"CLINICAL STUDY OF FEVER WITH THROMBOCYTOPENIA WITH SPECIAL REFERENCE TO INFECTIVE ETIOLOGY AND COMPLICATIONS ADMITTED TO GOVERNMENT ROYAPETTAH HOSPITAL, CHENNAI"

Dissertation submitted to

THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY

CHENNAI

In partial fulfillment of regulations

For award of the degree of

M.D (GENERAL MEDICINE)

BRANCH – 1

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BONAFIDE CERTIFICATE

This is to certify that dissertation named **"CLINICAL STUDY OF FEVER WITH THROMBOCYTOPENIA WITH SPECIAL REFERENCE TO INFECTIVE ETIOLOGY AND COMPLICATIONS ADMITTED TO GOVERNMENT ROYAPETTAH HOSPITAL, CHENNAI"** is a bonafide work performed by Dr. M.Manoj , post graduate student, Department of Medicine, Kilpauk Medical College, Chennai-10, under my guidance and supervision in fulfillment of regulations of the Tamilnadu Dr. M.G.R Medical University for the award of M.D. Degree Branch I (General Medicine) during the academic period from May 2011 to April 2014.

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DECLARATION

I solemnly declare that this dissertation **"CLINICAL STUDY OF FEVER WITH THROMBOCYTOPENIA WITH SPECIAL REFERENCE TO INFECTIVE ETIOLOGY AND COMPLICATIONS ADMITTED TO GOVERNMENT ROYAPETTAH HOSPITAL, CHENNAI"** was prepared by me at Government Kilpauk Medical College and Hospital, Chennai, under the guidance and supervision of **Dr. S. Mayilvahanan M.D.**, Professor, Department of Internal Medicine, Government Royapettah Hospital, Chennai.

This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfillment of the University regulations for the award of the degree of **M.D. Branch I (General Medicine)**.

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Date: (Dr. M. MANOJ)

