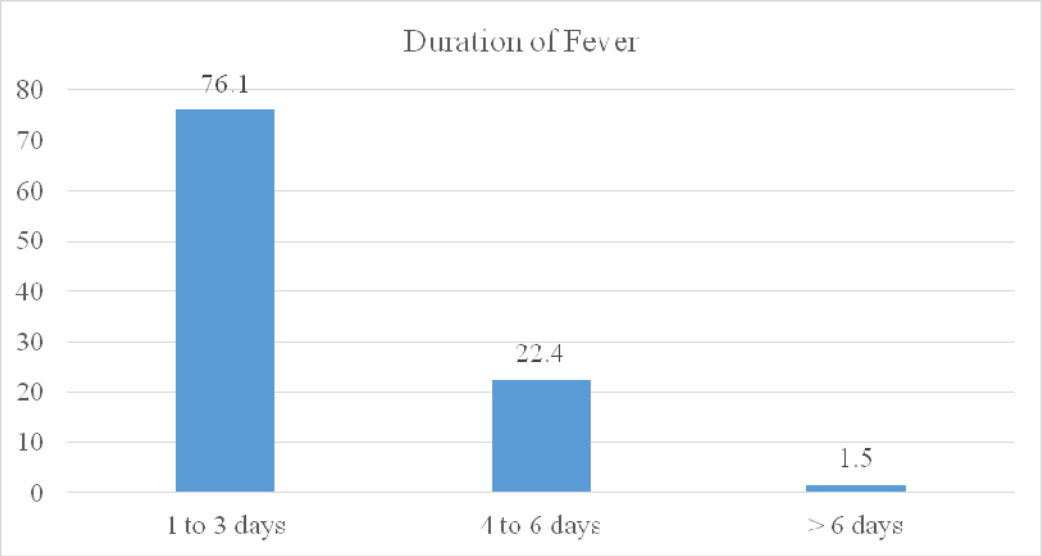


Figure4: Bar diagram showing Duration of Fever

None of the patients had Drug History

Table 5: Descriptive statistics of Vital Signs

	Temperature	Pulse	SBP	DBP
Number of patients	134	134	134	134
Mean	99.99	99.73	106.42	67.46
SD	0.95	5.89	15.57	7.82
Median	100.00	102.00	110.00	70.00
Minimum	98	82	70	50
Maximum	104	110	140	80
Range	6	28	70	30

Mean Temperature is 99.99 ± 0.95 degree F, Mean Pulse rate is 99.73 ± 5.89 bpm, Mean SBP is 106.42 ± 15.57 mm/Hg and Mean DBP is 67.46 ± 7.82 mm/Hg.

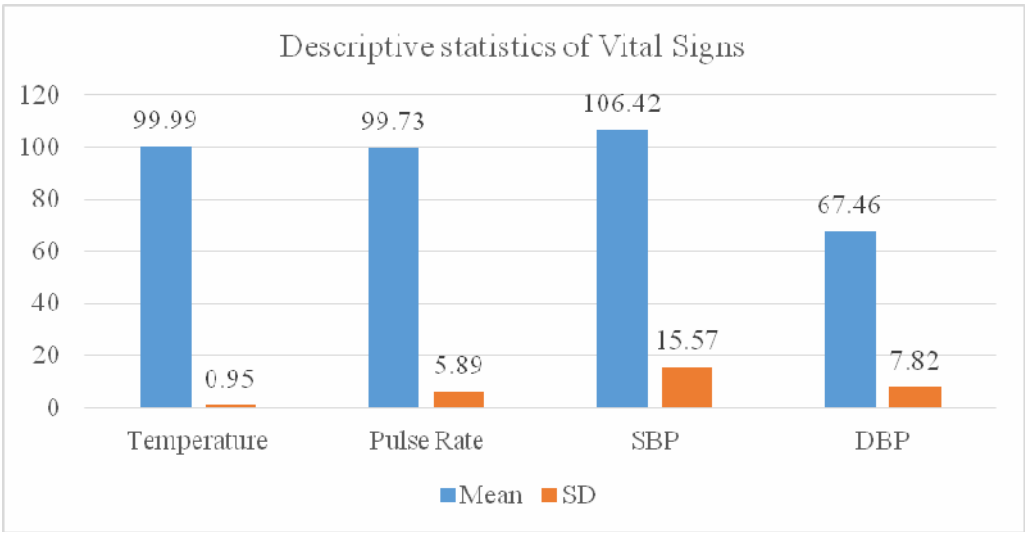


Figure 5: Bar diagram showing Mean and SD of Vital signs

Table 6: Hemorrhagic manifestations in subjects

	Present		Absent	
	Frequency	**Percent**	**Frequency**	**Percent**
Conjunctival Hemorrhage	37	27.6	97	72.4
Bleeding Gums	24	17.9	110	82.1
Petechiae	25	18.7	109	81.3
Hematuria	4	3.0	130	97.0

In this study 27.6% presented with Conjunctival Hemorrhage, 17.9% with Bleeding Gums, 18.7% with Petechiae and 3% with Hematuria

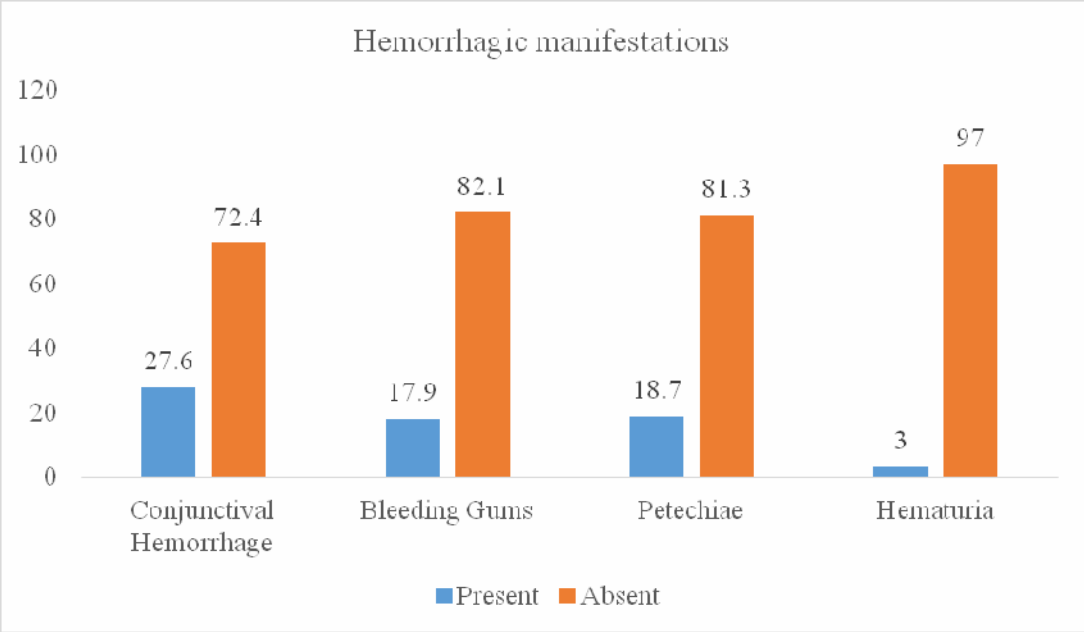


Figure 6: Bar diagram showing Hemorrhagic manifestations in subjects

Table 7: Classification of Hemorrhagic Manifestations

Hemorrhagic Manifestations		Frequency	Percent
Absent		73	54.5
Present	Conjunctival Hemorrhage	13	9.7
	Conjunctival Hemorrhage + Bleeding Gums	12	9.0
	Petechiae	12	9.0
	Bleeding Gums	9	6.7
	Conjunctival Hemorrhage + Petechiae	8	6.0
	Bleeding Gums + Petechiae	3	2.2
	Conjunctival Hemorrhage + Hematuria	2	1.5
	Conjunctival Hemorrhage + Petechiae + Hematuria	2	1.5
	Total	134	100.0

Conjunctival Hemorrhage is the most common bleeding manifestation in this study.

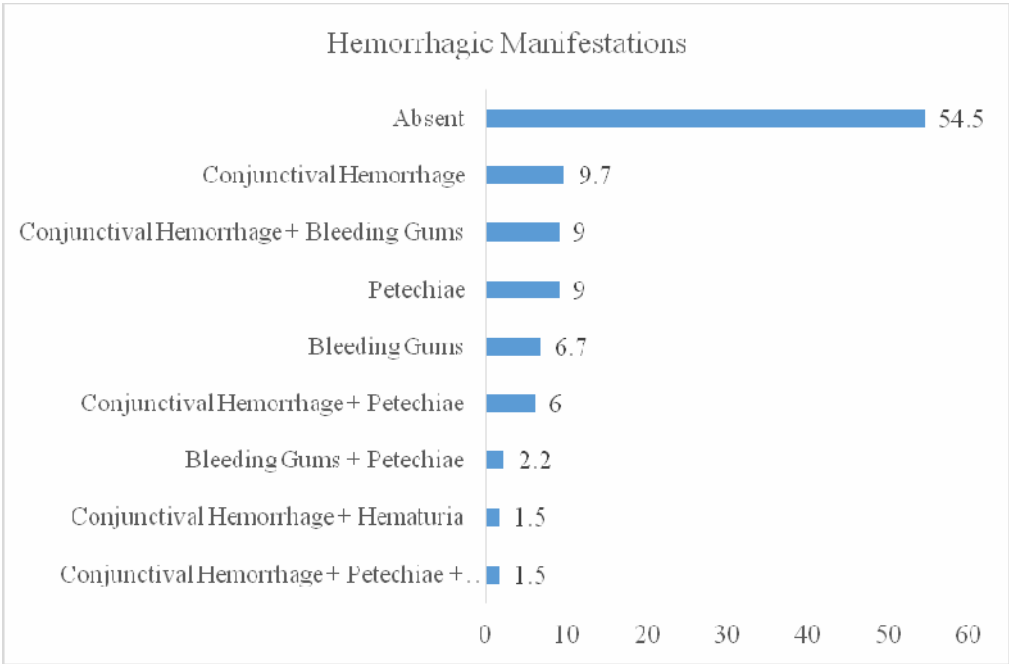


Figure 7: Bar diagram showing Hemorrhagic manifestation in subjects

Table 8: Findings of Systemic Examination

		Frequency (n=134)	Percent
Respiratory System	Normal	115	85.8
	Crepitation (B/L – 17 &Rt -1)	18	13.4
	Pleural effusion (B/L)	1	0.7
Per Abdomen	Normal	115	85.8
	Abdominal distension	10	7.5
	Hepatomegaly	5	3.7
	Splenomegaly	4	3.0
Central Nervous System	Irritable	1	0.7

Respiratory System examination showed that 13.4% had crepitation and 0.7% had Pleural effusion. Per Abdomen examination showed 7.5% had abdominal distension, 3.7% had hepatomegaly and 3% had splenomegaly. Cardiovascular system is normal in all subjects

Only one subject is irritable on Central Nervous system examination

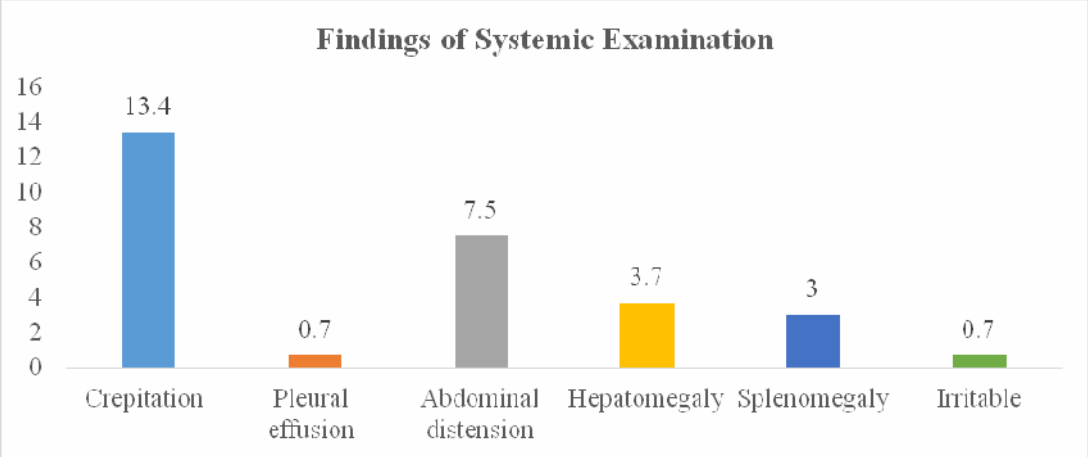


Figure 8: Bar diagram showing Findings of Systemic Examination

Table 9: Grading of Platelet count on Day 1, Day 3, Day 5 and Day 7

	Grade 1		Grade 2		Grade 3		Grade 4	
	Frequency	**%**	**Frequency**	**%**	**Frequency**	**%**	**Frequency**	**%**
Day 1	4	3.0	50	37.3	43	32.1	37	27.6
Day 3	16	11.9	59	44.0	38	28.4	20	14.9
Day 5	57	42.5	29	21.6	25	18.7	4	3.0
Day 7	54	40.3	0	0	0	0	0	0

In this study on day 1, 3% had Grade 1 platelet count, 37.3% had Grade 2, 32.1% had Grade 3 and 27.6% had Grade 4 Platelet count.

On Day 3, 11.9% had Grade 1, 44% had Grade 2, 28.4% had Grade 3 and 14.9% had Grade 4 Platelet count.

On Day 5, 42.5% had Grade 1, 21.6% had Grade 2, 18.7% had Grade 3 and 3% had Grade 4 platelet count.

On Day 7, 40.3% had Grade 1 only. Hence with increase in duration there is improvement in subjects.

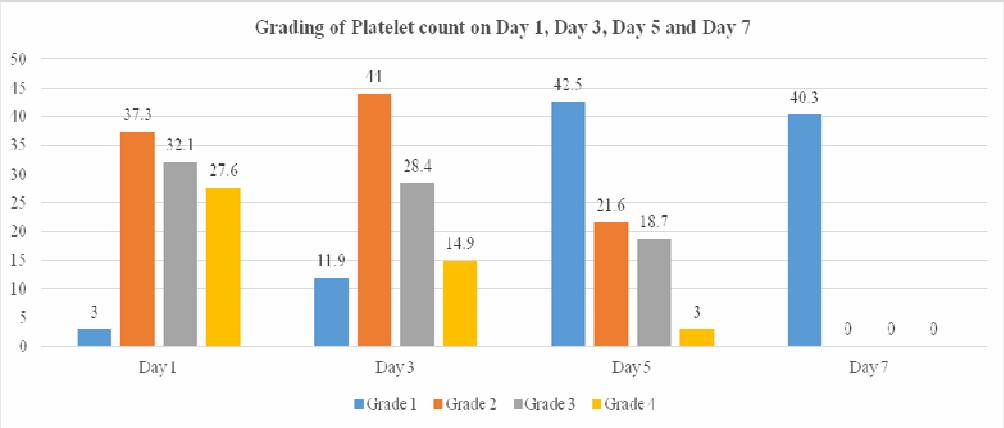


Figure 9: Bar diagram showing Grading of Platelet count

Table 10: Etiology in subjects with Fever with Thrombocytopenia

	Etiology			
	Present		Absent	
	Frequency	Percent	Frequency	Percent
Sepsis	26	19.4	109	80.6
Dengue	87	64.9	47	35.07
Malaria	32	23.8	102	76.11
Mixed (Dengue + Malaria)	9	6.7	125	93.28

In this study 19.4% are diagnosed to have Sepsis (TLC > 10000), 64.9% are positive for Dengue, 23.8% are positive for Malarial parasite and 6.7% had Mixed Infection.

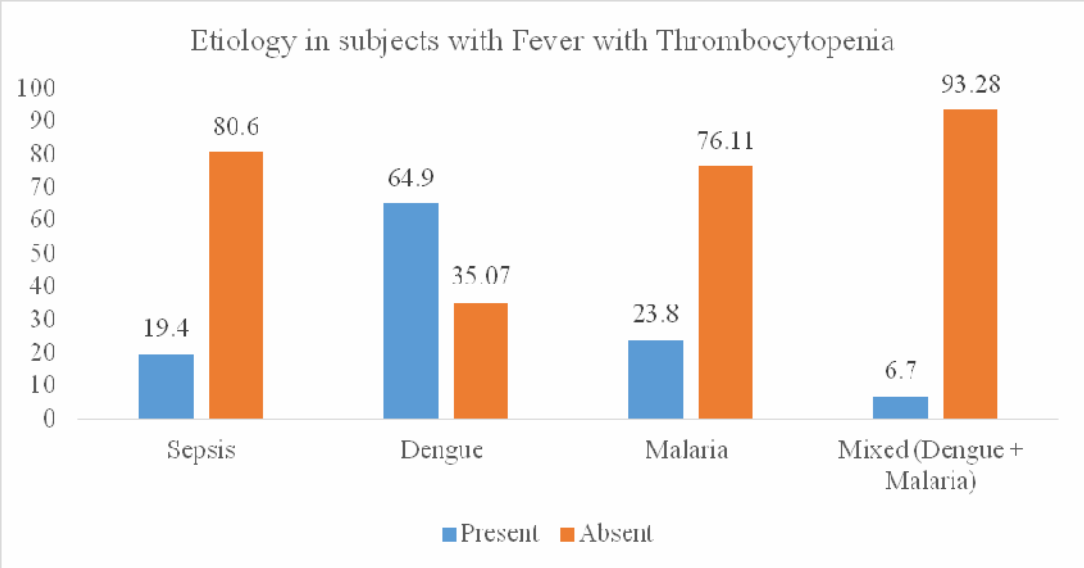


Figure 10: Bar diagram showing Etiology in subjects with Fever with Thrombocytopenia

Table 11: Etiology split up in subjects

		Frequency	Percent
Dengue Serology	NS1 Ag Positive	50	37.3
	IgM Positive	25	18.7
	Both NS1 Ag & IgM Positive	12	9.0
Malaria	P. vivax	23	17.2
	P.falciparum	9	6.7
Mixed Infection (Dengue + Malaria)	Dengue + PV	5	3.7
	Dengue + PF	4	3.0

Among Dengue Positive cases 37.3% are positive for NS1 Ag, 18.7% are positive for IgM antibodies and 9% are positive for Both NS1 and IgM ab.

17.2% are positive for P.vivax and 6.7% for P. falciparum.

3.7% had Dengue + P. vivax and 3% had Dengue + P. falciparum

No cases of Leptospira and Rickettsia

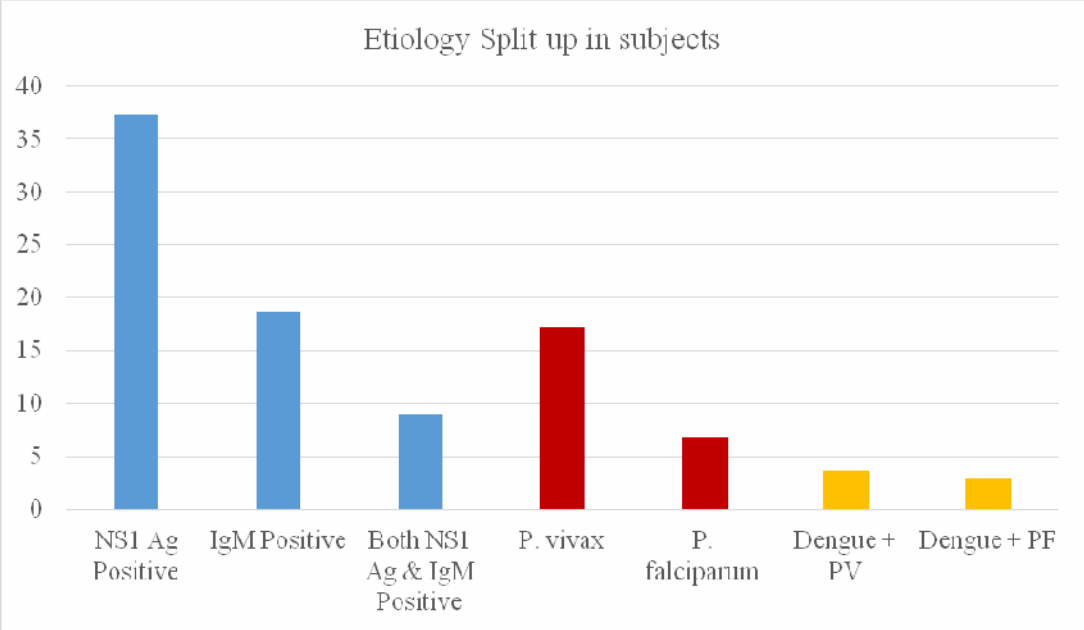


Figure 11: Bar diagram showing Etiology split up in subjects

Table 12: Chest X ray(CXR) findings in Subjects

		Frequency	Percent
CXR	Normal	116	86.6
	ARDS	13	9.7
	B/L lower zone non homogenous opacities	2	1.4
	Rt. lower zone non homogenous opacity	1	0.7
	B/L Pleural Effusion	1	0.7
	Left Lung Fibrosis	1	0.7
	Total	134	100.0

In this study on chest X ray, 9.7% had ARDS and 5 cases had other findings shown in the above table.