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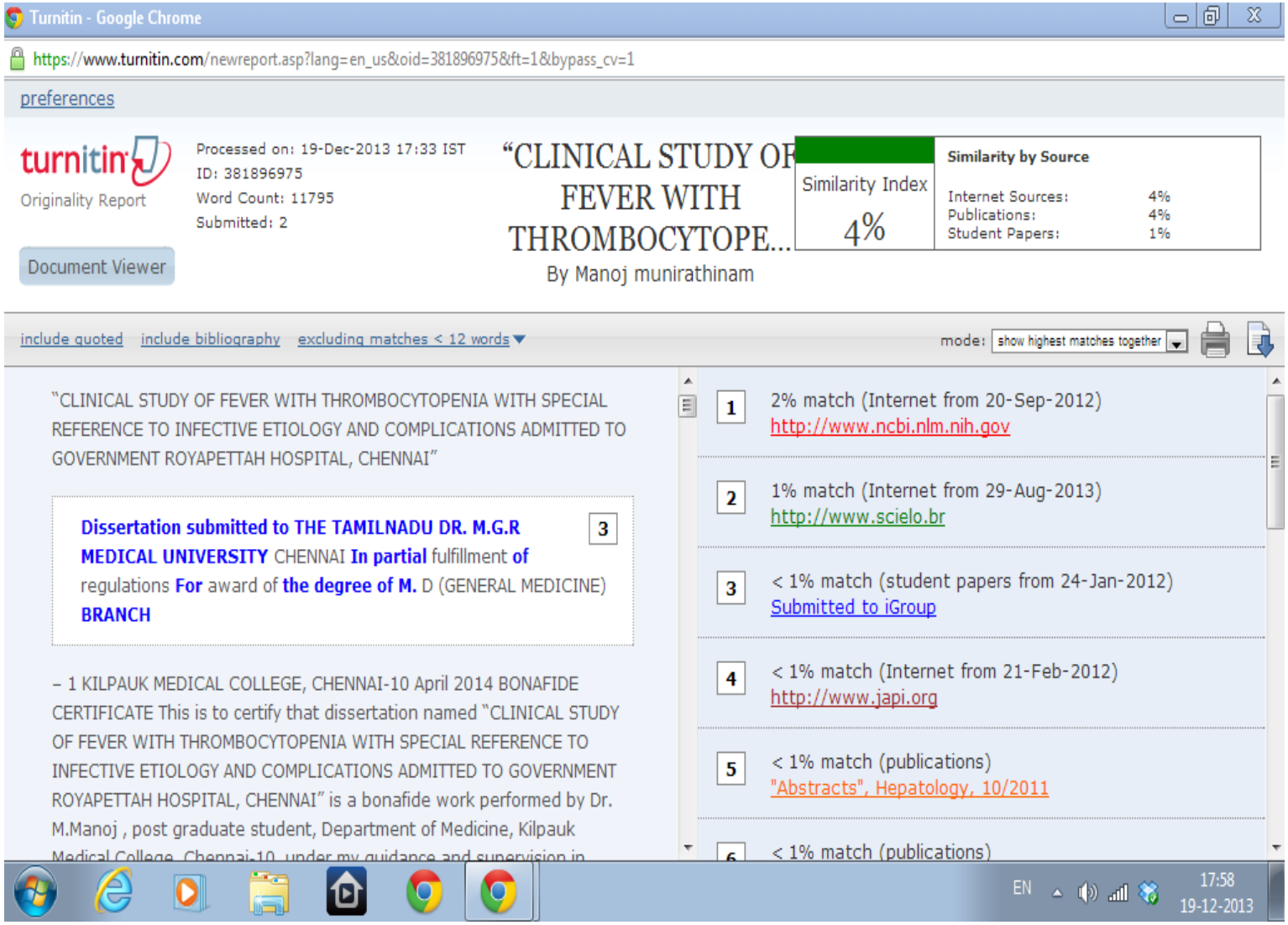
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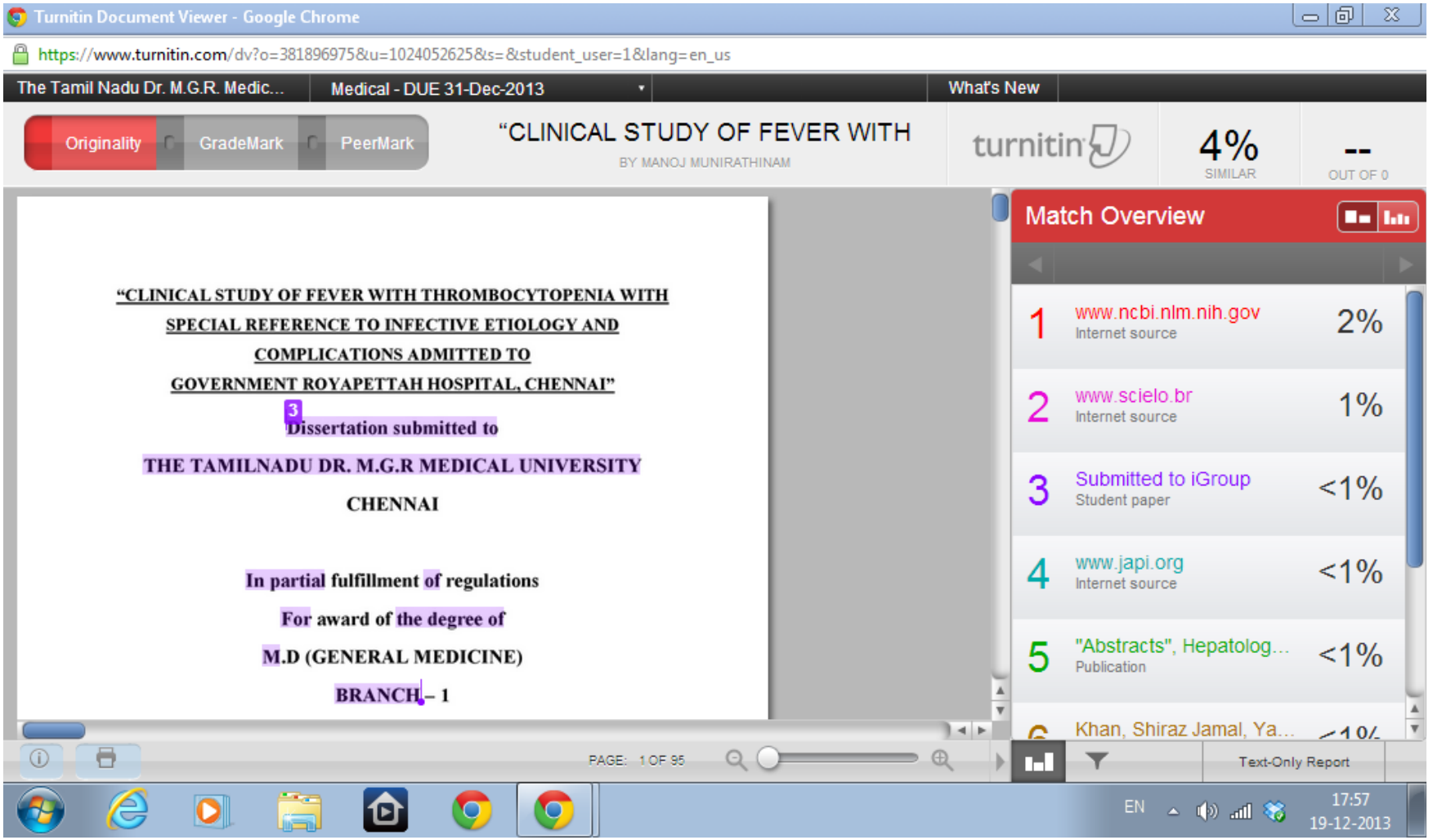
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ABSTRACT

BACKGROUND:

Fever with thrombocytopenia is a common condition that is associated with an increased risk of morbidity and mortality. Infections like Malaria, Dengue, Leptospirosis, Typhoid, HIV & septicemia are some of the common causes of fever with thrombocytopenia. Therefore a well organized systemic approach that is carried out with an awareness of causes of fever with thrombocytopenia can shorten the duration of investigations and bring out diagnosis. Hence, a need for study to know the causes and complications of fever with thrombocytopenia.

AIMS AND OBJECTIVES

1) To study the etiology of short duration fever with thrombocytopenia

2) To study the clinical presentation and the laboratory profile of patients presenting with fever and thrombocytopenia.

3) To assess the correlation of severity of thrombocytopenia with the bleeding manifestation .

MATERIALS AND METHODS :

This was a cross sectional study which included all new patients above 18 years with fever **(**temperature > 99.9 F**)** and thrombocytopenia (platelet count less than 1,50,000cells/ cu.mm) admitted to Government Royapettah hospital. The data of each patient was collected on a proforma specially designed for this study which includes demographic details, clinical features, past medical history, clinical and Lab values which will be analysed for statistical significance and correlation.

RESULTS :

In our study the leading cause of febrile thrombocytopenia was malaria. The 2nd leading cause of febrile thrombocytopenia was dengue fever. Typhoid fever accounted for 6% of cases. Patients in whom diagnosis could not be made was 16%. Among the 100 patients in the study group, the maximum number of patients (54%) had a platelet count between 50,000 to 100000. Platelet count less than 20000 were found in only three patients. Only 11% of patients had bleeding manifestations. A total of 9 patients had received transfusion of blood products.7 patients had received fresh whole blood alone and 2 of them had been transfused both fresh whole blood and platelets. The two patients who had received platelet transfusion were having sepsis and malaria.

CONCLUSION AND INTERPRETATION:

1) Infections are one of the most common causes of thrombocytopenia. The leading cause of fever with thrombocytopenia in our study was Malaria. 2) In malarial infection, the most common species was Plasmodium vivax followed by Plasmodium falciparum. 3) Dengue fever was the second commonest cause of febrile thrombocytopenia. 4) There is no direct correlation between the severity of thrombocytopenia and the bleeding manifestation. 5) Bleeding manifestation was present only in 11% of patients in the study. So in majority of patients, the thrombocytopenia was transient and asymptomatic. 6) Prophylactic platelet transfusion may not be required in all cases of severe thrombocytopenia. It may be restricted to selected patients with bleeding manifestation or platelets <10,000/cumm which may indicate bone marrow compromise.7) Most of the patients in our study did not require platelet or blood transfusion and the platelet count significantly increased after the treatment of the underlying infection.

KEYWORDS :

Fever, thrombocytopenia, malaria, dengue, bleeding, platelet count, platelet transfusion

INTRODUCTION

There is an alarming increase in the incidence of fever with thrombocytopenia. Routinely we come across many cases, both as inpatients and outpatients presenting with fever with thrombocytopenia. Infection is one of the common cause of thrombocytopenia. Thrombocytopenia in fever can predict the cause and thus helps in early diagnosis and treatment, preventing further fatal outcome associated with it.

Though patients can initially present with simple fever, in due course it can lead to unpredictable outcomes including death at times, therefore the aim of the study is to analyse the clinical profile of fever with thrombocytopenia, as early diagnosis and timely intervention prevents adverse outcomes and can save lives.

Fever with thrombocytopenia is a common condition that is associated with an increased risk of morbidity and mortality. Infections like Malaria, Dengue, Leptospirosis, Typhoid, HIV & septicemia are some of the common causes of fever with thrombocytopenia. Therefore a well organized systemic approach that is carried out with an awareness of causes of fever with thrombocytopenia can shorten the duration of investigations and bring out diagnosis. Hence, a need for study to know the causes and complications of fever with thrombocytopenia.

AIM OF THE STUDY

1) To study the etiology of short duration fever with thrombocytopenia

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REVIEW OF LITERATURE

THROMBOCYTOPENIA IN MALARIA

Thrombocytopenia is one of the most common complications of both Plasmodium vivax and Plasmodium falciparum malaria. It is pertinent that the finding of thrombocytopenia in patient, may be an indication for a thorough lookout into the blood smear to rule out malaria as the cause. This fact is especially important in the workup for thrombocytopenia in febrile patients.

Malaria affects almost all blood components and is a true haematological infectious disease. Anaemia and thrombocytopenia are the most frequent malaria-associated haematological complications (Wickramasinghe & Abdalla 2000)[1] and have received more attention in the scientific literature due to their associated mortality.

In the current field of Travel Medicine, the rapid increase in the number of people travelling to tropical areas has added a great challenge for malaria diagnosis because the thick blood smear (the standard diagnosis in endemic areas) has high specificity but only when performed by experienced microscopists.