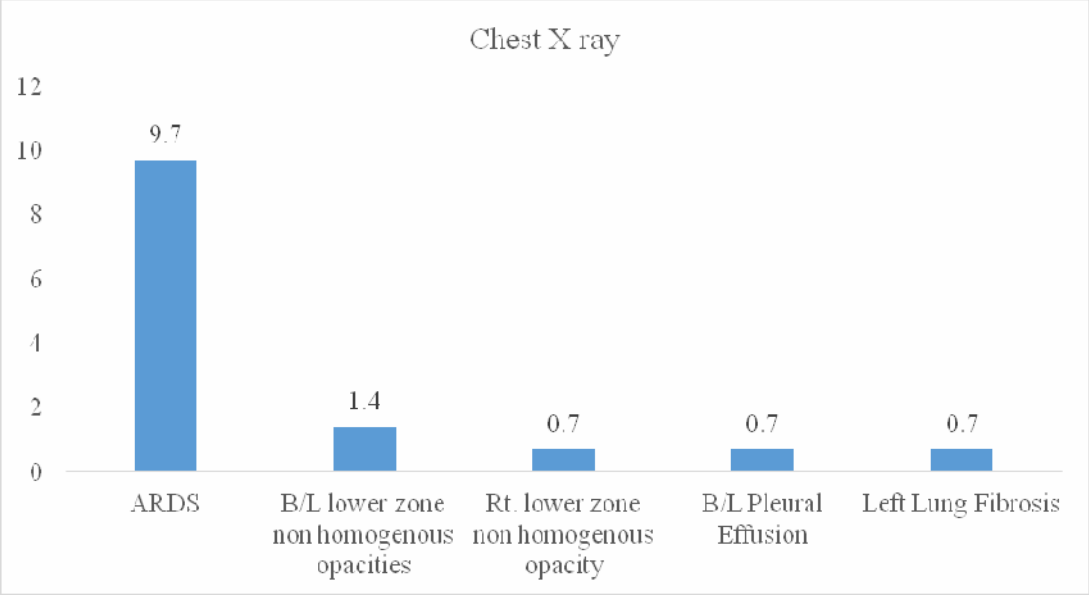


Figure 12: Bar diagram showing Chest X ray Findings

Table 13: Ultrasonography(USG) abdomen findings in subjects

		Frequency	Percent
USG abdomen	Normal	105	78.4
	GB Sludge	11	8.2
	Ascites	10	7.5
	Hepatomegaly	5	3.7
	Splenomegaly	3	2.2
	Total	134	100.0

On USG, 8.2% had Gall bladder sludge, 7.5% had ascites, 3.7% had hepatomegaly and 2.2% had splenomegaly.

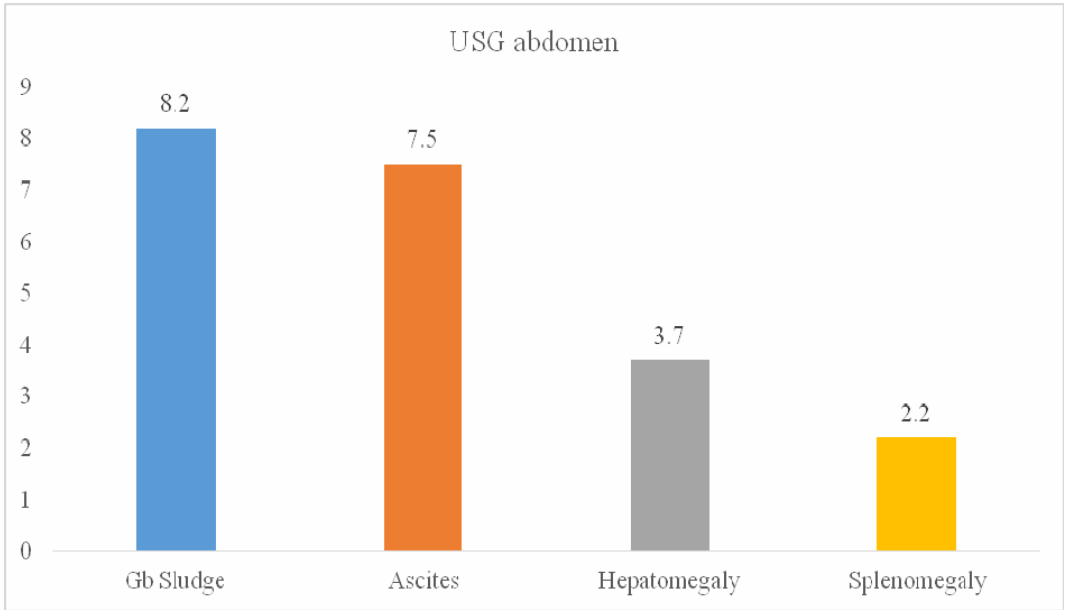


Figure 13: Bar diagram showing USG abdomen Findings

Only one case is positive for AFB (both samples).

Table 14: Platelet transfusion in Subjects

			Frequency	Percent
Platelet transfusion	**Not given**		100	74.6
	Given	**4 pints**	12	9.0
		6 pints	17	12.7
		8 pints	4	3.0
		12 pints	1	0.7
	Total		134	100.0

25.4% of subjects required Platelet transfusion. Of them 12.7% are transfused with 6 pints, 9% with 4 pints, 3% with 8 pints and 0.7% with 12 pints.

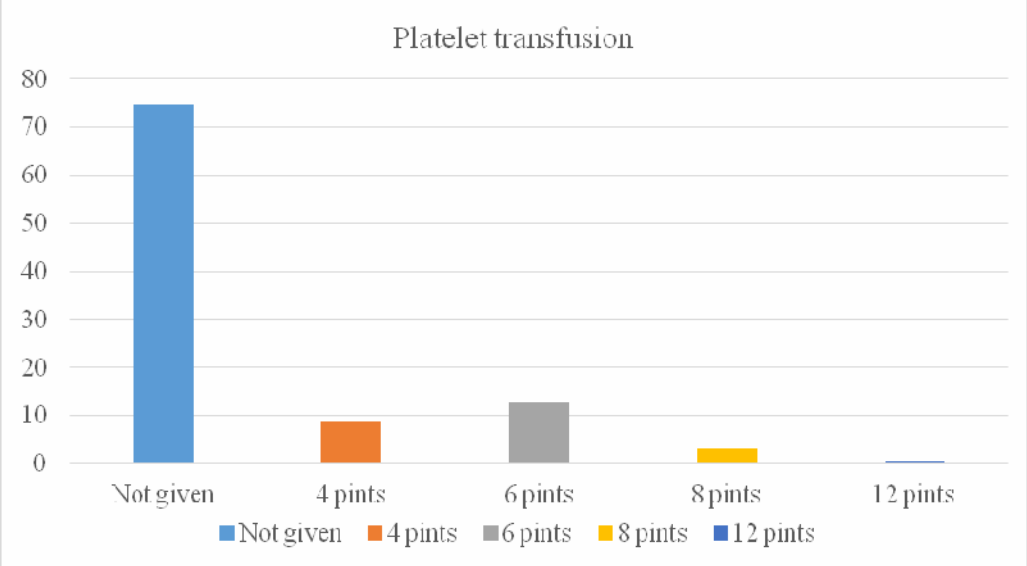


Figure 14: Bar diagram showing Platelet transfusion in Subjects

Table 15: Outcome in subjects with Fever and Thrombocytopenia

		Frequency	Percent
Outcome	Death	8	6.0
	Discharge	126	94.0
	Total	134	100.0

Prognosis is good in 94% of subjects and are discharged and 6% had poor prognosis and died during the stay.

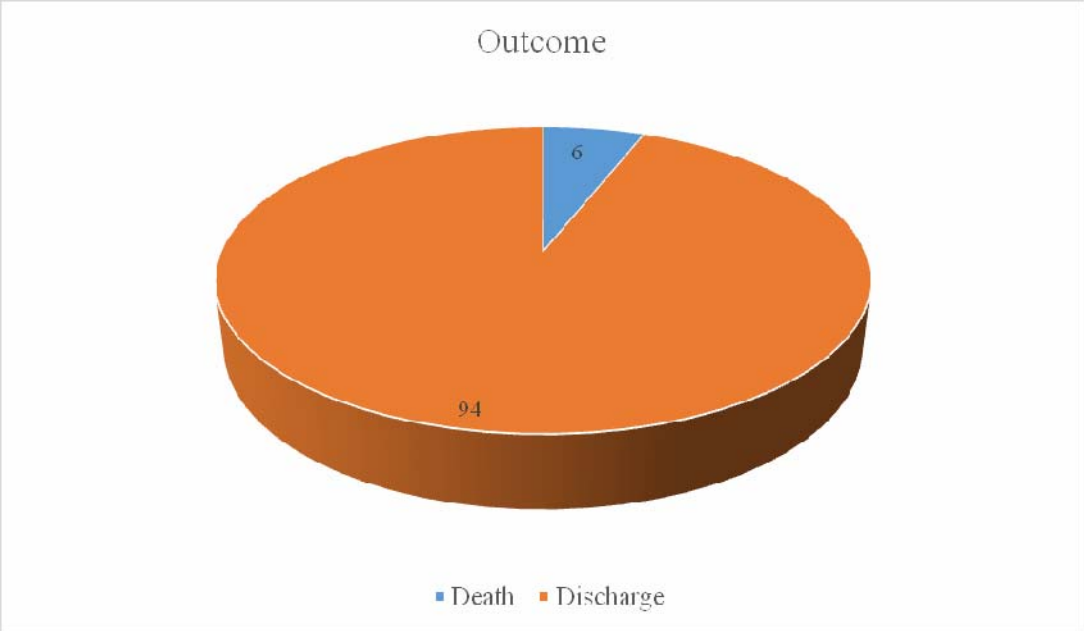


Figure 15: Pie chart showing Outcome in subjects

Table 16: Association between Platelet count grading and Bleeding Manifestations At Presentation

		Day1								P value
		Grade 1		Grade 2		Grade 3		Grade 4		
		Count	%	Count	%	Count	%	Count	%	
Bleeding	Present	0	0.0%	2	4.0%	27	62.8%	32	86.5%	<0.001*
	Absent	4	100.0%	48	96.0%	16	37.2%	5	13.5%	

It is observed that with increase in grade of platelet count there is increase in bleeding tendency. In Grade 1 no bleeding, in grade 2 4% had bleeding, in grade 3 62.8% had bleeding and in Grade 4 86.5% had bleeding manifestations. This observation is statistically significant.

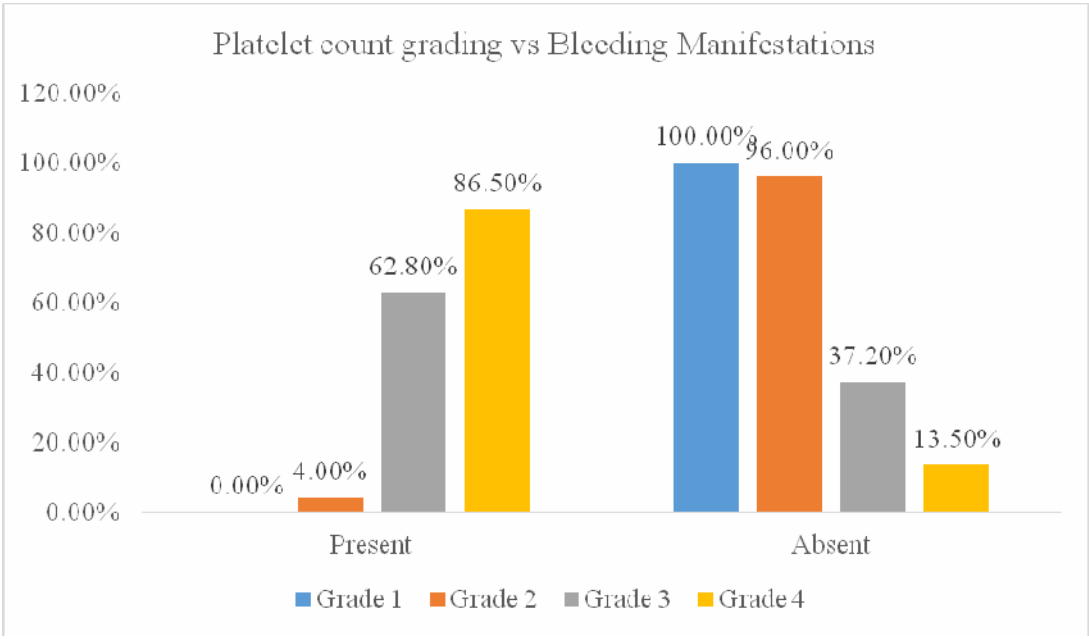


Figure 16: Bar diagram showing Platelet count grading and Bleeding Manifestatio

Table 17: Association between Various Hemorrhagic Manifestations and Platelet Grading on day 1

Hemorrhagic Manifestations	1ST DAY					
	Grade 2		Grade 3		Grade 4	
	Count	%	Count	%	Count	%
BG	0	0.0%	9	33.3%	0	0.0%
BG+Petechiae	0	0.0%	0	0.0%	3	9.4%
CH	2	100.0%	6	22.2%	5	15.6%
CH+BG	0	0.0%	0	0.0%	12	37.5%
CH+Hematuria	0	0.0%	1	3.7%	1	3.1%
CH+Petechiae	0	0.0%	2	7.4%	6	18.8%
CH+Petechiae+Hematuria	0	0.0%	0	0.0%	2	6.2%
Petechiae	0	0.0%	9	33.3%	3	9.4%

p <0.001**

It is observed that Conjunctival hemorrhage (CH) was common in Grade 2, Bleeding gums (BG) & Petechiae was common in Grade 3 and Conjunctival hemorrhage with Bleeding Gums was common in Grade 4. This observation is statistically significant.

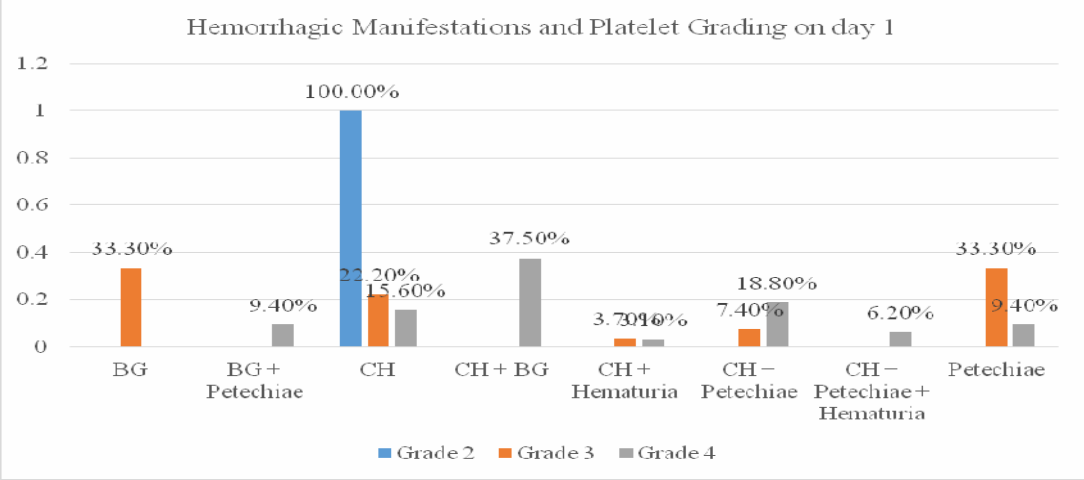


Figure 17: Bar diagram showing Various Hemorrhagic Manifestations and Platelet Grading on day 1

Table 18: Association between Diagnosis and Platelet Grades

		1st day								P value
		Grade 1		Grade 2		Grade 3		Grade 4		
		Count	%	Count	%	Count	%	Count	%	
Sepsis	Present	0	0.0%	9	18.0%	8	18.6%	9	24.3%	0.656
	Absent	4	100.0%	41	82.0%	35	81.4%	28	75.7%	
Dengue	Present	2	50.0%	31	62.0%	27	62.8%	27	73.0%	0.633
	Absent	2	50.0%	19	38.0%	16	37.2%	10	27.0%	
Malaria	Present	2	50.0%	13	26.0%	11	25.6%	6	16.2%	0.409
	Absent	2	50.0%	37	74.0%	32	74.4%	31	83.8%	
Mixed infection	Present	0	0.0%	4	8.0%	2	4.7%	3	8.1%	0.843
	Absent	4	100.0%	46	92.0%	41	95.3%	34	91.9%	

There is no significant association between grade of platelet count and Diagnosis. In higher grades of platelet count dengue is the common etiology.

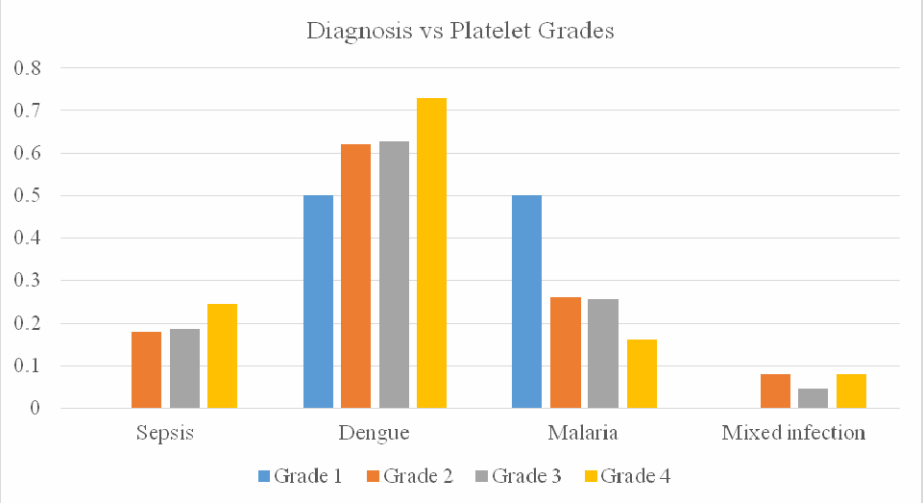


Figure 18: Bar diagram showing Association between Diagnosis and Platelet Grades

Table 19: Dengue serology and Platelet Grading association

Dengue Serology	1st Day								P value
	Grade 1		Grade 2		Grade 3		Grade 4		
	Count	%	Count	%	Count	%	Count	%	
NS1 Ag Positive	2	50.0%	17	34.0%	18	41.9%	13	35.1%	0.032*
IgM Positive	0	0.0%	13	26.0%	7	16.3%	5	13.5%	
Both NS1 Ag & IgM Positive	0	0.0%	1	2.0%	2	4.7%	9	24.3%	
Negative	2	50.0%	19	38.0%	16	37.2%	10	27.0%	

In this study there is significant association between Grade of Platelet count and Dengue serology. i.e. in higher grades both NS1 and IgM is positive and at Lower grade Ns1 Ag is positive.