The presence of thrombocytopenia in acute febrile travellers returning from tropical areas has become a highly sensitive clinical marker for

malaria diagnosis (D'Acremont et al. 2002)[2]. Another study has reported 60% sensitivity and 88% specificity of thrombocytopenia for malaria diagnosis in acute febrile patients (Lathia & Joshi 2004)[3].

The sensitivity of thrombocytopenia together with the acute febrile syndrome was 100% for malaria diagnosis, with a specificity of 70%, a positive predictive value of 86% and a negative predictive value of 100% (Patel et al.2004)[4]

In 2005, 138 of 684 (20.1%) malarial cases hospitalised in a tertiary care centre in Manaus had thrombocytopenia as the cause of admission, which corresponded to 6.8% of hospitalisations due to all causes in this reference institution (unpublished observations). Hospitalisation, however, does not add any benefit to the patient and because there is no evidence for any intervention, this simply increases public health costs in underdeveloped and under-resourced areas.

Since the beginning of the 1970s, there have been reports proposing that malaria-associated thrombocytopenia is quite similar in *Plasmodium vivax* and *Plasmodium falciparum* infections (Beale et al. 1972)[5]. However, more recent data in India has shown how thrombocytopenia exhibited a **heightened frequency and severity among patients with *P. vivax* infection** (Kochar et al. 2010)[6].

It is a general consensus that thrombocytopenia is very common in malaria and previously it was believed that it is more common in Falciparum

malaria. Recent studies have shown that thrombocytopenia is equally or even more common in *P. vivax* malaria contrary to the popular belief that it may be observed in *P. falciparum* malaria. More recent data in India has shown how thrombocytopenia exhibited a heightened frequency and severity among patients with *P. vivax* infection. Thrombocytopenia was seen in 40-90 percent of patients infected with *P. falciparum* infection in India. Maximum thrombocytopenia occurred on the fifth or sixth day of infection, and gradually returned to normal within 5-7 days after parasitemia ceased.

HOW LOW IS THE PLATELET COUNT IN MALARIA?

In a systematic review of literature, platelet counts less than 150,000/mm*3* occurred in 24-94% in patients with acute malaria and this frequency was not different between the two major species that affected humans.

Minor bleeding is mentioned in case reports of patients with Plasmodium vivax infection. The relatively lesser incidence of major bleeds may be explained by **medullary compensation with the release of mega platelets** in the peripheral circulation by megakaryocytes, thus maintaining a good primary haemostasis.

MECHANISM OF THROMBOCYTOPENIA IN MALARIA :

The speculated mechanisms leading to thrombocytopenia are:

1) coagulation disturbances,

2) splenomegaly,

3) bone marrow alterations,

4) antibody-mediated platelet destruction,

5) oxidative stress and the role of platelets as cofactors in triggering severe malaria.

1) Coagulation disturbance - A study based on 31 American soldiers in Vietnam with chloroquine-resistant falciparum malaria noted the following changes in the acute phase of the disease using the same patients as their own controls during convalescence: decrease in the platelet count and prothrombim activation time, increase in the activated thromboplastin time, and reduction in factors V, VII and VIII with normal fibrinogen (Dennis et al. 1967)[7].

In Manaus, 2004, a study with falciparum and vivax patients demonstrated a negative correlation between platelet counts, thrombin-anti-thrombin complex and D-dimers, suggesting that the activation of coagulation could be partially responsible for thrombocytopenia (Marques et al. 2005)[8].

2) Splenomegaly - The spleen in malaria has played a crucial role in the immune response against the parasite, as well as controlling parasitaemia due to the phagocytosis of parasitised red blood cells (RBCs) (Engwerda et al. 2005)[9]. Some data suggested that platelets were sequestered in the spleen during the acute infection (Skudowitz et al. 1973)[10].

3) Bone marrow alterations - a "dysmegakaryopoiesis" was proposed, similar to what happened in the human malarial anaemia model, where dyserythropoiesis was triggered by cytokines (Menendez et al. 2000)[11]. In the few studies that examined the bone marrow for this purpose, megakaryocytic lineage was apparently preserved (Naveira 1970, Beale et al. 1972)[12]. Thrombopoietin indeed seems to rise during the acute disease even in the presence of liver compromise, suggesting that no bone marrow inhibition is seen (Kreil et al. 2000)[13]. Additional data from FBC samples in vivax patients showed that there is a significant negative correlation between platelet count and mean platelet volume (Lacerda 2007)[14], suggesting that megakaryocytes are able to release mega platelets in the circulation to compensate for the low absolute number of platelets in the periphery. Similar results were shown in children with falciparum malaria (Maina et al. 2010)[15]. These mega platelets are probably able to sustain a good primary haemostasis that could explain the low frequency of severe bleeding in malarial patients.