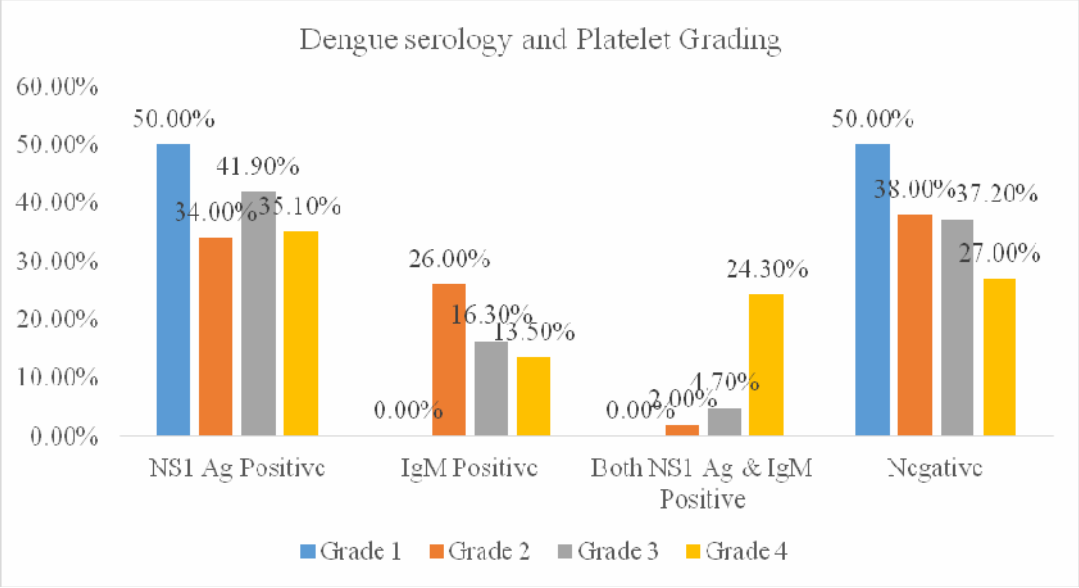


Figure 19: Bar diagram showing Dengue serology and Platelet Grading association

Table 20: Association between Platelet Grading and Diagnosis of Malaria

		PS for MP				P value
		Present		Absent		
		Count	%	Count	%	
Day1Platelet Grading	Grade 1	2	6.2%	2	2.0%	0.409
	Grade 2	13	40.6%	37	36.3%	
	Grade 3	11	34.4%	32	31.4%	
	Grade 4	6	18.8%	31	30.4%	

In this study among Malaria Positive patients 40.6% had Grade 2 platelet count, 34.4% had Grade 3 and 18.8% had Grade 4 platelet count. But there is no significant association between malaria diagnosis and platelet grading.

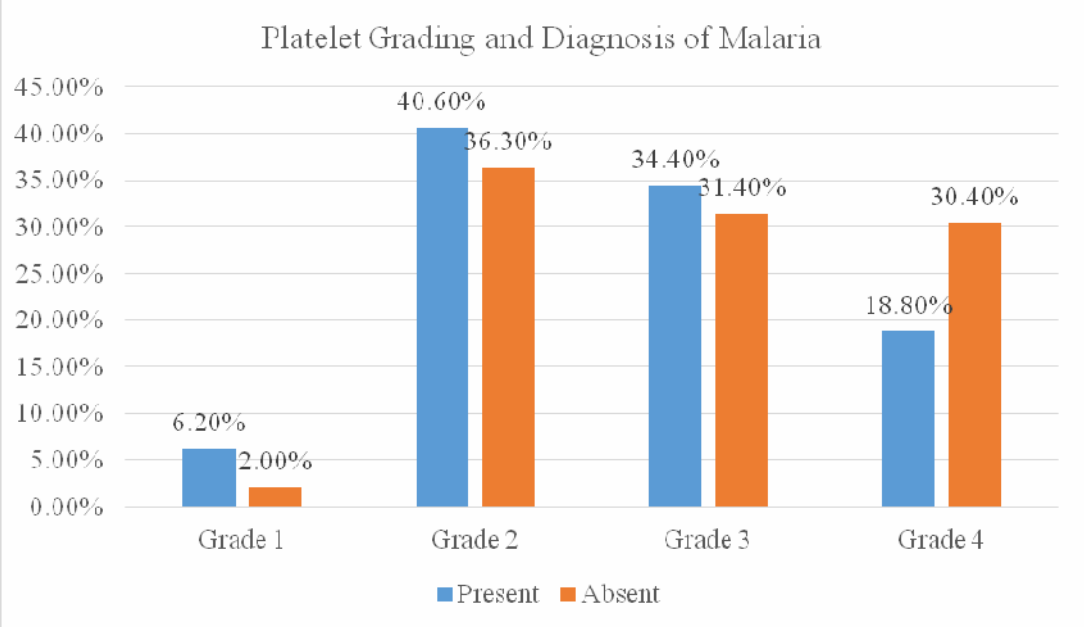


Fig 20 : Platelet Grading and Diagnosis of Malaria

Table 21: Association between Platelet Grading and Plasmodium Vivax Infection

		P.vivax				P value
		Absent		Present		
		Count	%	Count	%	
Day1Platelet Grading	Grade 1	2	1.8%	2	8.7%	0.207
	Grade 2	42	37.8%	8	34.8%	
	Grade 3	34	30.6%	9	39.1%	
	Grade 4	33	29.7%	4	17.4%	

In this study among 23 P.vivax positive patients 34.8% had Grade 2 platelet count, 39.1% had Grade 3 and 17.4% had Grade 4 platelet count. But there is no significant association between P.vivax infection and platelet grading.

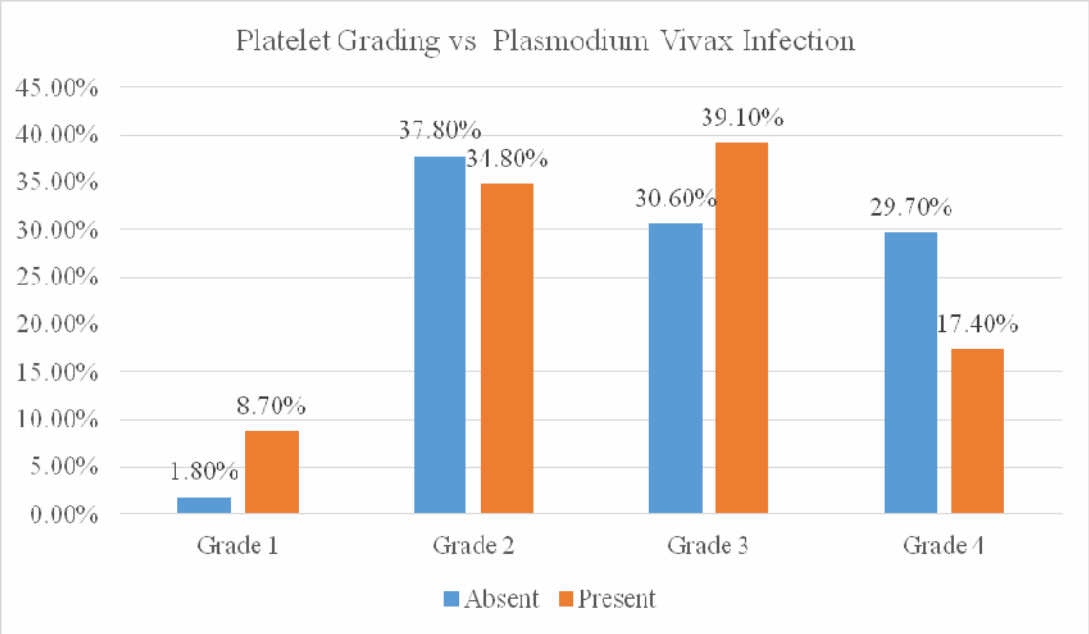


Fig 21 : Platelet Grading and Plasmodium Vivax Infection

Table 22: Association between Platelet Grading and Plasmodium Falciparum Infection

		P. Falciparum				P value
		Absent		Present		
		Count	%	Count	%	
Day1 Platelet Grading	Grade 1	4	3.2%	0	0.0%	0.672
	Grade 2	45	36.0%	5	55.6%	
	Grade 3	41	32.8%	2	22.2%	
	Grade 4	35	28.0%	2	22.2%	

In this study among 9 P.vivax Positive patients 55.6 % had Grade 2 platelet count, 22.2 % had Grade 3 and Grade 4 platelet grade respectively. But there is no significant association between P.falciparum infection and platelet grading.

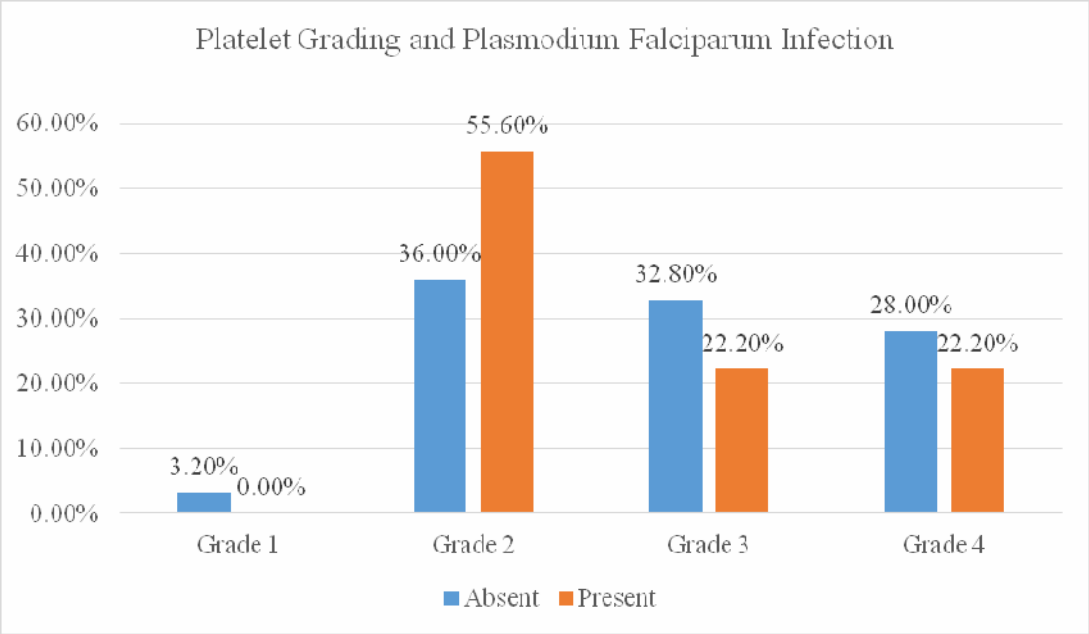


Fig 22 : Platelet Grading and Plasmodium Falciparum Infection

Table 23: Grade of Platelet count and Mean difference in Renal and Liver parameters

	1st day								P value
	Grade 1		Grade 2		Grade 3		Grade 4		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
BU	13.38	13.88	15.13	16.62	20.97	23.68	21.64	31.11	0.511
SC	0.76	0.09	0.93	0.47	1.01	0.76	1.01	1.11	0.888
TB	0.80	0.40	0.82	0.65	0.97	0.87	1.02	1.14	0.710
SGOT	20.50	9.88	28.42	23.05	37.91	35.77	36.68	43.47	0.429
SGPT	30.50	4.43	30.04	12.66	34.12	18.49	34.92	23.16	0.573

There is no significant difference in mean Renal and Liver function parameters with respect to Grades.

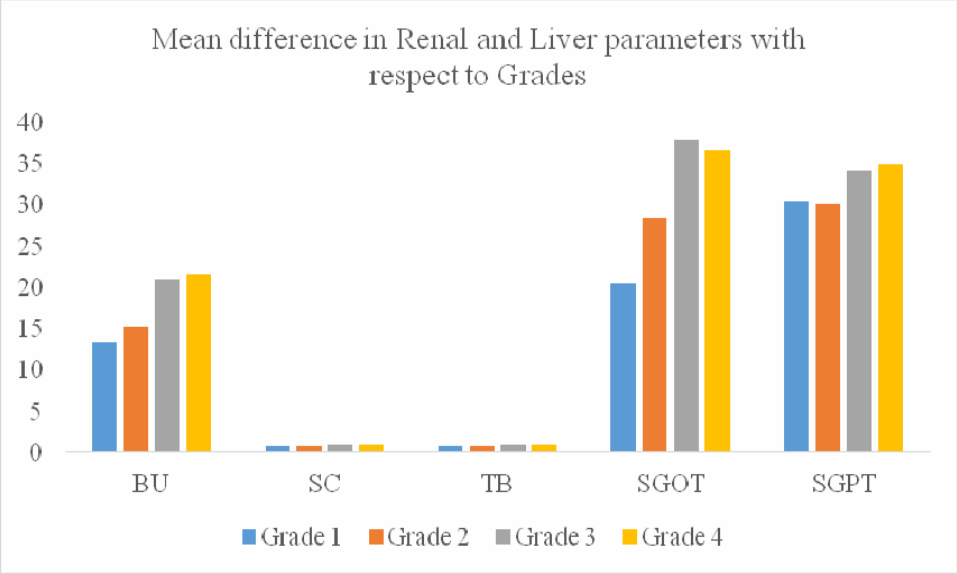


Figure 23: Bar diagram showing Mean difference in Renal and Liver parameters with respect to grades

Table 24: Grade of Platelet count and Organ Failure in subjects

		Day1								P value
		Grade 1		Grade 2		Grade 3		Grade 4		
		Count	%	Count	%	Count	%	Count	%	
Blood urea	Normal	4	100.0%	49	98.0%	40	93.0%	35	94.6%	0.658
	Raised	0	0.0%	1	2.0%	3	7.0%	2	5.4%	
Serum creatinine	Normal	4	100.0%	49	98.0%	40	93.0%	35	94.6%	0.658
	Raised	0	0.0%	1	2.0%	3	7.0%	2	5.4%	
Total bilirubin	Normal	4	100.0%	49	98.0%	39	90.7%	33	89.2%	0.319
	Raised	0	0.0%	1	2.0%	4	9.3%	4	10.8%	
SGOT	Normal	4	100.0%	49	98.0%	39	90.7%	33	89.2%	0.319
	Raised	0	0.0%	1	2.0%	4	9.3%	4	10.8%	
SGPT	Normal	4	100.0%	49	98.0%	39	90.7%	33	89.2%	0.319
	Raised	0	0.0%	1	2.0%	4	9.3%	4	10.8%	

There is no significant difference in Renal and Liver failure with respect to Grades of platelet count.

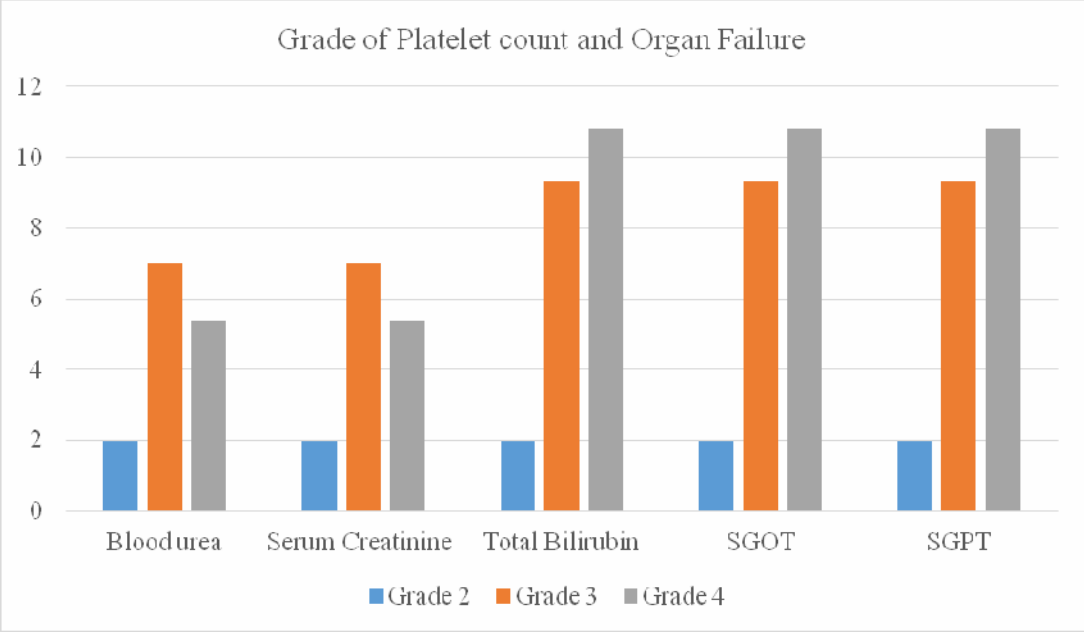


Figure 24: Bar diagram showing Grade of Platelet count versus Organ Failure

Table 25: Association between X ray findings and Platelet Grading

CXR	1st day							
	Grade 1		Grade 2		Grade 3		Grade 4	
	Count	%	Count	%	Count	%	Count	%
ARDS	0	0.0%	0	0.0%	3	7.0%	10	27.0%
B/L lower zone non homogenous opacities	0	0.0%	0	0.0%	1	2.3%	1	2.7%
B/L pleural effusion	0	0.0%	0	0.0%	0	0.0%	1	2.7%
Left lung fibrosis	0	0.0%	0	0.0%	1	2.3%	0	0.0%
Normal	4	100.0%	50	100.0%	38	88.4%	24	64.9%
Rt. lower zone non homogenous opacity	0	0.0%	0	0.0%	0	0.0%	1	2.7%

P value = 0.017*

There is significant association between X ray findings and platelet grading. i.e. in grade 3 and grade 4 ARDS and features of hemo perfusion is seen.

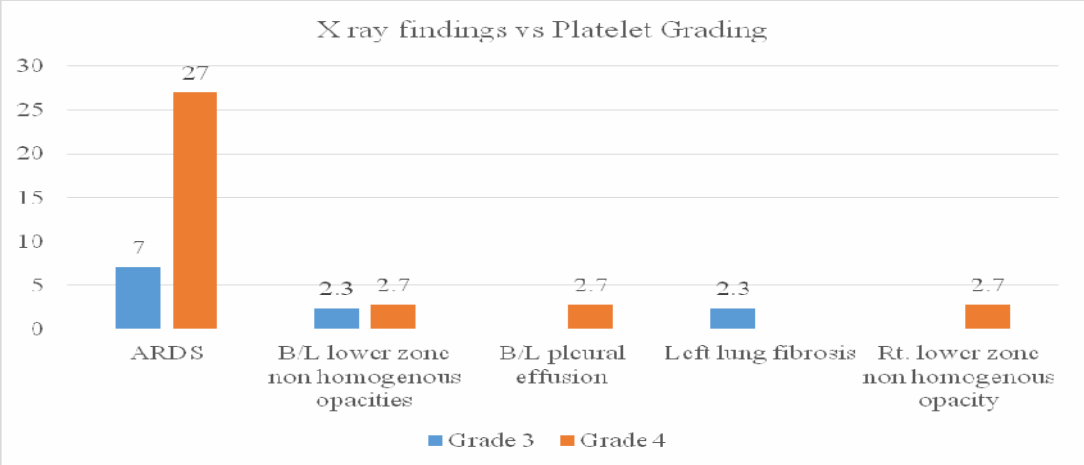


Figure 25: Bar diagram showing X ray findings vs Platelet Grading

Table 26: Association between Platelet Grading and USG findings

		1st day							
		Grade 1		Grade 2		Grade 3		Grade 4	
		Count	%	Count	%	Count	%	Count	%
USG	Ascites	1	25.0%	5	10.0%	4	9.3%	0	0.0%
	GB Sludge	0	0.0%	4	8.0%	2	4.7%	5	13.5%
	Hepatomegaly	0	0.0%	2	4.0%	0	0.0%	3	8.1%
	Normal	3	75.0%	38	76.0%	35	81.4%	29	78.4%
	Splenomegaly	0	0.0%	1	2.0%	2	4.7%	0	0.0%

p = 0.362

There is no significant association between Platelet grading and USG findings.

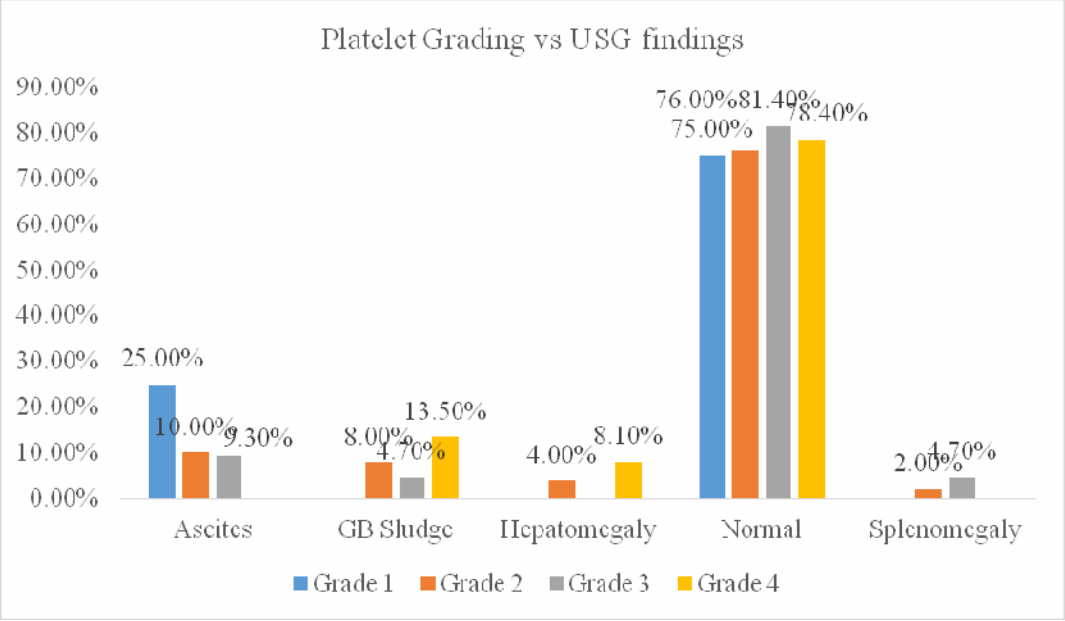


Figure 26: Bar diagram showing Platelet Grading and USG findings

Table 27: Association between Platelet Transfusion versus Grade of Platelet counts

		1st day				P value
		Grade 3		Grade 4		
		Count	%	Count	%	
Platelet transfusion	4	2	66.7%	10	32.3%	0.266
	6	0	0.0%	17	54.8%	
	8	1	33.3%	3	9.7%	
	12	0	0.0%	1	3.2%	

In this study there is no significant association between platelet transfusion and grade of platelet count.

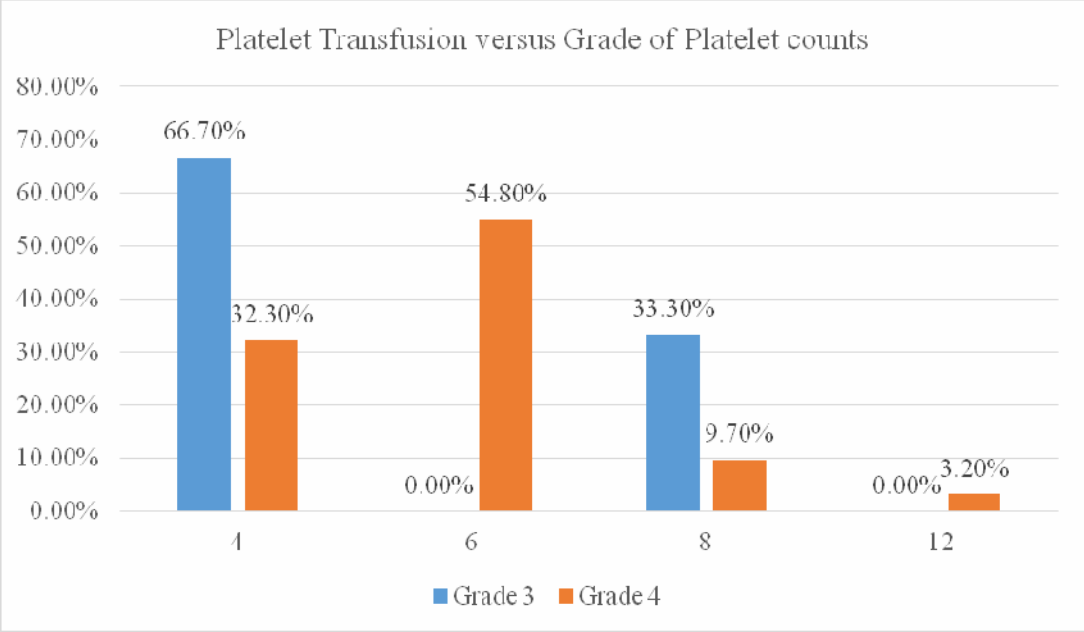


Figure 27: Bar diagram showing Platelet Transfusion versus Grade of Platelet counts

Table 28: Association between Outcome and Platelet count Grading

		1st day							
		Grade 1		Grade 2		Grade 3		Grade 4	
		Count	%	Count	%	Count	%	Count	%
Outcome	Death	0	0.0%	0	0.0%	3	7.0%	5	13.5%
	Discharge	4	100.0%	50	100.0%	40	93.0%	32	86.5%

p = 0.064

In this study higher grade had poor outcome in 13.5%. But this observation is not statistically significant.

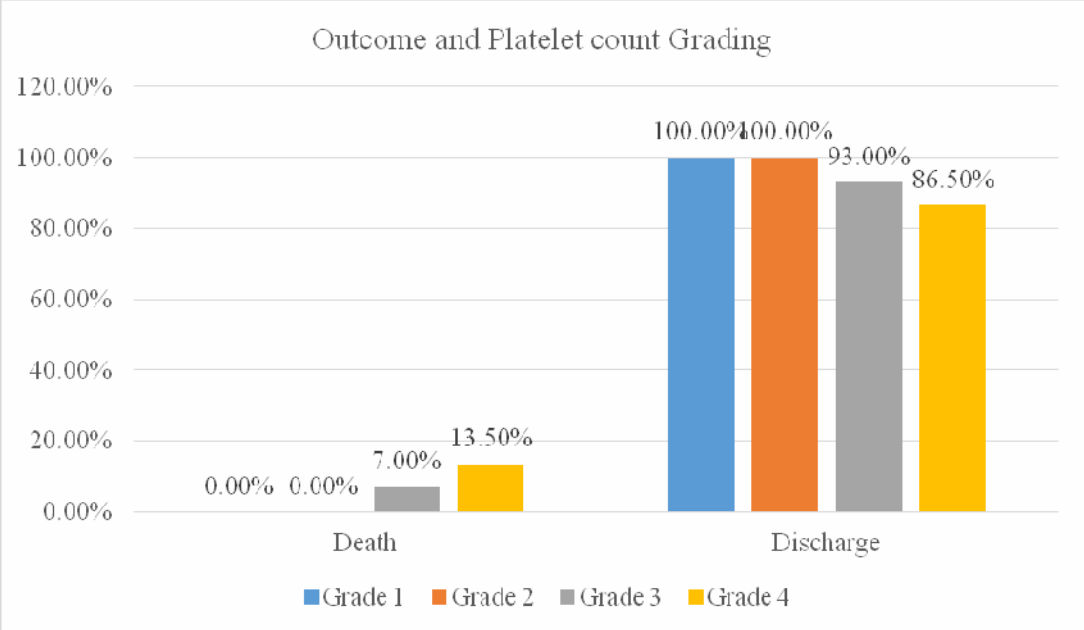


Fig 28 : Association between Outcome and Platelet count Grading

Table 29: Association between Outcome and Duration of Fever

		Outcome coded				P value
		Discharged		Death		
		Count	%	Count	%	
Duration of Fever	**1 to 3 days**	102	81.0%	0	0.0%	<0.001*
	4 to 6 days	23	18.3%	7	87.5%	
	> 6 days	1	0.8%	1	12.5%	

In this study there is significant association between duration of fever and outcome. i.e. Mortality is commonly seen in subjects with duration of fever > 3 days (100%).

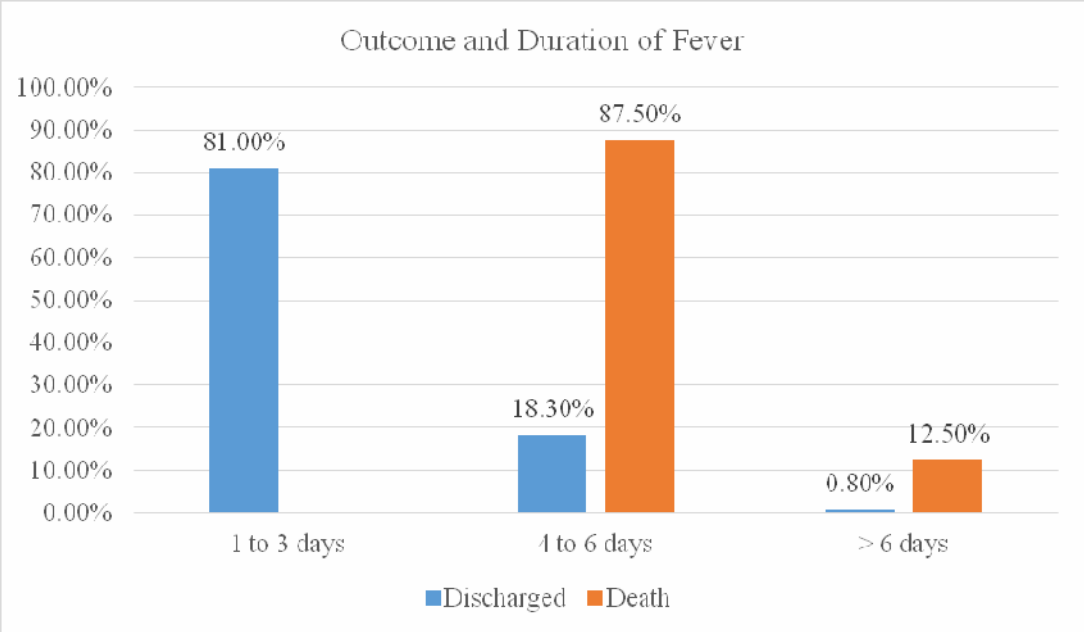


Figure 29: Bar diagram showing Outcome versus Duration of Fever

Table 30: Association between Outcome and Vital signs

		Outcome				P value
		Discharged		Death		
		Count	%	Count	%	
Pulse Rate	61 to 100 bpm Normal	56	44.4%	1	12.5%	0.76
	> 100 bpm Tachycardia	70	55.6%	7	87.5%	
Systolic blood pressure	< 90 mm/hg Hypotension	24	19.0%	6	75.0%	<0.001*
	90 to 140 mm/hg Normal	102	81.0%	2	25.0%	
Diastolic blood Pressure	< 60 mm/hg Hypotension	51	40.5%	7	87.5%	0.009*
	60 to 90 Normal	75	59.5%	1	12.5%	

There is significant association between SBP and DBP with outcome. i.e. 75% of death cases had SBP hypotension and 87.5% had DBP hypotension.

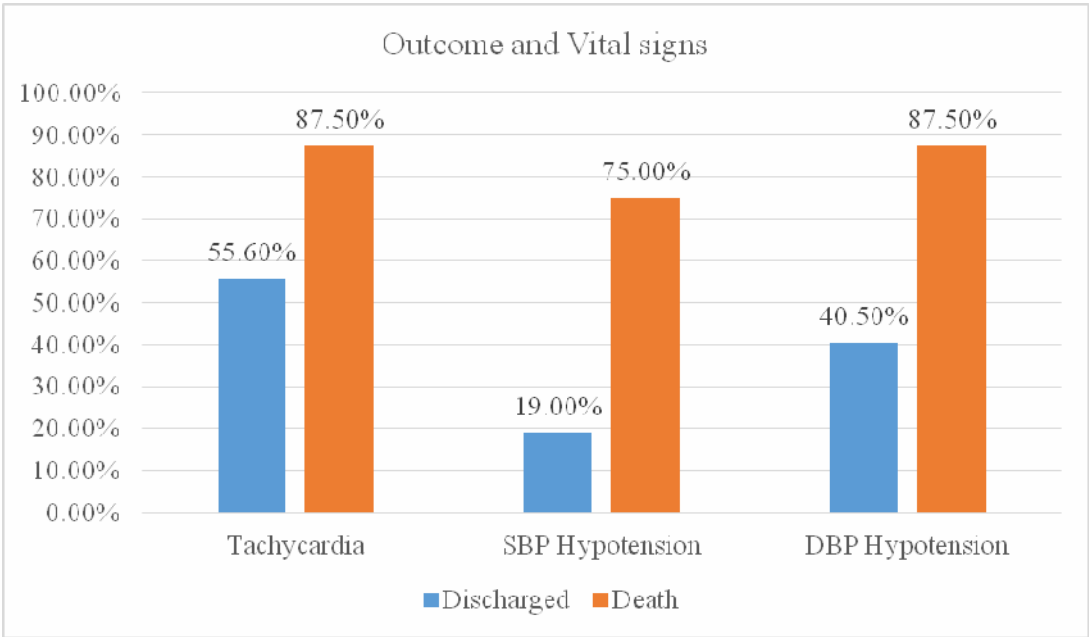


Figure 30: Bar diagram showing Outcome versus Vital signs

Table 31: Association between Outcome and Bleeding

		Outcome				P value
		Discharged		Death		
		Count	%	Count	%	
Bleeding	Present	56	44.4%	5	62.5%	0.320
	Absent	70	55.6%	3	37.5%	

There is no significant association between Outcome and bleeding.

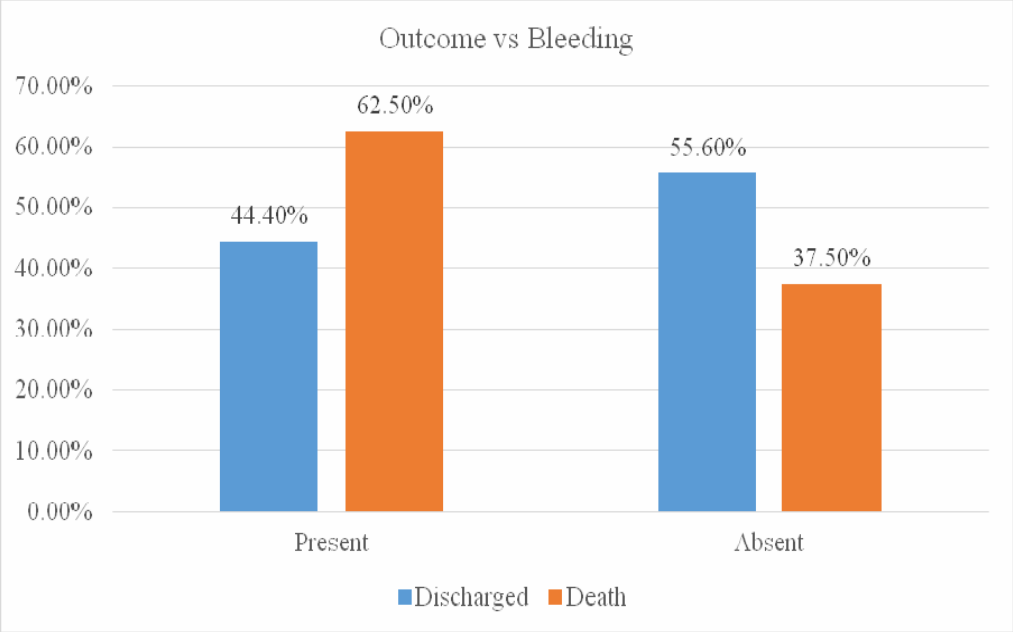


Figure 31: Bar diagram showing Outcome and Bleeding

Table 32: Association between Outcome and Dengue Serology

		Outcome coded				P value
		Discharged		Death		
		Count	%	Count	%	
Dengue serology	NS1 Ag Positive	48	38.1%	2	25.0%	0.359
	IgM Positive	23	18.3%	2	25.0%	
	Both NS1 Ag & IgM Positive	10	7.9%	2	25.0%	
	Negative	45	35.7%	2	25.0%	

There is no significant association between outcome and Dengue serology

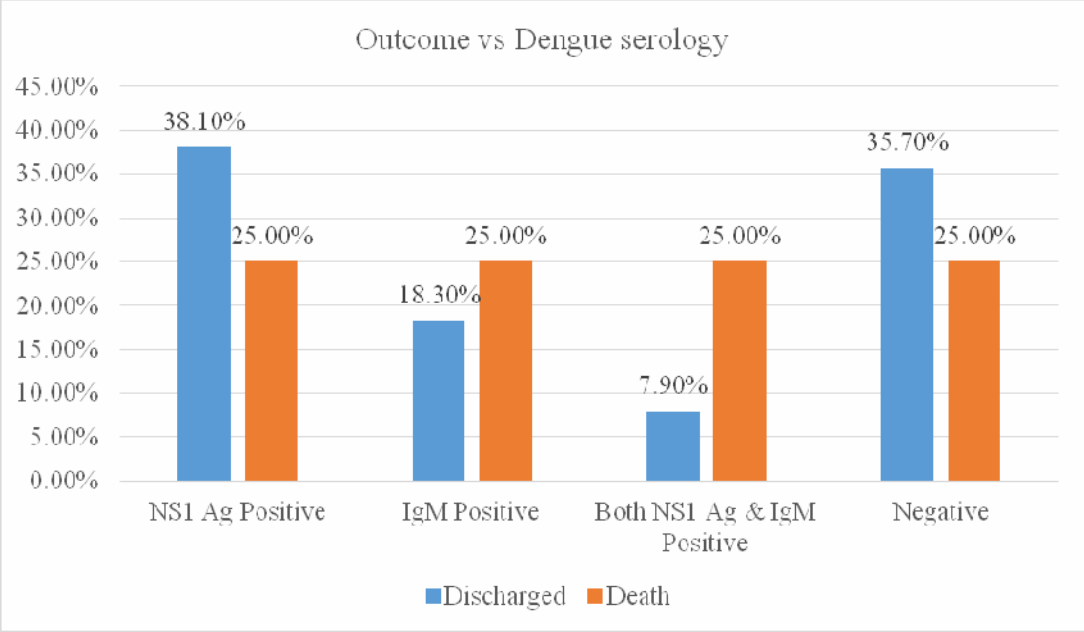


Figure 32: Bar diagram showing outcome vs Dengue serology

Table 33: Association between Outcome and Diagnosis

		Outcome coded				P value
		Discharged		Death		
		Count	%	Count	%	
Sepsis	Present	21	16.7%	5	62.5%	0.001*
	Absent	105	83.3%	3	37.5%	
Dengue	Present	81	64.3%	6	75.0%	0.538
	Absent	45	35.7%	2	25.0%	
PS for MP	Present	32	25.4%	0	0.0%	0.102
	Absent	94	74.6%	8	100.0%	
Mixed infection	Present	9	7.1%	0	0.0%	0.434
	Absent	117	92.9%	8	100.0%	

There is significant association between Sepsis and Outcome. i.e. 62.5% of the subjects who died had sepsis. There is no significant association with other diagnosis.

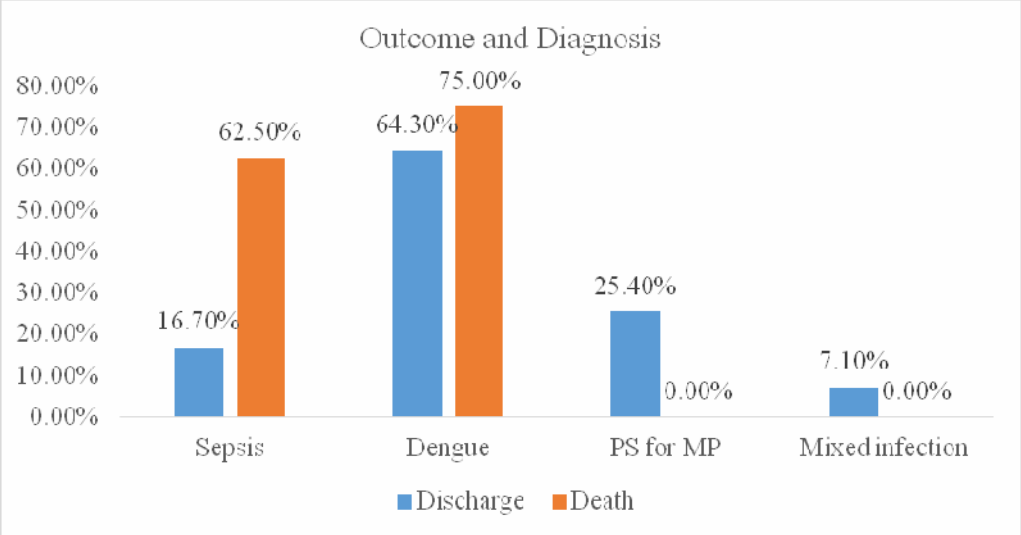


Figure 33: Bar diagram showing outcome vs diagnosis

Table 34: Association between Outcome Vs Total leucocyte count(TLC)

	Outcome	N	Mean	Std. Deviation	P value
TLC	Discharged	126	8643.65	3455.928	0.009*
	Death	8	12112.50	5298.366	

There is significant difference in mean TLC with respect to outcome. i.e. Subjects who died had higher TLC.