4) Antibody-mediated platelet destruction - There is evidence that platelet-associated IgG (PAIgG) is increased in malaria and is associated with thrombocytopenia. During acute malaria, thrombocytopenia is most probably associated with the binding of parasite antigens to the surface of platelets to which antimalarial antibodies also bind, leading to the *in situ* formation of immune complexes (Kelton et al. 1983)[16].

Because the generation of immune complexes is proportional to the amount of available antigen, the negative correlation between platelet count and peripheral parasitaemia reported in many studies (Lacerda 2007, Silva 2009)[17,18] corroborates immune mechanisms as a potential mechanism of platelet destruction.

5) Oxidative stress - Free radicals may play an important role in the platelet destruction in malarial infection.

6) Platelet aggregation - platelets from patients with acute malaria are highly sensitive to adenosine diphosphate (ADP) addition in vitro (Essien & Ebhota 1981)[19], and it is believed that ADP release following haemolysis could contribute to higher platelet aggregation.

The Relationship Between Thrombocytopenia And Severe Malaria

Severe thrombocytopenia (platelet count under 50,000/mm3), despite not being considered severe malaria according to World Health Organization criteria (WHO 2010) due to the inability to cause death *per se*, has been occasionally associated with severity (Gerardin et al. 2002, Rogier et al. 2004)[20,21].

17 patients from Manaus affected by any of the WHO malaria severity criteria with confirmed *P. vivax* monoinfection, 14 presented with thrombocytopenia, suggesting that this haematological complication can be explored as a marker of the severity for this species (Alexandre et al. 2010)[22].

From the case reports available, the association between severe cases with thrombocytopenia is evident. However, that can be due to bias publication, where prospective studies would be needed to validate this association. On the other hand, considering that many studies point to a clear negative correlation between platelet count and parasitaemia (Grynberg et al. 2007, Silva 2009)[23,24], it should be investigated if thrombocytopenia could be used in the surveillance of drug resistance, where higher parasitaemias for prolonged periods are usually found.

MANAGEMENT OF THROMBOCYTOPENIA IN MALARIA :

Data from experimental models are presented and, despite not being rare, there is no clear recommendation on the adequate management of this haematological complication.

In most cases, a conservative approach is adopted and platelet counts usually revert to normal ranges a few days after efficacious antimalarial treatment.

More studies are needed to specifically clarify if thrombocytopenia is the cause or consequence of the clinical disease spectrum.

Platelet transfusion has been widely followed, but with no confirmed efficacy. The indication of prophylactic platelet transfusion when platelet counts are under 10,000/mm3 probably applies only when the bone marrow is compromised and is not able to release efficacious platelets (Rebulla 2000). This does not seem to be the case in malaria. Keeping platelet counts between 50,000 and 100,000/mm3 is a formal indication only in patients undergoing surgical procedures (Rebulla 2001)[25]. In a tertiary care centre in the Western Brazilian Amazon over a 12-month period, 10.4% (20/191) of patients who received platelet transfusion were diagnosed with vivax or falciparum malaria (Lacerda et al. 2006)[26]. The dosage was usually below that recommended in the literature (Schlossberg & Herman 2003)[27]. In 40% of patients, the only justifications for

transfusion were maintaining a platelet count below 10,000/mm3 and discrete bleeding. In a further 6% of patients, only a very low platelet count was described. In this group of 40% of patients, the alleged reason was minor bleeding despite having non-severe thrombocytopenia; in 33%, no indication was verified. These data point to the little existing evidence of the recommendations for platelet transfusion in these patients. The corrected count increment to evaluate transfusion efficacy was not calculated for any patient. The low efficacy of platelet transfusion in general is well described for several acute infectious diseases (de Paula et al. 1993)[28], probably due to **peripheral immune mechanisms of destruction that do not spare the transfused platelets**.

Indications for platelet transfusion in cases when DIC is suspected and diagnosed, the formal clinical indication persists, as recommended elsewhere (Franchini 2005)[29]. Due to the impossibility of using frozen platelets in routine clinical practice, other platelet substitutes and preparations are being investigated (Blajchman 2003)[30]. Except in atypical cases of ITP with severe bleeding, there is no evidence for the use of human intravenous immunoglobulin, even in cases of severe thrombocytopenia (Lacerda et al. 2004)[31].

The use of corticoids has never been followed, probably due to the fact that the recovery of thrombocytopenia following antimalarial treatment is seen in almost all cases, with good prognosis for all species that infect humans (Lacerda

2007)[32] and with the lack of robust evidence of immune-mediated destruction of platelets as a major mechanism. It was also found that in patients with cerebral falciparum malaria, dexamethasone exacerbated the neurological symptoms and increased the frequency of gastrointestinal bleeding (Warrell et al. 1982, Hoffman et al. 1988)[33,34]. However, in none of these studies was platelet recovery analysed as a secondary endpoint.