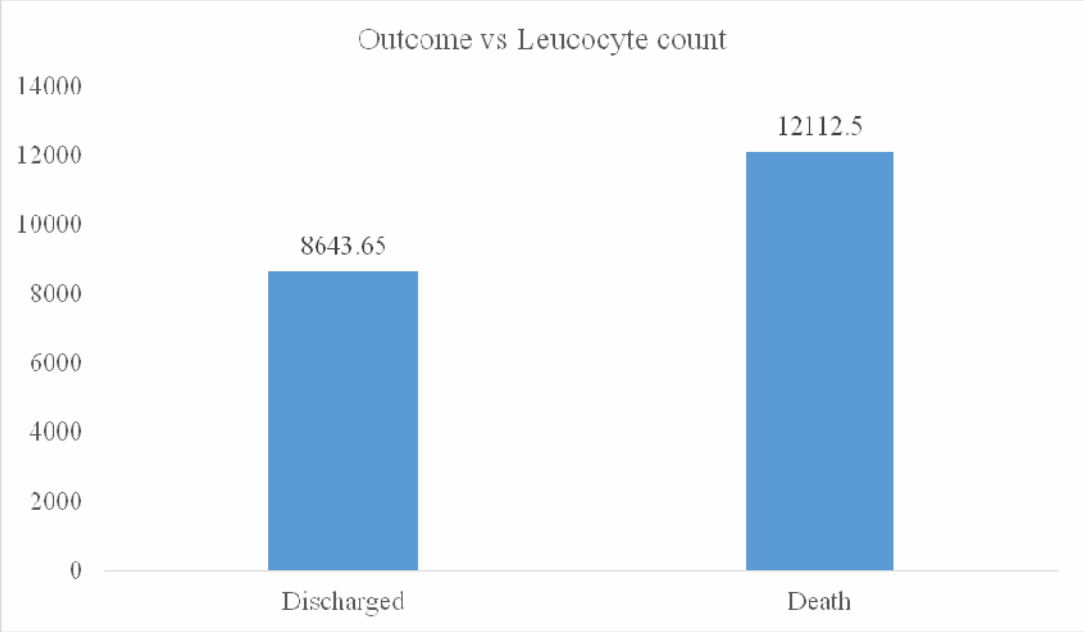


Figure 34: Bar diagram showing Outcome vs Leucocyte count

Table 35: Mean Difference of Renal and Liver Function parameters with respect to Outcome

	Outcome				P value
	Discharged		Death		
	Mean	SD	Mean	SD	
Blood Urea	16.27	15.97	57.82	64.29	<0.001*
Serum Creatinine	0.89	0.47	2.27	2.33	<0.001*
Total Bilirubin	0.85	0.75	2.04	1.70	<0.001*
SGOT	30.09	27.02	87.38	71.00	<0.001*
SGPT	31.15	15.27	57.25	33.74	<0.001*

There is significant difference in renal parameters and liver function parameters with respect to outcome. i.e. .in subjects who had mortality had higher Blood urea, Serum creatinine, Total bilirubin, SGOT and SGPT.

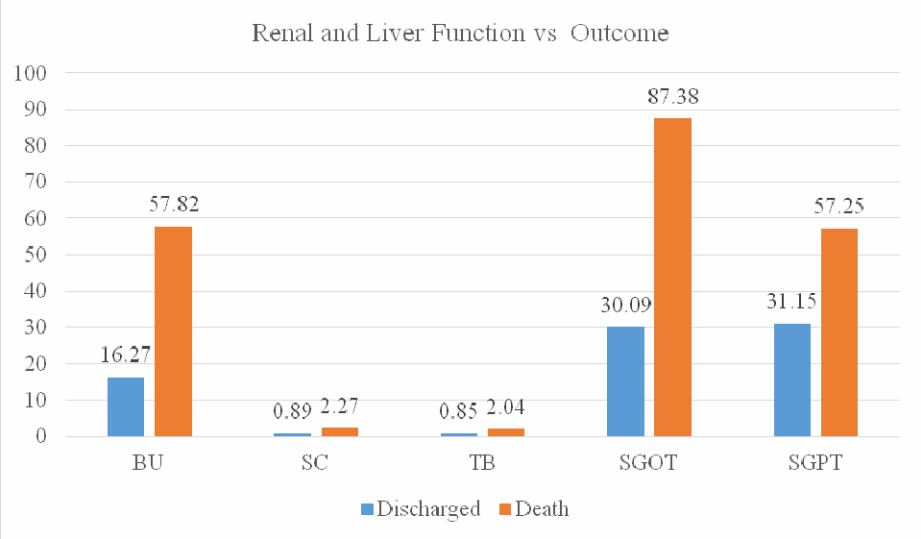


Figure 35: Bar diagram showing Renal and Liver Function parameters with respect to Outcome

Table 36: Association between Outcome and Organ Failure

		Outcome				P value
		Discharged		Death		
		Count	%	Count	%	
Blood urea	Normal	123	97.6%	5	62.5%	<0.001*
	Raised	3	2.4%	3	37.5%	
Serum creatinine	Normal	123	97.6%	5	62.5%	<0.001*
	Raised	3	2.4%	3	37.5%	
Total bilirubin	Normal	121	96.0%	4	50.0%	<0.001*
	Raised	5	4.0%	4	50.0%	
SGOT	Normal	121	96.0%	4	50.0%	<0.001*
	Raised	5	4.0%	4	50.0%	
SGPT	Normal	121	96.0%	4	50.0%	<0.001*
	Raised	5	4.0%	4	50.0%	

There is significant difference in renal parameters and Liver function parameters with respect to outcome. i.e. .in subjects who had mortality had higher Blood urea, Serum creatinine, Total bilirubin, SGOT and SGPT.

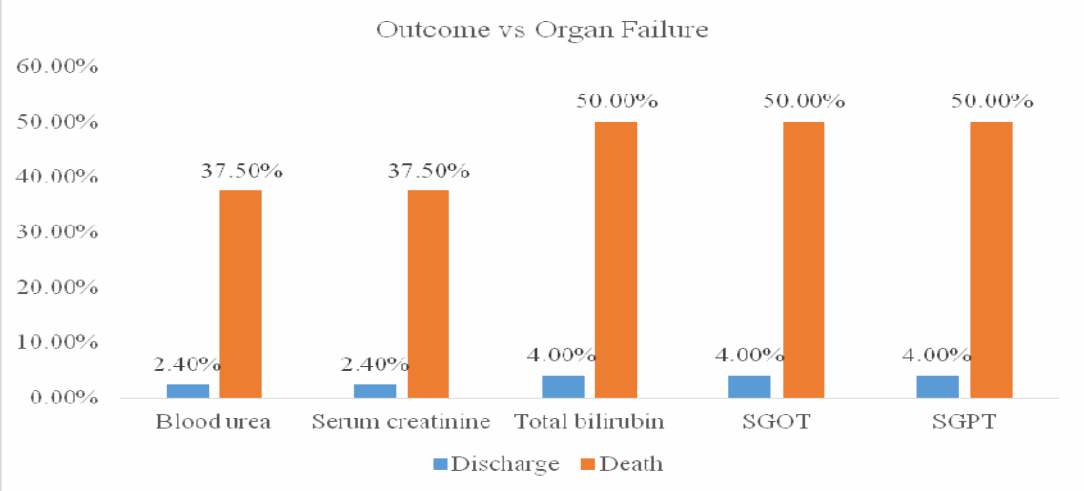


Figure 36: Bar diagram showing Renal and Liver Function parameters with respect to Outcome

Table 37: Association between Chest X ray findings and Outcome

		Outcome				P value
		Discharged		Death		
		Count	%	Count	%	
CXR	ARDS	10	7.9%	3	37.5%	<0.001*
	B/L lower zone non homogenous opacities	2	1.6%	0	0.0%	
	B/L pleural effusion	0	0.0%	1	12.5%	
	Left lung fibrosis	1	0.8%	0	0.0%	
	Normal	112	88.9%	4	50.0%	
	Rt. lower zone non homogenous opacity	1	0.8%	0	0.0%	

In this study there is significant association between Chest X ray findings and Outcome. i.e 37.5% of .Subjects with Chest X ray findings (ARDS) had mortality.

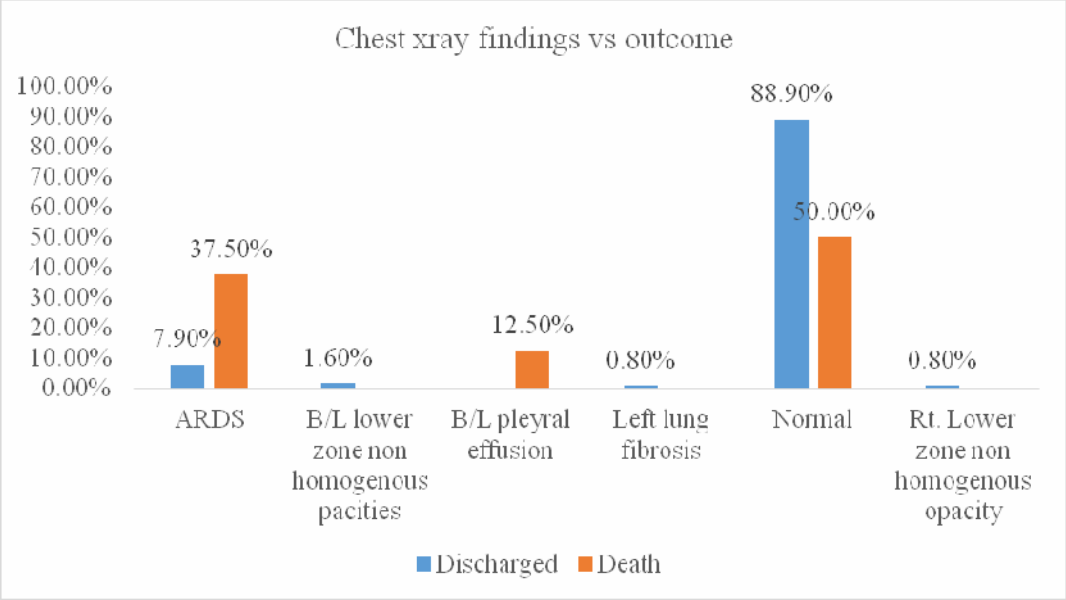


Figure 37: Bar diagram showing Chest X ray findings vs Outcome

Table 38: Association between USG findings and Outcome

		Outcome				P value
		Discharged		Death		
		Count	%	Count	%	
USG	Ascites	10	7.9%	0	0.0%	0.015*
	Gall Bladder Sludge	8	6.3%	3	37.5%	
	Hepatomegaly	4	3.2%	1	12.5%	
	Normal	101	80.2%	4	50.0%	
	Splenomegaly	3	2.4%	0	0.0%	

There is significant association between outcome and USG findings. i.e. 50% of subjects who had mortality had abnormal findings such as Gall Bladder(GB) sludge (37.5%) and Hepatomegaly (12.5%).

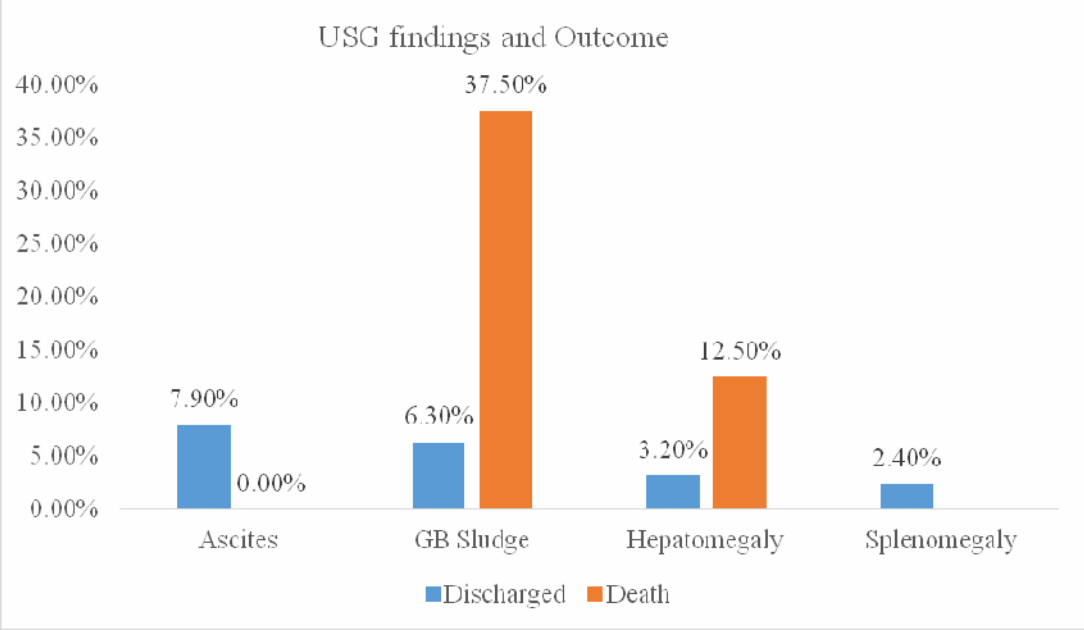


Figure 38: Bar diagram showing USG findings vs Outcome

Table 39: Association between Outcome and Platelet transfusion

		Outcome				P value
		Discharged		Death		
		Count	%	Count	%	
Platelet transfusion	4	10	37.0%	2	28.6%	0.075
	6	15	55.6%	2	28.6%	
	8	2	7.4%	2	28.6%	
	12	0	0.0%	1	14.3%	

There is no significant association between platelet transfusion and outcome.

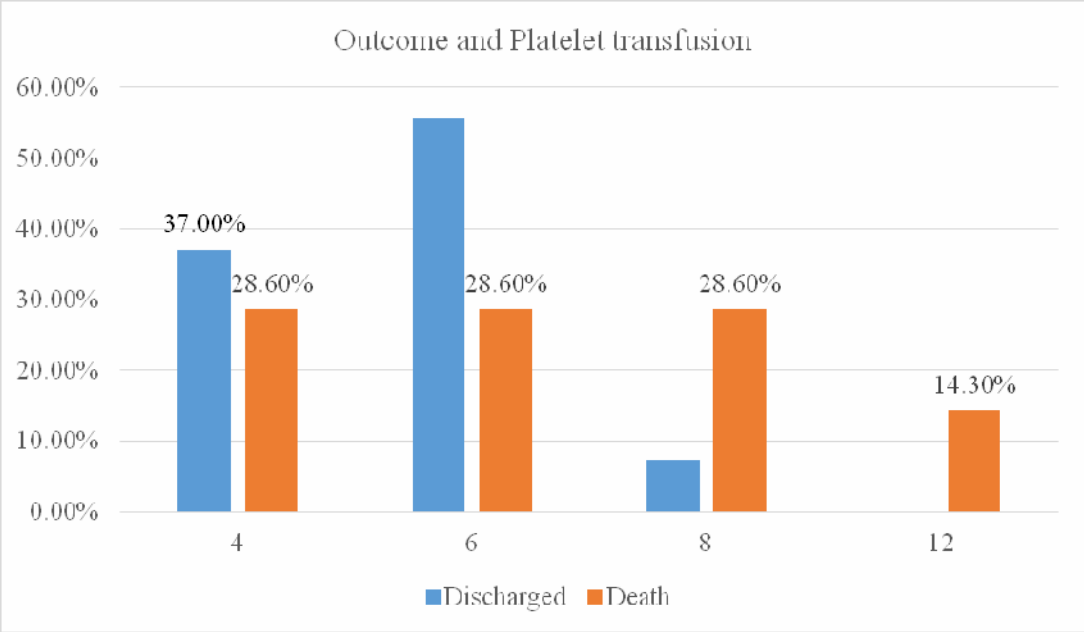


Figure 39: Bar diagram showing Outcome and Platelet transfusion

DISCUSSION

A prospective study of 134 patients, who presented with fever and thrombocytopenia, was carried out at Sri Devraj URS Medical college, Tamaka, Kolar.

In our study majority 32.8% of subjects were in the age group 21 to 30 years followed by 27.6% in 31 to 40 years. Least number of cases were seen in < 20 years (10.4%) and > 50 years (10.4%). Mean age of subjects was 35.49 ± 12.94. This is in consistent with the study done by Monira Pervin et al, where the age group in the study was 20 – 29 yrs (37 %) and a study done by Ekta Gupta et al, had included patients with age group of 21 – 30 yrs (34.2%) which is again in consistent with our study.[95]

In our study Majority of the patients are males (51.5%) and 48.5% are females. This is consistent with study done by Nair PS et al, where 69.7% males and 30.3% females.[51] A study done by Putta Suresh ,the majority of the patients were male (54%)[89] and females 46%, which is consistent with our study.

In our study all the cases had fever, mean duration of fever was 2.69 ± 1.71 days. 63.4% had headache, 12.7% had joint pains, 72.4% had vomiting, 67.2% had myalgia, 26.9% had abdominal pain & rashes respectively, 10.4% had dyspnea and 44.8% had bleeding manifestations. In a study done by Monira Pervin et al, the common symptoms were myalgia (84.5%), headache (82.5%), arthralgia (68%), lethargy (80.4%) and retro orbital pain (49.5%)[94]. In a study done by Kumar A et al, most common presentation was myalgia (64.6%), vomiting (47.6%) ,headache (47.6%) and abdominal pain (37.6%).[97]

CLINICAL FEATURES	Monira Pervin et al (2004)	Kumar A et al(2010)	Present study
FEVER	100%	100%	**100%**
HEADACHE	82.5%	47.6%	**63.4%**
JOINT PAINS	68%	NM	**12.7%**
MYALGIA	84.5%	64.6%	**67.2%**
VOMITING	NM	47.6%	**72.4%**

In the above studies headache and mayalgia are the common presenting symptoms followed by arthralgia and vomiting, which is consistent with our present study.

In the present study 44.8% had bleeding manifestations. In that 27.6% presented with Conjunctival Hemorrhage, 17.9% with Bleeding Gums, 18.7% with Petechiae and 3% with Hematuria.

BLEEDING MANIFESTATION	Putta Suresh study (2015)	Gandhi AA et al study (2015)	Kumar A et al study(2010)	PS Nair et al study (2003)	Present study
Petechiae	16%	29.4%	67.2%	22.2%	**18.7%**
Bleeding gums	8%	6%	35.2%	15.6%	**17.9%**
Conjunctival haemorrhage	NM	NM	NM	NM	**27.6%**
Haematuria	8%	1%	NM	NM	**3%**

In a study done by Kumar A et al, most common bleeding manifestations were petechiae (67.2%), gum bleed (5.2%), melena (4.7%), hemetemesis (3%) and epistaxis (2.6%).[97] In a study done by PS Nair et al, petechiae / purpura was the commonest bleeding manifestations (22.22%,n=45) and GI bleed (22.22%) followed by epistaxis(15.56%,n=45), bleeding gums (13.33%,n=45), and other bleeding accounting for 26.67%(n=45).[51]

In a study done by Putta Suresh the commonest bleeding manifestation was cutaneous in the form of petechiae and purpura, which was seen in 8 cases (16%), followed by hematemesis (12%), malena (12%), bleeding gums (8%), hematuria (8%) and epistaxis (2%).[89] In a study done by Gandhi AA et al the common bleeding manifestation was petechiae (29.4%) followed by bleeding gums (6%).[84]

In the present study conjunctival haemorrhage is the most common bleeding manifestation (27.6%). Conjunctival haemorrhage + Bleeding gums seen in 12 patients (9%), conjunctival haemorrhage + petechiae seen in 8 patients (6%), bleeding gums + petechiae seen in 3 patients (2.2%), conjunctival haemorrhage + hematuria seen in 2 patients (1.5%), conjunctival haemorrhage + petechiae + hematuria seen in 2 patients (1.5%)(TABLE 7)

Grading of thrombocytopenia is carried out according to National Cancer Institute (NCI)

Common Terminology Criteria.[90]

Grade 0: Within normal limit, platelet count 150,000 or above.

Grade I: Platelet count between 75,000 and 150,000.

Grade II: Platelet count between 50,000 and 75,000.

Grade III: Platelet count between 25,000 and 50,000.

Grade IV: Platelet count less than 25,000.

PLATELET COUNT AT PRESENTATION	PS Nair et al study (2003)	Gandhi AA et al study (2015)	Putta Suresh study (2015)	Bhalara et al study (2015)	Present study
<10,000	8.2%	<50,000	<20,000	6%	**GRADE 1 - 3%**
10,000-20,000	9.2%	18%	15%	9.7%	**GRADE 2- 37.3%**
20,000-50,000	25.7%		13.3%	23.5%	**GRADE 3-32.1%**
50,000-1,00,000	56.8%	14%	64%	28.4%	**GRADE 4- 27.6%**
1,00,000-1,50,000				31.4%	

In the present study

On Day 1, 3% had Grade 1 platelet count, 37.3% had Grade 2, 32.1% had Grade 3 and 27.6% had Grade 4 Platelet count.

On Day 3, 11.9% had Grade 1, 44% had Grade 2, 28.4% had Grade 3 and 14.9% had Grade 4 Platelet count.

On Day 5, 42.5% had Grade 1, 21.6% had Grade 2, 18.7% had Grade 3 and 3% had Grade 4 platelet count.

On Day 7, 40.3% had Grade 1 only. Increase in duration there was improvement in subjects.

In a study, conducted by Nair PS et al, 56.8% had platelet count between 50,000-1,00,000 followed by 28 patients (25.7%) between 20,000 to 50,000,and 9.2% between10,000 to 20,000 , and 8.2% had <10,000. This is consistent with our study.[51]

In Gandhi AA et al study distribution of platelet count in the range of > 50000-150000/mm3 was seen in 57.14%. Platelet count in the range of 20-50000/mm3 was seen in 29.47% and Platelet count in the range of 0-20000/mm3 was

seen in 13.39%.[84] In Bhalara et al study 1,00,000- 1,50,000 present in 31.4%, 50,000 - 1,00,000 present in 28.4%, 20,000-50,000 present in 23.5%, 10,000-20,000 present in 9.7% and <10,000 present in 6%.[87]

In the present study we observed that with increase in grade of platelet count there was increase in bleeding tendency. At presentation In Grade 1 no bleeding, in grade 2 % had bleeding, in grade 3 62.8% had bleeding and in Grade 4. 86.5% had bleeding manifestations. This observation was statistically significant.

	Platelet counts association with bleeding manifestations			
Gandhi AA et al study (2015)	<20,000- 16.9%	20,000 - 50,000 24.1%	>50,000-1.7%	
Present study	**GRADE 4 - 86.5%**	**GRADE - 3 62.8%**	**GRADE 2- 4%**	**GRADE 1- 0%**

In Gandhi AA et al study 16.9% of cases with <20,000 platelet count had bleeding manifestations,24.1% of cases with range of 20,000 - 50,000, 1.7% of cases with >50,000 platelet count had bleeding manifestations.[84]

In our study we observed that Conjunctival hemorrhage was common in Grade 2, Bleeding gums & Petechiae was common in Grade 3 and Conjunctival hemorrhage with Bleeding Gums was common in Grade 4. This observation was statistically significant. (TABLE 17)

In the present study 19.4% were diagnosed to have Sepsis (TLC > 10000), 64.9% were positive for Dengue, 23.8% were positive for Malarial parasite, 6.7% had Mixed Infection and one case is positive for both sputum AFB samples.

Etiology for thrombocytopenia	Bhalara et al Study (2015)	Gandhi AA et al study (2015)	Putta Suresh study (2015)	PS Nair et al study (2003)	Present study
DENGUE	28.6%	26.7%	14%	13.7%	**64.9%**
MALARIA	22.8%	36.6%	8%	9.1%	**23.8%**
SEPSIS	6.3%	4.4%		26.6%	**19.4%**
DENGUE + MALARIA					**6.7%**
OTHERS			8%	14.6%	

In the present study among Dengue Positive cases 37.3% were positive for NS1 Ag, 18.7% were positive for IgM antibodies and 9% were positive for Both NS1 and IgM ab. 17.2% were positive for P.vivax and 6.7% for P. falciparum. 3.7% had Dengue + P. vivax and 3% had Dengue + P. falciparum .No cases of Leptospira and Rickettsia (TABLE 11)

In Bhalara et al most common etiology responsible for newly diagnosed thrombocytopenia in adult patients is dengue (28.6%) , second common etiology was malaria (22.8%) which is consistent with our study.[87] In Putta Suresh study common etiology is dengue (14%), followed by malaria (8%) which is consistent with our study.[89] Whereas in PS Nair et al study common etiology is sepsis(26.6%) followed by enteric fever(14.6%), dengue(13.7%) and malaria (9.1%).[51]

In Gandhi AA et al study dengue positive in 30 cases in that 36.6% cases of dengue had > 50,000 platelet count, 50% cases of dengue had 20,000-50,000 platelet count range, 10% cases of dengue are in 10000- 20000 platelet count range and 3% 0f cases are in 5000- 10000 range. Malaria positive in 41 cases in that 63.4% of cases had >50000 platelet count, 24.3% cases are within range of 20000-50000, 9.7% cases are in 10000- 20000 platelet count range and 2% are within 5000-10000 platelet count

range. Septicemia in 4 cases, in that 80% had > 50000 and 20% are in 5000-10000 platelet count range.[84]

Gandhi AA et al study etiology of fever with thrombocytopenia in different platelet count range					
Etiology	**Plateletcount >50000**	**20000-50000**	**10000-20000**	**5000-10000**	**<5000**
Dengue	36.6%	50%	10%	3%	0
Malaria	63.4%	24.3%	9.7%	2%	0
Septicemia	80%	0	0	20%	0

In the present study dengue positive in 87 cases in that 2% of cases are presented with GRADE 1 thrombocytopenia, 35.6% of cases presented with GRADE 2 thrombocytopenia, 31% of cases presented with GRADE 3 thrombocytopenia and 31% of cases presented with GRADE 4 thrombocytopenia. There was significant association between Grade of Platelet count and Dengue serology. I.e. in higher grades both NS1 and IgM was positive and at Lower grade Ns1 Ag was positive.

In the present study Malaria positive in 32 cases in that 6% of cases presented with GRADE 1 thrombocytopenia, 40% cases presented with GRADE 2 thrombocytopenia, 34% cases presented with GRADE 3 thrombocytopenia and 18% cases presented with GRADE 4 thrombocytopenia.

In the present study Sepsis is seen in 26 cases in that 34% cases presented with GRADE 2 thrombocytopenia, 30% cases presented with Grade 3 thrombocytopenia, 34% cases presented with GRADE 4 thrombocytopenia.

In the present study Mixed infection (Dengue + Malaria) seen in 9 cases in that 44% cases presented with GRADE 2 thrombocytopenia, 22% cases presented with GRADE 3 thrombocytopenia, 33% cases presented with GRADE 4 thrombocytopenia.(TABLE 18)

In our study radiologically on chest X ray, 9.7% had ARDS and 2 cases had b/l lower zone non homogenous opacities, 1 case had Rt lower zone non homogenous opacity, 1 case had b/l pleural effusion and 1 case had left lung fibrosis. On USG 8.2% had GB sludge, 7.5% had ascites, 3.7% had Hepatomegaly and 2.2% had Splenomegaly.

In our study 25.4% of subjects required Platelet transfusion. Of them 12.7% were transfused with 6 pints, 9% with 4 pints, 3% with 8 pints and 0.7% with 12 pints.

In the present study Prognosis was good in 94% of subjects and were discharged and 6% had poor prognosis and died during the stay. 126 cases are discharged and 8 cases are died, in that 8 cases 3(7%) cases presented with GRADE 3 thrombocytopenia, 5 (13.5%) presented with GRADE 4 thrombocytopenia. Higher grade thrombocytopenia had poor outcome in 13.5%.

In the present study there was significant association between Duration of fever and outcome. I.e. Mortality was commonly seen in subjects with duration of fever > 3 days. In 8 cases, 7(87.5%) cases presented with duration of 4-6 days, 1(12.5%) case presented with duration of fever >6 days.

In the present study 61 cases presented with bleeding manifestations, in that 56(91.8%) cases are discharged and 5(8.1%) cases are died.

In our study there was significant association between Sepsis and Outcome. I.e. 62.5% of the subjects who died had sepsis. In 8 cases, 5(62.5%) cases has sepsis and 6 (75%) are dengue positive.

In the present study there was significant difference in renal parameters and Liver function parameters with respect to outcome. i.e. .In subjects who had mortality had higher Blood urea, Serum creatinine, Total bilirubin, SGOT and SGPT. (TABLE 36) There was significant association between Chest X ray findings and Outcome. I.e 37.5% of .Subjects with Chest X ray findings (ARDS) had mortality. ARDS seen in 13 cases in that 3 cases are died. There was significant association between outcome and USG findings. I.e. 50% of subjects who had mortality had abnormal findings such as GB sludge (37.5%) and Hepatomegaly (12.5%).

CONCLUSION

This study shows that dengue fever (64.9%) is the most common diagnosis made in patients who are presented with febrile illness with thrombocytopenia followed by malaria(23.8%) and sepsis (19.4%). Among Dengue positive patients 37.3% are positive for NS1Ag, 18.7% positive for IgM antibodies and 9% are positive for both NS1 and IgM antibodies. Among Malaria, 17.2% are positive for P.vivax and 6.7% for P.falciparum. 3.7% had Dengue + P.vivax and 3% had Dengue + P.falciparum. No cases of Leptospira and Rickettsia. Sixty one patients tend to have bleeding manifestations, most common being the conjunctival haemorrhage. In this study we observed that with increase in grade of platelet count there was increase in bleeding tendency. Majority of bleeding manifestations occurred in patients with GRADE 4 thrombocytopenia.

SUMMARY

- In our study we included 134 patients who presented with Fever with thrombocytopenia.
- 32.8% were between age group 21-30 years.
- 51.5% were males and 48.5% were females.
- Mean duration of fever was 2.69+_ 1.7 days.
- In our study all patients presented with fever, followed by vomiting(72.4%),myalgia (67.2%), headache(63.4%) and joint pains (12.7%).
- In our study 44.8% had bleeding manifestations. In that 27.6% presented with Conjunctival Hemorrhage, 17.9% with Bleeding Gums, 18.7% with Petechiae and 3% with Hematuria.
- In a present study conjunctival haemorrhage is the most common bleeding manifestation (27.6%). Conjunctival haemorrhage + Bleeding gums seen in 12 patients (9%), conjunctival haemorrhage + petechiae seen in 8 patients (6%), bleeding gums + petechiae seen in 3 patients (2.2%), conjunctival haemorrhage + hematuria seen in 2 patients (1.5%), conjunctival haemorrhage + petechiae + hematuria seen in 2 patients (1.5%).
- In our study 25.4% of subjects required Platelet transfusion. Of them 12.7% were transfused with 6 pints, 9% with 4 pints, 3% with 8 pints and 0.7% with 12 pints.
- In our study

  On Day 1, 3% had Grade 1 platelet count, 37.3% had Grade 2, 32.1% had Grade 3 and 27.6% had Grade 4 Platelet count.

  On Day 3, 11.9% had Grade 1, 44% had Grade 2, 28.4% had Grade 3 and 14.9% had Grade 4 Platelet count.

On Day 5, 42.5% had Grade 1, 21.6% had Grade 2, 18.7% had Grade 3 and 3% had Grade 4 platelet count.

On Day 7, 40.3% had Grade 1 only. Increase in duration there was improvement in subjects.

- In our study we observed that with increase in grade of platelet count there was increase in bleeding tendency. At presentaion In GRADE 1 no bleeding, in GRADE 2 4% had bleeding, in GRADE 3 62.8% had bleeding and in GRADE 4 86.5% had bleeding manifestations. This observation was statistically significant.
- In present study 64.9% were positive for Dengue, 19.4% were diagnosed to have Sepsis , 23.8% were positive for Malarial parasite, 6.7% had Mixed Infection and one case is positive for both sputum AFB samples. No cases of Leptospira and Rickettsia.
- Mortality was commonly seen in subjects with duration of fever > 3 days.
- In present study 61 cases presented with bleeding manifestations, in that 56(91.8%) cases are discharged and 5(8.1%) cases are died.
- In subjects who had mortality had higher Blood urea, Serum creatinine, Total bilirubin, SGOT and SGPT.

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ANNEXURES

PROFORMA

1. OP/IP No.: 2.Date:

3. Serial No.:

4. Name: 5.Age: 6. Gender:

7. Occupation:

8. Date of Admission:

9. Date of Discharge:

10. Address with Phone no.:

11. Chief Complaints:

12. Past history:

13. Drug / Treatment history:

14. Personal History:

15. General Physical Examination: (At admission)

PR: BP: Temp:

Resp Rate: Spo2:

Conjunctival haemorrhage : Bleeding gums:

Petechia :

Pallor: Icterus: Cyanosis:

Clubbing: Lymphdenopathy: Oedema:

16. Systemic examination:

CVS:

RS:

PA:

CNS:

17. Diagnosis:

18. Duration of hospital stay:

19. INVESTIGATIONS:

1)Complete blood picture. (At admission)

	Day 1	Day 3	Day 5	Day 7
Platelet count				
Grading				

2)Specific serology tests for

Dengue(NS1Ag,IgM,IgG)

Leptospirosis,

Peripheral smear for malarial parasite,

Rapid card test malaria .

3. Weil Felix test.

4. Chest X-ray.

5. Sputum for Acid Fast Bacilli I &II

6. ECG .

7. Renal function tests.

8.Urine routine.

9.Liver function tests.

Signature

INFORMED CONSENT FORM

Name of the investigator: **Dr K.SABARI GIRISH**

Name of the organization: R L Jalappa Hospital and Research centre attached to Sri Devaraj Urs Medical College

Name of the participant: Sl no:

CLINICAL AND ETIOLOGICAL PROFILE OF PATIENTS WITH ACUTE FEBRILE ILLNESS WITH THROMBOCYTOPENIA.

I have been invited to take part in this research study. The information in this document is meant to help me to decide whether or not to take part. I have clarified my doubts regarding this study with the principal investigator.

I have been asked to participate in this study because I satisfy the eligibility criteria which are mentioned in synopsis.

I request and authorize Dr. K.Sabari Girish to perform the designated tests for my blood sample. My signature below constitutes my acknowledgment that the benefits, risks and limitations of this testing have been explained to my satisfaction by a qualified health professional.

Participation is totally voluntary and there would be no payment for sample collection. All test results are treated with medical confidentiality and will not be disclosed to any outsider except if it is required by the law.

I give my consent to allow my sample to be used for medical research, test validation or education as long as my privacy is maintained.

I understand that I remain free to withdraw from this study at any time and this will not change my future care.

I have read and received a copy of patient information sheet. I understand the information provided in this document and I have had the opportunity to ask questions I might have about the testing, the procedure, the associated risk and alternatives.

Subject name and signature/ Thumb impression DATE:

Parents / Guardians name / Thumb impression DATE:

Signature of the person taking consent DATE:

KEY TO MASTER CHART

M	Male
F	Female
Y	Yes
N	No
SBP	Systolic blood pressure
DBP	Diastolic blood pressure

Bleeding coded

0	No bleeding
1	Bleeding present
CH	Conjunctival haemorrhage
BG	Bleeding gums
CVS	Cardio vascular system
RS	Respiratory system
b/l	Bilateral
P/A	Per abdomen
CNS	Central nervous system
TLC	Total leukocyte count

Sepsis

1	Absent
2	Present

Dengue serology

1	NS1Ag
2	IgM
3	NS1Ag + IgM
4	Absent
PS for MP	Peripheral smear for malarial parasite

PS for MP

0	Absent
1	Present
P.Vivax	Plasmodium vivax
P.Falciparum	Plasmodium Falciparum

Mixed infection

0	Absent
1	Present
ECG	Electro cardio gram
CXR	Chest X Ray
USG	Ultra sono graphy
AFB	Acid Fast Bacilli
RFT	Renal Function Test
BU	Blood Urea
SC	Serum Creatinine
LFT	Liver Function Test
TB	Total Bilirubin
SGOT	Serum Glutamic Oxaloacetic Transaminase
SGPT	Serum Glutamic Pyruvic Transaminase

MASTER CHART

Slno	NAME	AGE	GENDER	OCCUPATION	IPNO	Chiefcomplaints	FEVER	DURATIONOFFEVERAT PRESESNTATION	HEADACHE	JOINTPAINS	VOMITING	MYALGIA	ABDOMINALPAIN	DYSPNOEA	RASHES	BLEEDING MANIFESTATIONS	DRUGHISTORY	TEMP	PULSE	SBP	DBP	Bleedingcoded	HEMORRHAGIC MANIFESTATIONS	CONJUNCTIVAL HEMORRHAGE	BLEEDINGGUMS	PETECHIA	HEMATURIA	SYSTEMICEXAMINATION	CVS
1	Lakshmamma	75	F	Housewife	10956		Y	3	N	N	Y	Y	N	N	N	N	N	100	96	110	70	0	Absent	N	N	N	N		Normal
2	Prasad	23	M	Student	23219		Y	2	Y	N	Y	Y	N	N	N	Y	N	100	92	130	80	1	CH	Y	N	N	N		Normal
3	Doddapillaiah	41	M	Agriculture	28482		Y	4	Y	N	N	Y	N	N	N	N	N	101	102	120	80	0	Absent	N	N	N	N		Normal
4	Sridhar	30	M	Driver	28338		Y	4	Y	N	Y	Y	N	N	Y	Y	N	101	106	110	70	1	CH+Petechiae	Y	N	Y	N		Normal
5	Nagaraj	40	M	Agriculture	8162		Y	3	Y	N	Y	Y	Y	N	N	N	N	103	108	130	70	0	Absent	N	N	N	N		Normal
6	Sreenath	18	M	Student	13543		Y	2	Y	N	Y	N	N	N	N	Y	N	102	98	80	60	1	CH+BG	Y	Y	N	N		Normal
7	Anandh	25	M	Student	21361		Y	2	Y	N	Y	Y	Y	N	N	N	N	102	102	110	70	0	Absent	N	N	N	N		Normal
8	Shivanna	20	M	Student	8095		Y	1	Y	N	Y	Y	N	N	N	Y	N	104	110	120	80	1	CH	Y	N	N	N		Normal
9	Bebejahn	60	F	Housewife	8670		Y	4	Y	N	N	Y	N	Y	N	Y	N	100	102	130	80	1	BG	N	Y	N	N		Normal
10	Manjunath	30	M	Driver	7792		Y	4	Y	N	Y	Y	N	N	N	N	N	100	104	110	70	1	Petechiae	N	N	Y	N		Normal
11	Navya	20	F	Student	161240		Y	8	Y	N	N	Y	N	N	N	Y	N	101	102	80	60	1	Petechiae	N	N	Y	N		Normal
12	Santosh kumar	19	M	Student	34199		Y	5	Y	N	Y	N	N	N	N	Y	N	102	102	120	80	1	CH+Petechiae	Y	N	Y	N		Normal
13	Veerappa	74	M	School teacher	34169		Y	2	Y	N	Y	N	N	N	N	N	N	100	102	110	70	0	Absent	N	N	N	N		Normal
14	Raja reddy	40	M	Labour	35856		Y	2	N	N	Y	Y	Y	N	Y	N	N	100	102	120	80	1	CH	Y	N	N	N		Normal
15	Suresh pandey	27	M	Labour	34998		Y	3	N	N	N	Y	N	N	N	Y	N	99	88	100	70	1	BG	N	Y	N	N		Normal
16	Ramana	28	M	Labour	8763		Y	1	N	N	Y	Y	N	N	Y	N	N	100	98	110	70	0	Absent	N	N	N	N		Normal
17	Suhab	19	M	Student	10518		Y	3	Y	N	Y	Y	Y	N	N	Y	N	100	96	90	60	1	CH	Y	N	N	N		Normal
18	Pruthvi raj	21	M	Student	17226		Y	4	Y	N	N	Y	N	N	N	N	N	100	94	100	60	0	Absent	N	N	N	N		Normal
19	Manjunath	41	M	Labour	1007191		Y	4	Y	N	Y	Y	Y	Y	N	N	N	99	92	110	70	0	Absent	N	N	N	N		Normal
20	Ravi	22	M	Student	14130		Y	3	Y	N	Y	N	N	N	Y	Y	N	99	92	90	60	1	CH+Petechiae	Y	N	Y	N		Normal
21	Rmakrishnappa	69	M	Student	12232		Y	5	Y	N	Y	N	N	Y	N	N	N	99	94	100	60	1	Petechiae	N	N	Y	N		Normal
22	Shabeer pasha	35	M	Shop keeper	18223		Y	3	N	N	N	Y	Y	N	N	Y	N	100	102	110	70	1	BG	N	Y	N	N		Normal
23	Kamalamma	48	F	Housewife	15464		Y	3	Y	N	Y	Y	N	N	N	N	N	99	92	110	60	0	Absent	N	N	N	N		Normal
24	Rajesh	25	M	Student	19950		Y	2	N	N	Y	Y	N	N	N	Y	N	100	104	100	60	1	CH	Y	N	N	N		Normal
25	Vijay kumar	25	M	Driver	397950		Y	1	N	N	N	Y	Y	N	Y	N	N	102	106	120	80	0	Absent	N	N	N	N		Normal
26	Manjunath	41	M	Labour	400649		Y	1	N	N	Y	N	N	N	N	Y	N	100	102	90	60	1	CH	Y	N	N	N		Normal
27	Byrappa	53	M	Agriculture	403549		Y	2	Y	N	Y	Y	N	N	N	N	N	100	98	110	60	0	Absent	N	N	N	N		Normal
28	Markondappa	53	M	Labour	403543		Y	3	N	N	Y	Y	N	N	N	Y	N	102	106	100	60	1	BG+Petechiae	N	Y	Y	N		Normal
29	Nanjappa	72	M	Agriculture	403518		Y	4	Y	N	Y	Y	N	N	N	N	N	99	92	120	80	0	Absent	N	N	N	N		Normal
30	Sakamma	62	F	Labour	403549		Y	3	N	N	N	Y	N	N	Y	N	N	100	106	130	80	0	Absent	N	N	N	N		Normal
31	Tamilarasim	42	F	Housewife	61897		Y	2	N	N	Y	N	Y	Y	N	N	N	101	108	100	60	0	Absent	N	N	N	N		Normal
32	Amarnath	34	M	Labour	179493		Y	6	N	N	N	N	N	Y	Y	Y	N	101	106	100	60	1	CH+BG	Y	Y	N	N		Normal
33	Parvathamma	50	F	Labour	59068		Y	2	Y	Y	Y	Y	N	N	N	N	N	100	96	110	70	0	Absent	N	N	N	N		Normal
34	Lakshmamma	50	F	Housewife	67838		Y	5	Y	N	Y	N	Y	N	Y	Y	N	100	98	90	60	1	CH+Petechiae +Hematuria	Y	N	Y	Y		Normal
35	Shivamma	45	F	Labour	73837		Y	3	N	N	Y	Y	N	N	N	N	N	100	92	130	80	0	Absent	N	N	N	N		Normal
36	Sukanya	18	F	Student	66143		Y	2	N	N	N	N	N	N	N	N	N	102	106	110	70	0	Absent	N	N	N	N		Normal
37	Radhamma	45	F	Housewife	65639		Y	4	Y	N	Y	Y	N	N	Y	Y	N	99	88	120	80	1	CH	Y	N	N	N		Normal
38	Venkatamma	40	F	Agriculture	62785		Y	1	Y	N	Y	Y	N	N	N	N	N	100	102	110	70	0	Absent	N	N	N	N		Normal