Immune modulators are also candidates in the adjuvant antimalarial therapy (Muniz-Junqueira et al. 2005, Mohanty et al. 2006)[35,36], based on the drug-induced inhibition of adhesion molecules in RBCs and platelets (Muniz-Junqueira 2007)[37]. The exploration of drugs known by their anti-inflammatory effect, modulating TNF, e.g., pentoxyfylline and thalidomide, upon severe malaria, could not only contribute to the understanding of the mechanisms of severity but also clarify the association between platelets and severe disease.

The frequency of thrombocytopenia (i.e., platelet count below 150,000/mm3) in malarial infection ranges from 24-94% in the literature, despite the low occurrence of severe bleeding, even in the case of severe malaria. It is still unclear whether this haematological complication is more frequent in *P. vivax* or *P. falciparum* malaria. The clinical management of malarial thrombocytopenia is expectant and the level of evidence for platelet transfusion is insufficient to

recommend this practice. It is not clear whether platelets are diminished during acute malarial infection as a consequence of the immune response to the parasite present or whether platelets are actually involved in the generation of severe disease.

SYSTEMATIC REVIEW OF STUDIES,

ESTIMATING THROMBOCYTOPENIA IN MALARIAL PATIENTS IN INDIA (2002-2011)

REFERENCES	TYPE OF PATIENTS	AGE RANGE	SPECIES	N	THROMBOCYTOPENIA %
Mohapatra et al. (2002)	Inpatients and outpatients	15-60 y	*P.v.*	110	3.6 (< 100,000)
Jadhav et al. (2004)	Inpatients and outpatients	All ages	*P.v.*	973	65 (50,000-150,000)
Kumar and Shashirekha (2006)	Inpatients and outpatients	All ages	*P.v.*	27	88.8 (< 150,000)
Prasad et al. (2009)	Inpatients	< 5 y	*P.f.*	40	85 (< 150,000)
Kochar et al. (2010)	Inpatients and outpatients	All ages	*P.v./P.f. and mixed*	1,064	24.6 (< 150,000)
George and Alexander (2010)	Inpatients	18-66 y	*P.v.*	30	93.3 (< 150,000)
Srivastava et al. (2011)	Inpatients	All ages	*P.v.*	50	82 (< 150,000)

COLLATED CASE REPORTS OF *PLASMODIUM VIVAX*-ASSOCIATED THROMBOCYTOPENIA IN INDIA (2002-2011)

REFERENCES	PLATELET COUNT (X 1,000/MM3)	BLEEDING	PLATELET TRANSFUSION	OBSERVATION
Makkar et al. (2002)	8	Gingival bleeding	Yes	-
Aggarwal et al. (2005)	6	Petecchiae	Yes	-
Katira and Shah (2006)	14-92	No	Yes	-
Kaur et al. (2007)	30	No	No	Acute renal failure
Kaur et al. (2007)	30	Petecchiae	No	Acute renal failure
Vij et al. (2008)	NA	Gingival bleeding	No	NA
Parakh et al. (2009)	5-42	Petecchiae	No	Cerebral malaria, shock and acute renal failure
Thapa et al. (2009)	11	Petecchiae and mucosal bleeding	Yes	Hepatitis and shock
Harish and Gupta (2009)	1	Intracranial bleed	No	Seizures
Bhatia and Bhatia (2010)	NA	Yes	NA	NA

THROMBOCYTOPENIA IN DENGUE FEVER

Dengue Haemorrhagic Fever is a probable case of dengue and haemorrhagic tendency evidenced by one or more of the following:

1) Positive tourniquet test

2) Petechiae, ecchymosis or purpura

3) Bleeding from mucosa (mostly epistaxis or bleeding from gums), injection sites or other sites

4) Haematemesis or melena

5) Thrombocytopaenia (platelets 100,000/cu.mm or less) and

6) Evidence of plasma leakage due to increased capillary permeability manifested by one or more of the following:

– A >20% rise in haemotocrit for age and sex

– A >20% drop in haemotocrit following treatment with fluids as compared to baseline

– Signs of plasma leakage (pleural effusion, ascites or hypoproteinaemia).

Dengue Shock Syndrome (DSS) - All the above criteria of DHF plus signs of circulatory failure manifested by rapid and weak pulse, narrow pulse pressure (< or equal to 20 mm Hg); hypotension for age, cold and clammy skin and restlessness.

CAUSE OF THROMBOCYTPENIA IN DENGUE:

Although not fully elucidated, recent evidence indicates that severe Dengue viral infections increase vascular permeability that leads to decreased intravascular fluid volume and consequent hemoconcentration and hypotension in infected patients. Another feature of Dengue viral infection is thrombocytopenia, which is common in both mild and severe diseases.