Slno	RS	PA	CNS	PLATELETCOUNT				TLC	Sepsis	DENGUESEROLOGY	NS1AG	IGM	IGG	PSFORMP	P.vivax	P.Falciparum	MIxedinfection	LEPTOSPIRA
				@1STDAY	@3RDDAY	@5THDAY	@7THDAY											
1	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 1	12000	2	4			Absent	0			0	absent
2	Normal	Mild hepatomegal	No deficits	GRADE 2	GRADE 1	GRADE 0	GRADE 0	7800	1	1	Present		Absent	1		Present	1	absent
3	Normal	Normal	No deficits	GRADE 1	GRADE 0			5600	1	1	Present		Absent	0			0	absent
4	Normal	Normal	No deficits	GRADE 3	GRADE 3	GRADE 2	GRADE 0	5600	1	1	Present		Absent	0			0	absent
5	Normal	bdominal distensi	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	9000	1	4			Absent	0			0	absent
6	b/l basal crepts	Normal	No deficits	GRADE 4	GRADE 4	GRADE 3	GRADE 1	14500	2	4			Absent	0			0	absent
7	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 2	GRADE 1	8900	1	3	Present	Present	Absent	0			0	absent
8	Normal	bdominal distensi	No deficits	GRADE 3	GRADE 2	GRADE 2	GRADE 1	8900	1	1	Present		Absent	0			0	absent
9	Normal	Normal	No deficits	GRADE 3	GRADE 4	GRADE 2	GRADE 1	7800	1	1	Present		Absent	0			0	absent
10	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 2	GRADE 1	7800	1	2		Present	Absent	0			0	absent
11	b/l basal crepts	Normal	No deficits	GRADE 3	GRADE 4	GRADE 4		13500	2	3	Present	Present	Absent	0			0	absent
12	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 3	GRADE 1	6700	1	1	Present		Absent	0			0	absent
13	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 3	GRADE 1	14000	2	4			Absent	0			0	absent
14	b/l basal crepts	Normal	No deficits	GRADE 4	GRADE 4	GRADE 3	GRADE 1	7900	1	1	Present		Absent	0			0	absent
15	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 1	GRADE 0	6700	1	1	Present		Absent	1	Present		1	absent
16	Normal	Mild hepatomegal	No deficits	GRADE 2	GRADE 2	GRADE 1		6700	1	1	Present		Absent	1	Present		1	absent
17	t lower lobes crep	Normal	No deficits	GRADE 4	GRADE 4	GRADE 2	GRADE 1	15000	2	4			Absent	0			0	absent
18	Normal	Normal	No deficits	GRADE 3	GRADE 3	GRADE 1		6000	1	4			Absent	1	Present		0	absent
19	Normal	Mild spleenomega	No deficits	GRADE 3	GRADE 2	GRADE 1		7800	1	4			Absent	1	Present		0	absent
20	Normal	Normal	No deficits	GRADE 4	GRADE 2	GRADE 1		5800	1	4			Absent	1	Present		0	absent
21	Normal	Normal	No deficits	GRADE 4	GRADE 4	GRADE 1	GRADE 1	13500	2	4			Absent	0			0	absent
22	Normal	Normal	No deficits	GRADE 3	GRADE 1	GRADE 0		7800	1	4			Absent	1	Present		0	absent
23	Normal	Normal	No deficits	GRADE 3	GRADE 1	GRADE 0		6700	1	4			Absent	1	Present		0	absent
24	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 2	GRADE 1	7600	1	3	Present	Present	Absent	0			0	absent
25	Normal	bdominal distensi	No deficits	GRADE 3	GRADE 3	GRADE 1	GRADE 0	6500	1	4			Absent	1	Present		0	absent
26	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 3	GRADE 1	6000	1	4			Absent	1	Present		0	absent
27	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 0		6800	1	4			Absent	1	Present		0	absent
28	b/l basal crepts	Normal	No deficits	GRADE 4	GRADE 4	GRADE 2	GRADE 1	8900	1	3	Present	Present	Absent	0			0	absent
29	Normal	bdominal distensi	No deficits	GRADE 3	GRADE 2	GRADE 2	GRADE 0	7800	1	1	Present		Absent	0			0	absent
30	Normal	Normal	No deficits	GRADE 2	GRADE 1	GRADE 0		6700	1	2		Present	Absent	0			0	absent
31	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 1	GRADE 0	14500	2	4			Absent	0			0	absent
32	b/l basal crepts	Normal	No deficits	GRADE 4	GRADE 3	GRADE 4		7000	1	2		Present	Absent	0			0	absent
33	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 2	GRADE 0	7000	1	1	Present		Absent	0			0	absent
34	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 1	GRADE 0	7300	1	3	Present	Present	Absent	1		Present	1	absent
35	Normal	Normal	No deficits	GRADE 2	GRADE 1	GRADE 0		7800	1	2		Present	Absent	0			0	absent
36	Normal	Normal	No deficits	GRADE 2	GRADE 1	GRADE 0		5600	1	1	Present		Absent	0			0	absent
37	Normal	Normal	No deficits	GRADE 3	GRADE 1	GRADE 0		5600	1	1	Present		Absent	0			0	absent
38	Normal	Normal	No deficits	GRADE 3	GRADE 3	GRADE 1	GRADE 0	14500	2	4			Absent	0			0	absent

Slno	WEILFELIX	ECG	CXR	USGABDOMEN	SPUTUM	AFB1	AFB2	RFT	BU	SC	LFT	TB	SGOT	SGPT	PLATELET TRANSFUSION	OUTCOME
1	absent	Normal	Normal	Normal		Absent	Absent		31.8	1.16		0.9	19	19		DISCHARGE
2	absent	Normal	Normal	mild hepatomegaly		Absent	Absent		7.6	0.93		0.2	31	33		DISCHARGE
3	absent	Normal	Normal	Normal		Absent	Absent		8.3	0.67		1	18	32		DISCHARGE
4	absent	Normal	Normal	Normal		Absent	Absent		5.6	0.68		0.5	34	35		DISCHARGE
5	absent	Normal	Normal	Minimal ascites		Absent	Absent		7.5	0.83		0.8	22	28		DISCHARGE
6	absent	Normal	e non homoger	Normal		Absent	Absent		20.1	1.16		3	124	96	4	DISCHARGE
7	absent	Normal	Normal	Normal		Absent	Absent		5.8	0.76		0.6	23	33		DISCHARGE
8	absent	Normal	Normal	Minimal ascites		Absent	Absent		18.4	0.69		0.9	42	21		DISCHARGE
9	absent	Normal	Normal	Normal		Absent	Absent		14.6	0.72		0.3	24	23		DISCHARGE
10	absent	Normal	Normal	Normal		Absent	Absent		20.1	0.75		0.8	12	22	4	DISCHARGE
11	absent	Normal	ARDS	Gb sludge		Absent	Absent		34.1	1.11		3	98	76	4	DEATH
12	absent	Normal	Normal	Normal		Absent	Absent		31.8	0.73		0.3	26	32	6	DISCHARGE
13	absent	Normal	Normal	Normal		Absent	Absent		32	0.72		0.4	18	34		DISCHARGE
14	absent	Normal	ARDS	Normal		Absent	Absent		8.4	0.58		0.1	34	24	4	DISCHARGE
15	absent	Normal	Normal	Normal		Absent	Absent		5.3	0.76		0.1	19	21		DISCHARGE
16	absent	Normal	Normal	mild hepatomegaly		Absent	Absent		22	0.7		0.6	34	28		DISCHARGE
17	absent	Normal	ne non homoge	Normal		Absent	Absent		34.1	1.31		5	164	106	4	DISCHARGE
18	absent	Normal	Normal	Normal		Absent	Absent		9.2	0.93		0.8	19	31		DISCHARGE
19	absent	Normal	Normal	Mild splenomegaly		Absent	Absent		14.6	0.87		0.5	27	34		DISCHARGE
20	absent	Normal	Normal	Normal		Absent	Absent		7.5	0.83		0.7	18	27	6	DISCHARGE
21	absent	Normal	Normal	Normal		Absent	Absent		5.3	0.44		0.9	18	16	4	DISCHARGE
22	absent	Normal	Normal	Normal		Absent	Absent		5.6	0.83		0.4	33	32		DISCHARGE
23	absent	Normal	Normal	Normal		Absent	Absent		22	0.86		0.9	29	24		DISCHARGE
24	absent	Normal	Normal	Normal		Absent	Absent		20.1	0.87		1	27	27	4	DISCHARGE
25	absent	Normal	Normal	Moderate ascites		Absent	Absent		9.3	0.76		0.7	31	29		DISCHARGE
26	absent	Normal	Normal	Normal		Absent	Absent		5.8	0.87		1	17	29		DISCHARGE
27	absent	Normal	Normal	Normal		Absent	Absent		5.3	0.87		1	34	33		DISCHARGE
28	absent	Normal	ARDS	Normal		Absent	Absent		8.4	0.67		1	12	34	6	DISCHARGE
29	absent	Normal	Normal	Minimal ascites		Absent	Absent		7.5	0.82		0.7	27	22		DISCHARGE
30	absent	Normal	Normal	Normal		Absent	Absent		36.4	1.11		0.8	27	28		DISCHARGE
31	absent	Normal	Normal	Normal		Absent	Absent		3.3	0.56		0.9	17	34		DISCHARGE
32	absent	Normal	ARDS	Gb sludge		Absent	Absent		5.8	0.44		0.8	24	32	8	DEATH
33	absent	Normal	Normal	Normal		Absent	Absent		13.1	0.69		0.8	12	24		DISCHARGE
34	absent	Normal	Normal	Normal		Absent	Absent		32	1.09		0.5	31	34	8	DISCHARGE
35	absent	Normal	Normal	Normal		Absent	Absent		20	1.16		0.8	20	28		DISCHARGE
36	absent	Normal	Normal	Normal		Absent	Absent		19.6	0.69		0.8	32	35		DISCHARGE
37	absent	Normal	Normal	Normal		Absent	Absent		15.9	0.69		0.9	12	19		DISCHARGE
38	absent	Normal	Normal	Normal		Absent	Absent		7.6	0.58		0.7	24	16		DISCHARGE

MASTER CHART

39	Dhanamma	47	F	Housewife	73367		Y	1	N	Y	Y	Y	Y	N	N	Y	N	100	106	100	60	1	BG	N	Y	N	N		Normal	Normal	Mild spleenomega	No deficits	GRADE 3	GRADE 2	GRADE 0		6400	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Mild splenomegaly		Absent	Absent		32	0.87		0.1	22	29		DISCHARGE
40	Varalakshmi	39	F	Housewife	72913		Y	2	Y	N	N	N	Y	N	N	N	N	101	106	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 3	GRADE 3	GRADE 0	8900	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		23.1	0.7		0.7	12	26		DISCHARGE
41	Mubarak ahmed	60	M	Labour	210210		Y	15	Y	N	N	N	N	N	N	N	N	101	110	100	70	0	Absent	N	N	N	N		Normal	b/l basal crepts	Normal	No deficits	GRADE 3	GRADE 2	GRADE 2	GRADE 1	31000	2	4			Absent	0			0	absent	absent	Normal	Left lung fibrosi	Normal		present	present		16.7	0.69		0.8	24	32		DISCHARGE
42	Lelavathi	47	F	Agriculture	66321		Y	2	N	N	Y	Y	Y	N	N	N	N	101	106	120	80	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 3	GRADE 2	GRADE 0	7800	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		36.4	0.72		0.5	12	21		DISCHARGE
43	Savithramma	46	F	Housewife	72257		Y	2	Y	N	Y	Y	N	N	Y	N	N	99	92	130	80	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 1	GRADE 3	GRADE 3	GRADE 1	7800	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		34.1	0.72		0.2	8	36		DISCHARGE
44	Shabeena parve	37	F	Housewife	66179		Y	2	Y	N	Y	Y	Y	N	N	N	N	100	102	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 0	GRADE 0	7800	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		36.4	1.31		1	31	34		DISCHARGE
45	Munirathnamma	28	F	Labour	67974		Y	1	N	Y	N	Y	N	Y	N	Y	N	100	108	110	70	1	CH	Y	N	N	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 0	GRADE 0	6700	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		20	0.73		0.6	33	28		DISCHARGE
46	Nagamani	34	F	Housewife	130744		Y	1	Y	N	Y	N	N	N	N	N	N	100	98	130	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 1	GRADE 1	GRADE 0	9800	1	4			Absent	1	Present		0	absent	absent	Normal	Normal	Normal		Absent	Absent		6.1	0.88		0.8	21	29		DISCHARGE
47	Aruna	25	F	Student	131322		Y	1	Y	N	Y	Y	N	N	Y	N	N	100	96	120	80	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 2	GRADE 1	7900	1	2		Present	Absent	1		Present	1	absent	absent	Normal	Normal	Normal		Absent	Absent		15.9	1.03		1	24	29		DISCHARGE
48	Nirmala	31	F	Housewife	131720		Y	1	N	N	Y	Y	N	N	N	Y	N	98	92	80	60	1	CH+Petechiae	Y	N	Y	N		Normal	b/l basal crepts	Normal	No deficits	GRADE 4	GRADE 3	GRADE 3	GRADE 1	6700	1	1	Present		Absent	0			0	absent	absent	Normal	ARDS	Normal		Absent	Absent		7.5	0.58		0.5	14	18	6	DISCHARGE
49	Shyla	26	F	Student	144265		Y	1	Y	N	Y	Y	N	N	Y	N	N	100	98	110	70	0	Absent	N	N	N	N		Normal	Normal	bdominal distensi	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	15000	2	4			Absent	0			0	absent	absent	Normal	Normal	Minimal ascites		Absent	Absent		3.3	0.8		1	29	29		DISCHARGE
50	Ashwini	24	F	Student	145965		Y	4	Y	Y	Y	N	Y	N	Y	Y	N	100	96	110	70	1	CH	Y	N	N	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 2	GRADE 1	6100	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		36.9	0.75		0.9	39	34		DISCHARGE
51	Lakshmi	27	F	Housewife	147294		Y	2	Y	N	N	Y	N	N	Y	N	N	100	92	130	80	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	6000	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		8.1	0.83		1	34	29		DISCHARGE
52	Krishnappa	45	M	Labour	171672		Y	4	N	N	Y	Y	N	N	N	N	N	100	96	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	7800	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		7.9	0.76		0.9	29	33		DISCHARGE
53	Suresh	23	M	Driver	173020		Y	5	Y	N	Y	Y	N	N	N	Y	N	98	90	90	60	1	BG	N	Y	N	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 3	GRADE 2	GRADE 1	16000	2	4			Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		86	3		4	152	86		DISCHARGE
54	Nizam pasha	17	M	Student	173051		Y	2	Y	N	Y	Y	Y	N	N	N	N	100	102	120	80	0	Absent	N	N	N	N		Normal	Normal	bdominal distensi	No deficits	GRADE 1	GRADE 1	GRADE 0		6500	1	4			Absent	1	Present		0	absent	absent	Normal	Normal	Moderate ascites		Absent	Absent		6.1	0.78		1	31	28		DISCHARGE
55	Fiyaz ahmed	38	M	Shop keeper	171790		Y	2	Y	N	Y	Y	N	Y	N	N	N	100	104	130	80	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	7800	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		4.7	0.76		0.5	19	26		DISCHARGE
56	Shivraj	42	M	Labour	189716		Y	4	Y	Y	N	N	N	N	N	N	N	100	102	80	60	1	Petechiae	N	N	Y	N		Normal	Normal	Normal	No deficits	GRADE 4	GRADE 4	GRADE 4		16000	2	3	Present	Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		156	5		5	212	102	12	DEATH
57	Lalitha	27	F	Housewife	149445		Y	4	Y	N	Y	Y	N	N	Y	Y	N	101	102	110	70	1	CH	Y	N	N	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 2	GRADE 1	7600	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		6.1	0.83		0.8	25	26		DISCHARGE
58	Arunamma	47	F	Housewife	149490		Y	4	N	N	N	N	Y	N	N	N	N	100	102	80	60	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 1	GRADE 0	6500	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		9.8	0.76		1	34	34		DISCHARGE
59	Arif pasha	31	M	Labour	174400		Y	1	Y	N	Y	Y	N	N	N	N	N	99	98	120	80	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 3	GRADE 2	GRADE 1	6000	1	4			Absent	1		Present	0	absent	absent	Normal	Normal	Normal		Absent	Absent		9.3	0.87		1	27	34		DISCHARGE
60	Muniraju	32	M	Labour	175138		Y	1	Y	N	Y	Y	N	N	Y	Y	N	100	102	80	60	1	CH+Petechiae	Y	N	Y	N		Normal	b/l basal crepts	Mild hepatomegal	No deficits	GRADE 4	GRADE 4	GRADE 2	GRADE 1	6800	1	1	Present		Absent	0			0	absent	absent	Normal	ARDS	mild hepatomegaly		Absent	Absent		16.8	0.55		0.2	16	12	6	DISCHARGE
61	Nalina	29	F	Housewife	149037		Y	2	Y	N	Y	N	Y	N	N	N	N	100	104	120	80	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	16000	2	4			Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		8.1	0.61		1	25	34		DISCHARGE
62	Hayath khan	57	M	Agriculture	177740		Y	3	Y	N	Y	Y	N	N	Y	N	N	98	92	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	7800	1	1	Present		Absent	1	Present		1	absent	absent	Normal	Normal	Normal		Absent	Absent		6.1	0.93		0.6	24	24		DISCHARGE
63	Manjunath redd	35	M	Shop keeper	177756		Y	2	Y	Y	Y	Y	N	N	Y	Y	N	100	102	130	70	1	CH+Hematuria	Y	N	N	Y		Normal	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 3	GRADE 1	6700	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		16.8	0.76		1	22	31	6	DISCHARGE
64	Asha	34	F	Housewife	150412		Y	2	N	N	N	Y	N	Y	Y	N	N	98	96	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	8000	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Gb sludge		Absent	Absent		8.3	0.94		0.5	27	29		DISCHARGE
65	Kalavathi	29	F	Housewife	151266		Y	1	Y	N	Y	N	Y	N	N	N	N	100	102	130	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	9200	1	4			Absent	1	Present		0	absent	absent	Normal	Normal	Normal		Absent	Absent		7.5	0.89		0.3	32	32		DISCHARGE
66	Ramchandrappa	43	M	Labour	177762		Y	2	Y	N	Y	N	N	N	N	N	N	100	110	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 2	GRADE 1	7000	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		8.9	0.78		1	27	24		DISCHARGE
67	Rajanna	35	M	Labour	177825		Y	2	Y	N	N	Y	N	N	N	Y	N	100	96	130	70	1	BG+Petechiae	N	Y	Y	N		Normal	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 3	GRADE 1	7300	1	3	Present	Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		36.9	0.87		1	30	32	6	DISCHARGE
68	Manjula	32	F	Housewife	151554		Y	3	Y	Y	Y	Y	N	N	N	Y	N	99	86	100	60	1	CH+Hematuria	Y	N	N	Y		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 4	GRADE 3	GRADE 1	7800	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		7	0.8		1	19	34		DISCHARGE
69	Venkatravanapp	30	M	Labour	178359		Y	3	Y	N	N	N	N	N	N	Y	N	100	92	100	60	1	BG	N	Y	N	N		Normal	Normal	bdominal distensi	No deficits	GRADE 3	GRADE 3	GRADE 2	GRADE 1	5600	1	4			Absent	1		Present	0	absent	absent	Normal	Normal	Minimal ascites		Absent	Absent		18.4	0.86		0.2	28	26		DISCHARGE
70	Ashraf pasha	21	M	Student	178727		Y	4	N	N	Y	Y	N	N	Y	N	N	100	96	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	5600	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		19.6	0.86		0.6	24	31		DISCHARGE
71	Nagamani	40	F	Housewife	153320		Y	4	Y	N	Y	Y	N	N	N	Y	N	99	92	100	60	1	BG	N	Y	N	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 3	GRADE 2	GRADE 1	9000	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		8.4	0.8		0.5	31	23		DISCHARGE
72	Raheen bee	62	F	Housewife	76519		Y	6	N	N	Y	Y	N	N	N	N	N	99	96	80	60	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 4	GRADE 3		6400	1	4			Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		112	4		3	162	86	4	DEATH
73	Munnabhai	48	F	Labour	153742		Y	2	Y	N	Y	N	Y	N	Y	Y	N	100	104	90	60	1	CH	Y	N	N	N		Normal	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 3	GRADE 1	14000	2	4			Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		6.1	0.55		0.3	28	15	4	DISCHARGE
74	Rajareddy	32	M	Labour	179529		Y	5	Y	N	Y	Y	N	N	Y	N	N	100	102	100	60	0	Absent	N	N	N	N		Normal	Normal	bdominal distensi	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	8900	1	1	Present		Absent	1	Present		1	absent	absent	Normal	Normal	Moderate ascites		Absent	Absent		12.1	0.8		1	22	34		DISCHARGE
75	Srinivasa	38	M	Labour	179967		Y	3	N	Y	N	N	Y	N	N	N	N	100	104	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 1	GRADE 1	GRADE 0	7800	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		7.6	0.82		0.8	18	35		DISCHARGE
76	Subramani	35	M	Agriculture	180228		Y	3	N	N	Y	N	N	N	Y	N	N	99	106	100	60	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 1	GRADE 0		7800	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		31.8	0.87		0.5	24	33		DISCHARGE
77	Nagaveni	27	F	Housewife	155609		Y	2	Y	N	Y	Y	Y	Y	N	Y	N	100	98	80	60	1	CH+BG	Y	Y	N	N		Normal	b/l basal crepts	Normal	No deficits	GRADE 4	GRADE 3	GRADE 3	GRADE 1	7800	1	1	Present		Absent	0			0	absent	absent	Normal	ARDS	Normal		Absent	Absent		12.1	0.61		1	17	26	6	DISCHARGE
78	Lalitha	30	F	Housewife	156037		Y	2	Y	N	N	N	N	N	N	Y	N	100	86	100	60	1	Petechiae	N	N	Y	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 3	GRADE 2	GRADE 1	6700	1	4			Absent	1	Present		0	absent	absent	Normal	Normal	Gb sludge		Absent	Absent		22	1.09		1	32	33		DISCHARGE
79	Syed yasir	22	M	Student	180471		Y	2	N	N	Y	Y	N	N	N	Y	N	100	98	90	60	1	CH+BG	Y	Y	N	N		Normal	Normal	Normal	No deficits	GRADE 4	GRADE 4	GRADE 3	GRADE 1	9800	1	3	Present	Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		16.8	0.88		0.9	27	34	4	DISCHARGE
80	Masud	30	M	employee	180486		Y	2	N	N	Y	N	Y	N	N	Y	N	99	92	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	7900	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		12.1	0.83		1	28	35		DISCHARGE