Dengue virus has been isolated from polymorphonuclear leukocytes, monocyte / macrophages, dendritic cells and others[38] .It has also been detected in megakaryocyte progenitors and circulating platelets [39,40,41] These findings suggest that Dengue virus may induce thrombocytopenia via direct interactions with megakaryocytes and platelets. Dengue virus has also been shown to reduce circulating platelet counts independent of virus attachment or entry into platelets or their precursors. Thus, two mechanisms are probably involved in dengue-induced thrombocytopenia:

1) impaired thrombopoiesis and

2) peripheral platelet destruction

1) IMPAIRED THROMBOPOIESIS

Marrow suppression within 2–4 days of dengue viral infection can contribute to thrombocytopenia . Viral RNA has been isolated from bone marrow specimens of infected individuals, suggesting that dengue targets the marrow and hematopoietic system.[42] Bone marrow studies also reveal diminished megakaryopoiesis during the onset of dengue infection and clinical recovery is associated with normal megakaryocyte topography and platelet counts [43] Suppression of megakaryopoiesis occurs either directly, due to infection and suppression of hematopoietic progenitor cells or indirectly, via impairment of stromal cells that function by altering the repertoire of cytokines in the bone marrow microenvironment. In regard to direct effects, Nakao et al. [44] demonstrated that Dengue virus- 4 propagates in human bone marrow progenitors in vitro and alters their proliferative capacity. Dengue viral infection suppresses proliferation of human cord blood progenitors and Dengue Virus -2 inhibits the differentiation of CD34+ progenitors into megakaryocytes, presumably by inducing apoptosis in infected cells[45,46]

Together, these data support that DV is able to directly infect hematopoietic progenitors and suppress megakaryopoiesis and thrombopoiesis. Dengue virus can also infect stromal cells, which in turn suppresses hematopoiesis. Rothwell et al.[47] infected long-term marrow cultures with Dengue Virus -2 and

characterized the viral antigen-positive cells. This investigation demonstrated two types of stromal cells that were positive for viral antigens: adventitial reticular cells and bone marrow dendritic cells. Altered cytokine production by infected stroma is the most probable mechanism of marrow suppression during DV infection. The in vitro findings described above and the hematological findings of leukopenia in conjunction with thrombocytopenia in dengue patients are used as argument in favor of dengue globally suppressing bone marrow hematopoiesis. [48] However, emerging evidence indicates that dengue infection also has extramedullary effects on circulating platelets.

2) INCREASED PERIPHERAL DESTRUCTION

a) Autoimmune-induced platelet activation and clearance

b) Platelet–leukocyte and platelet–endothelial cell interactions

c) Platelet dysfunction

d) Direct infection

e) Soluble mediators

Autoimmune-induced platelet activation and clearance

Several groups have put forth the autoimmune hypothesis, which postulates that host-generated anti-Dengue virus antibodies crossreact with platelets and facilitate their clearance [49] In support of this concept, serum from

dengue patients can bind platelets and higher levels of antiplatelet IgM are observed in severe DV infections when compared to classical dengue fever[50]. Moreover, dengue patient serum or rabbit anti nonstructural protein-1 (NS1) induce complementmediated lysis in platelets[51,52] which may contribute to the loss of circulating platelets during dengue illness. Autoantibodies directed against NS1 target human platelets and fibrinogen and induce thrombocytopenia in mice [53]

A molecular mimicry mechanism has been proposed in which the C-terminal region of NS1 shows sequence homology with integrins on the surface of platelets.

In clinical settings, increased levels of platelet-associated immunoglobulin (PAIgM or PAIgG) and phagocytosis of platelets by macrophages correlates with thrombocytopenia during the acute phase of secondary dengue infection [54] Similarly, anti-NS1 autoantibodies or pooled sera from dengue patients enhance the engagement of immunoglobulinopsonized platelets by macrophages.

Platelet–leukocyte and platelet–endothelial cell interactions

Similar to platelets, antibodies directed against Dengue Virus NS1 crossreact and activate endothelial cells . Endothelial cells infected with Dengue Virus display high expression of E-selectin and support the adherence of platelets. Platelets that adhere to dengue-infected endothelial cells express surface P-selectin. Increased interactions of platelets with leukocytes and endothelium are probably contributors to the pathogenesis of dengue disease, including thrombocytopenia.

Platelet dysfunction

There are a few studies examining platelet function in dengue disease. Among these, it has been shown that dengue serum abnormally activates platelets and inhibits platelet aggregation .

Direct infection

Recent studies indicate that dengue virus directly interacts and activates platelets. DV induces morphological changes in normal platelets typical of activation, including the presence of filopodia and degranulation . In parallel, Dengue virus increases the expression of surface P-selectin and fibrinogen binding . Dengue viral RNA and viral-like particles have also been detected in platelets of affected patients.