MASTER CHART

81	Naresh	18	M	Student	179983		Y	1	Y	N	Y	N	N	N	Y	N	N	100	102	100	60	0	Absent	N	N	N	N		Normal	Normal	bdominal distensi	No deficits	GRADE 2	GRADE 1	GRADE 1	GRADE 0	6700	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Minimal ascites		Absent	Absent		7.6	0.83		0.9	31	21		DISCHARGE
82	Varalakshmamr	48	F	Housewife	156150		Y	1	Y	N	N	Y	N	N	N	N	N	101	104	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	6700	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		9.2	0.83		1	17	22		DISCHARGE
83	Arathi	28	F	Housewife	120013		Y	1	N	N	Y	Y	Y	N	N	Y	N	100	102	130	70	1	BG	N	Y	N	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 3	GRADE 2	GRADE 1	6100	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		20	0.87		1	31	23		DISCHARGE
84	Syed sab	22	M	Student	180904		Y	1	N	N	Y	Y	N	N	Y	Y	N	101	102	100	60	1	CH	Y	N	N	N		Normal	b/l basal crepts	Normal	No deficits	GRADE 3	GRADE 3	GRADE 1	GRADE 0	15000	2	4			Absent	0			0	absent	absent	Normal	ne non homogen	Normal		Absent	Absent		96	4		4	162	104		DISCHARGE
85	Ravi	25	M	Student	181568		Y	1	N	N	N	Y	N	N	N	Y	N	100	102	110	70	1	CH+BG	Y	Y	N	N		Normal	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 3	GRADE 1	7800	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		13.1	0.86		0.3	18	34	4	DISCHARGE
86	Rajesh	30	M	Driver	182043		Y	1	N	Y	Y	N	Y	N	N	Y	N	99	98	90	60	1	Petechiae	N	N	Y	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 3	GRADE 1	GRADE 0	14500	2	4			Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		7.6	0.58		0.9	32	35		DISCHARGE
87	Lakshmidevi	25	F	Housewife	157562		Y	2	Y	N	Y	N	N	N	N	Y	N	100	102	100	60	1	CH	Y	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	6500	1	4			Absent	1	Present		0	absent	absent	Normal	Normal	Normal		Absent	Absent		8.1	0.93		0.9	20	28		DISCHARGE
88	Gauramma	54	F	Labour	158415		Y	1	Y	N	Y	N	N	Y	Y	N	N	100	104	110	70	0	Absent	N	N	N	N		Normal	Normal	Mild spleenomega	No deficits	GRADE 2	GRADE 1	GRADE 0		7800	1	3	Present	Present	Absent	0			0	absent	absent	Normal	Normal	Gb sludge		Absent	Absent		13.1	1.03		1	31	27		DISCHARGE
89	Sonappa	23	M	Shop keeper	183448		Y	3	Y	N	N	Y	N	N	N	Y	N	99	98	100	60	1	BG	N	Y	N	N		Normal	b/l basal crepts	Normal	No deficits	GRADE 3	GRADE 3	GRADE 1	GRADE 1	6700	1	1	Present		Absent	0			0	absent	absent	Normal	ARDS	Normal		Absent	Absent		9.2	0.61		1	15	24		DISCHARGE
90	Nagaraj	28	M	employee	183476		Y	3	Y	Y	Y	Y	Y	N	N	N	N	101	110	140	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	7600	1	4			Absent	1		Present	0	absent	absent	Normal	Normal	Normal		Absent	Absent		8.9	0.88		0.8	28	34		DISCHARGE
91	Subramani	18	M	Student	184862		Y	3	Y	N	Y	N	N	N	Y	Y	N	100	102	100	60	1	CH+BG	Y	Y	N	N		Normal	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 3	GRADE 1	6500	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Gb sludge		Absent	Absent		8.4	0.94		0.1	31	34	6	DISCHARGE
92	Lakshmidevamı	38	F	Housewife	85388		Y	5	N	N	Y	N	Y	N	N	N	N	101	110	80	60	0	Absent	N	N	N	N		Normal	b/l pleural effusior	Normal	No deficits	GRADE 4	GRADE 4			6000	1	1	Present		Absent	0			0	absent	absent	Normal	l pleural effusi	Gb sludge		Absent	Absent		7.9	0.53		0.4	32	12	6	DEATH
93	Sharadamma	48	F	Housewife	158920		Y	2	Y	N	Y	Y	N	N	N	Y	N	99	92	110	60	1	Petechiae	N	N	Y	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 2	GRADE 1	6800	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		36.4	0.87		0.7	19	23		DISCHARGE
94	Bharathi	29	F	Labour	159791		Y	2	Y	N	N	Y	Y	N	N	Y	N	100	102	90	60	1	CH+BG	Y	Y	N	N		Normal	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 3	GRADE 1	8900	1	1	Present		Absent	1	Present		1	absent	absent	Normal	Normal	Normal		Absent	Absent		18.4	0.99		1	27	23	6	DISCHARGE
95	Hyder	35	M	Agriculture	186064		Y	3	Y	N	Y	N	N	N	N	N	N	100	104	110	60	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	7800	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		9.8	0.88		0.8	33	24		DISCHARGE
96	Venkatramaiah	64	M	Labour	158518		Y	2	N	Y	Y	Y	N	N	Y	Y	N	98	92	130	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	6700	1	4			Absent	1	Present		0	absent	absent	Normal	Normal	Normal		Absent	Absent		22	0.83		0.3	27	29		DISCHARGE
97	Ayub khan	46	M	Labour	187516		Y	3	Y	N	Y	N	N	N	N	N	N	100	102	120	80	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 1	GRADE 1	GRADE 0	8000	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		34.1	0.87		0.9	20	22		DISCHARGE
98	Geetha	27	F	Student	159872		Y	2	N	N	N	Y	Y	N	N	Y	N	100	106	80	60	1	CH+BG	Y	Y	N	N		Normal	Normal	Mild hepatomegal	No deficits	GRADE 4	GRADE 3	GRADE 3	GRADE 1	9200	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	mild hepatomegaly		Absent	Absent		12.1	0.89		0.9	18	23		DISCHARGE
99	Baby rajani	22	F	Student	160244		Y	2	Y	N	Y	N	N	Y	N	Y	N	101	98	100	60	1	Petechiae	N	N	Y	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 2	GRADE 1	15000	2	4			Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		7.5	0.58		0.5	32	36		DISCHARGE
100	Harish kumar	19	M	Student	187589		Y	4	Y	N	N	Y	N	N	N	N	N	100	96	120	80	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	7300	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		4.7	0.88		0.7	18	28		DISCHARGE
101	Somsundhar	21	M	Student	189067		Y	3	Y	N	Y	Y	N	N	N	N	N	98	92	130	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 1	GRADE 0		7800	1	4			Absent	1		Present	0	absent	absent	Normal	Normal	Normal		Absent	Absent		7.6	0.89		0.5	29	29		DISCHARGE
102	Shivaraj	30	M	Labour	189716		Y	2	N	N	Y	Y	Y	N	Y	Y	N	100	102	90	60	1	CH+BG	Y	Y	N	N		Normal	b/l basal crepts	Normal	No deficits	GRADE 4	GRADE 4	GRADE 3	GRADE 1	5600	1	3	Present	Present	Absent	0			0	absent	absent	Normal	ARDS	Normal		Absent	Absent		7.5	0.68		1	24	24	6	DISCHARGE
103	Nagalakshmi	27	F	Student	1021664		Y	1	Y	N	N	N	N	N	N	N	N	101	92	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	13500	2	4			Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		9.3	0.52		0.7	40	24		DISCHARGE
104	Kavitha	20	F	Student	160264		Y	4	Y	Y	Y	Y	N	N	N	Y	N	100	102	100	60	1	Petechiae	N	N	Y	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 1	GRADE 1	9000	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		3.3	0.89		0.6	22	33		DISCHARGE
105	Narayanamma	38	F	Labour	160248		Y	4	N	N	Y	Y	N	N	N	N	N	101	102	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	6400	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Gb sludge		Absent	Absent		22	0.99		0.5	34	22		DISCHARGE
106	Chalapathi	39	M	Labour	190099		Y	2	Y	N	Y	Y	Y	N	N	N	N	100	102	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	16000	2	4			Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		6.1	0.61		1	38	24		DISCHARGE
107	Nagesh	32	M	Labour	191458		Y	2	Y	N	N	Y	N	N	N	Y	N	99	92	80	60	1	CH+BG	Y	Y	N	N		Normal	Normal	Normal	No deficits	GRADE 4	GRADE 3	GRADE 3	GRADE 1	8900	1	4			Absent	1	Present		0	absent	absent	Normal	Normal	Normal		Absent	Absent		16.7	0.83		0.5	21	33	6	DISCHARGE
108	Shabeena	39	F	Housewife	160309		Y	3	N	Y	Y	N	N	N	Y	N	N	100	98	120	80	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	7800	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		7	0.89		0.7	18	23		DISCHARGE
109	Lashmidevamm	42	F	Housewife	160230		Y	1	Y	N	Y	Y	N	N	N	Y	N	100	98	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 1	GRADE 1	GRADE 0	7800	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		7.5	0.93		0.3	22	26		DISCHARGE
110	Sandeep	23	M	Student	192554		Y	2	Y	N	Y	N	N	N	N	N	N	100	102	100	60	0	Absent	N	N	N	N		Normal	Normal	bdominal distensi	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	7800	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Moderate ascites		Absent	Absent		5	0.76		0.5	24	27		DISCHARGE
111	Ravi	28	M	Student	192283		Y	3	N	N	Y	Y	Y	N	Y	N	N	99	98	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 2	GRADE 1	6700	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		7.5	0.94		0.7	30	34		DISCHARGE
112	Anjamma	45	F	Housewife	85383		Y	5	N	Y	Y	Y	N	N	N	Y	N	100	106	80	60	1	CH+Petechiae	Y	N	Y	N		Normal	b/l basal crepts	Normal	No deficits	GRADE 3	GRADE 3	GRADE 4		19000	2	2		Present	Absent	0			0	absent	absent	Normal	ARDS	Normal		Absent	Absent		5	0.52		0.6	28	32	8	DEATH
113	Sheela	32	F	Housewife	161320		Y	1	Y	N	N	N	N	N	N	Y	N	100	96	80	60	1	CH+BG	Y	Y	N	N		Normal	b/l basal crepts	Normal	No deficits	GRADE 4	GRADE 4	GRADE 2	GRADE 1	7900	1	2		Present	Absent	1		Present	1	absent	absent	Normal	ARDS	Gb sludge		Absent	Absent		7	0.58		0.6	24	34	6	DISCHARGE
114	Muneeramma	49	F	Housewife	1021745		Y	2	N	N	Y	Y	N	N	Y	N	N	100	102	110	60	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	6700	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		5.6	0.94		0.9	17	23		DISCHARGE
115	Raghu	40	M	Labour	192371		Y	3	Y	N	Y	Y	N	N	N	N	N	99	98	130	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	12500	2	4			Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		36.9	1.31		1	24	26		DISCHARGE
116	Gopalappa	33	M	Labour	194673		Y	1	N	N	Y	Y	N	Y	N	N	N	100	102	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	6100	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		12.1	0.93		0.6	27	34		DISCHARGE
117	Gauravamma	39	F	Housewife	163921		Y	2	N	N	N	Y	Y	N	N	Y	N	100	104	90	60	1	Petechiae	N	N	Y	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 3	GRADE 1	GRADE 0	6000	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		16.7	0.99		1	25	33		DISCHARGE
118	Sumithra	29	F	Housewife	163302		Y	4	N	N	Y	N	N	N	N	N	N	100	104	120	80	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	7800	1	4			Absent	1		Present	0	absent	absent	Normal	Normal	Gb sludge		Absent	Absent		14.6	1.11		0.7	22	31		DISCHARGE
119	Anjanappa	39	M	Labour	190555		Y	2	Y	N	N	Y	N	N	Y	N	N	100	102	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	16000	2	4			Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		112	4		5	182	112		DISCHARGE
120	Venkatchalapatl	39	M	Labour	196290		Y	1	Y	Y	Y	Y	N	Y	N	Y	N	98	82	90	60	1	CH+BG	Y	Y	N	N		Normal	b/l basal crepts	Normal	No deficits	GRADE 4	GRADE 4	GRADE 3	GRADE 1	6500	1	3	Present	Present	Absent	0			0	absent	absent	Normal	ARDS	Normal		Absent	Absent		22	0.69		0.7	12	34	6	DISCHARGE
121	Praveen taj	34	F	Labour	165238		Y	2	Y	N	Y	Y	N	N	N	N	N	100	102	130	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	14000	2	4			Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		8.9	0.55		0.6	24	34		DISCHARGE
122	Bharathi	32	F	Housewife	164650		Y	3	N	N	N	N	Y	N	N	N	N	100	106	120	80	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	6700	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		8.4	0.83		0.9	27	33		DISCHARGE

MASTER CHART

123	Lakshmamma	28	F	Housewife	166183		Y	1	Y	Y	Y	Y	N	N	N	Y	N	98	92	70	50	1	CH+Petechiae +Hematuria	Y	N	Y	Y		Normal	Normal	Normal	No deficits	GRADE 4	GRADE 4	GRADE 3	GRADE 1	7600	1	3	Present	Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		8.4	0.89		0.4	24	27	8	DISCHARGE
124	Prince kumar	19	M	Student	197044		Y	2	Y	N	Y	Y	Y	N	N	N	N	100	102	120	80	0	Absent	N	N	N	N		Normal	Normal	Mild spleenomega	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	6500	1	4			Absent	1	Present		0	absent	absent	Normal	Normal	Mild splenomegaly		Absent	Absent		7.9	0.88		0.5	31	31		DISCHARGE
125	Murali	19	M	Student	194901		Y	3	N	N	Y	N	N	N	Y	Y	N	101	110	100	60	1	Petechiae	N	N	Y	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 2	GRADE 1	6000	1	4			Absent	1	Present		0	absent	absent	Normal	Normal	Normal		Absent	Absent		23.1	0.86		0.6	31	34		DISCHARGE
126	Munivenkatamr	46	F	Housewife	167163		Y	2	Y	N	N	Y	N	N	N	N	N	100	102	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 0	6800	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		19.6	1.03		1	18	32		DISCHARGE
127	Swetha	43	F	Housewife	167179		Y	3	N	N	Y	Y	N	N	N	Y	N	100	102	80	60	1	BG+Petechiae	N	Y	Y	N		Normal	Normal	Normal	No deficits	GRADE 4	GRADE 4	GRADE 3	GRADE 1	8900	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		8.3	0.83		0.6	31	23	4	DISCHARGE
128	Rani	20	F	Student	88266		Y	6	Y	N	N	N	N	N	N	N	N	101	110	70	50	0	Absent	N	N	N	N		Normal	Normal	Normal	Irritable	GRADE 4	GRADE 4			18000	2	4			Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		9.8	0.55		0.5	33	32		DEATH
129	Hemavathi	23	F	Student	167541		Y	1	Y	N	Y	Y	Y	N	N	N	N	99	92	100	60	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 1	13500	2	4			Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		4.7	0.53		0.3	10	18		DISCHARGE
130	Muzammil ahm	36	M	Shop keeper	77297		Y	2	N	Y	Y	N	N	N	Y	Y	N	99	88	90	60	1	CH+Petechiae	Y	N	Y	N		Normal	b/l basal crepts	Normal	No deficits	GRADE 4	GRADE 3	GRADE 3	GRADE 1	8000	1	1	Present		Absent	0			0	absent	absent	Normal	ARDS	Gb sludge		Absent	Absent		12.1	0.56		0.8	32	32	6	DISCHARGE
131	Sumangala	29	F	Housewife	170370		Y	2	Y	N	N	N	N	Y	N	N	N	100	102	110	70	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 1	GRADE 2	GRADE 1	GRADE 0	9200	1	4			Absent	1	Present		0	absent	absent	Normal	Normal	Normal		Absent	Absent		5	0.87		1	25	26		DISCHARGE
132	Kusuma	36	F	Housewife	171744		Y	3	N	N	Y	Y	Y	N	N	Y	N	100	102	80	60	1	Petechiae	N	N	Y	N		Normal	Normal	Normal	No deficits	GRADE 3	GRADE 2	GRADE 2	GRADE 1	7000	1	2		Present	Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		15.9	0.86		0.8	32	28		DISCHARGE
133	Kavya	32	F	Housewife	177826		Y	2	Y	N	N	Y	N	N	Y	N	N	100	102	120	80	0	Absent	N	N	N	N		Normal	Normal	Normal	No deficits	GRADE 2	GRADE 2	GRADE 1	GRADE 1	7800	1	1	Present		Absent	0			0	absent	absent	Normal	Normal	Normal		Absent	Absent		23.1	1.09		1	29	26		DISCHARGE
134	Venkatamma	65	F	Housewife	95396		Y	5	N	N	Y	Y	N	N	N	Y	N	100	108	110	70	1	CH+Petechiae	Y	N	Y	N		Normal	b/l basal crepts	Mild hepatomegal	No deficits	GRADE 4	GRADE 4			11000	2	1	Present		Absent	0			0	absent	absent	Normal	Normal	Hepatomegaly		Absent	Absent		132	6		3	110	86	6	DEATH