Soluble mediators

Key mediators that activate platelets and induce thrombocytopenia are often present in dengue infection. Monocytes from a donor infected with Dengue virus-1 respond to a second hit of dengue virus-2 by generating Platelet Activating Factor (PAF), a lipid mediator that augments platelet aggregation. This observation is in agreement with others demonstrating that thrombocytopenia and disease severity is reduced in mice lacking the PAF receptor (PAFr). Fibrin degradation products (D-dimers) and thrombin/ antithrombin complexes are typically increased after dengue infection[55] Von Willebrand factor is likewise

increased, creating a milieu for enhanced platelet activation. An array of cytokines, such as tumor necrosis factor-a (TNF-a) and interleukin-1b (IL-1b) are also produced during dengue infection. These cytokines have been linked to the onset and regulation of thrombosis and hemostasis and it has been demonstrated that increased TNF-a and IL-1 b in dengue patients correlates with thrombocytopenia .

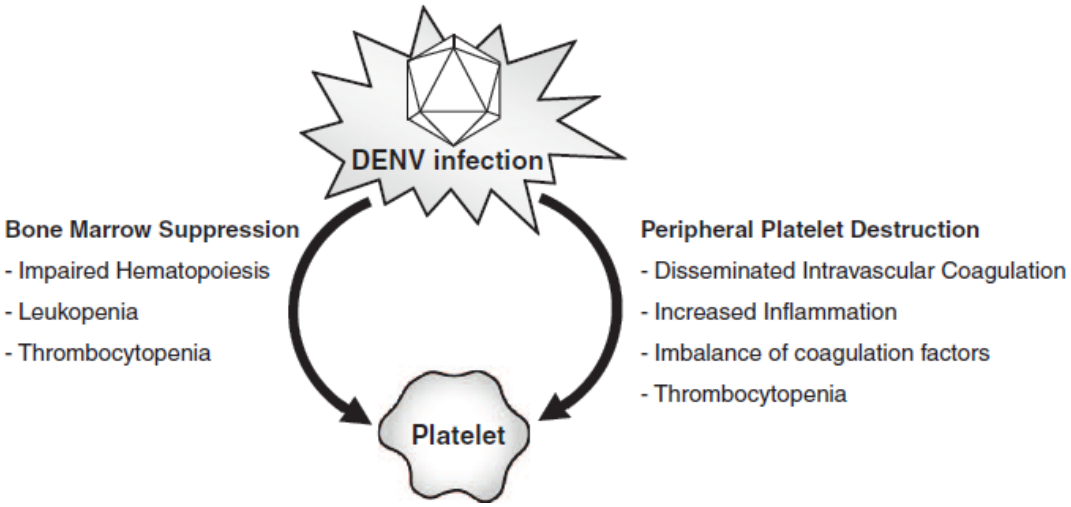
TARGETING PLATELETS IN THE TREATMENT OF DENGUE INFECTION

Although thrombocytopenia is frequently observed in patients with dengue, severe bleeding is rare. When it occurs, however, excessive bleeding is associated with a high lethality. It is controversial as to whether the intensity of thrombocytopenia predicts bleeding risk in dengue patients; nonetheless, it is well accepted that severe thrombocytopenia associates with hemorrhagic manifestations. In addition, it is probable that other factors, such as disseminated intravascular coagulation (DIC), hepatic impairment and/or vascular dysfunction, act in concert with thrombocytopenia to induce bleeding.

Platelet transfusion has been used as a strategy for the prevention or treatment of severe bleeding in patients with dengue. However, **recent WHO guidelines do not recommend platelet transfusion for hemodynamically stable patients with thrombocytopenia**. Even in patients who exhibit severe bleeding and hemodynamic instability, transfusion of platelets is only considered with

restrictions. Importantly, these recommendations are based solely on the opinions of experts or small observational studies rather than randomized clinical trials.

Other treatments considered for dengue-induced thrombocytopenia are anti-D immune globulin (anti-D) and PAFr antagonists.[56] Of these, anti-D has shown promise in the treatment of severe thrombocytopenia in DHF patients while a PAFr antagonist relieved thrombocytopenia in a mouse model of dengue infection . By contrast, IVIG did not hasten the recovery of thrombocytopenia in dengue patients with secondary DV infection. Moving forward, it will be important to consider nontraditional roles of platelets in the treatment of dengue. This includes their role in regulating viral infection and replication, inflammation and vascular integrity, which may identify new molecular targets for the treatment of dengue infection



Schematic representation of two major mechanisms involved in dengue-induced thrombocytopenia: bone marrow suppression and peripheral platelet destruction.

THROMBOCYTOPENIA IN HIV INFECTION

Thrombocytopenia in HIV was first described in 1982. The prevalence is more or less 40%, depending on which literature is quoted. Thrombocytopenia is associated with increased morbidity and mortality, accelerated deterioration in CD4 counts and accelerated progression to full-blown AIDS. In a meta-analysis of 5 trials involving > 3 000 patients, both treatment-naïve and treatment-experienced patients, thrombocytopenia was found to be one of 8 factors that correlated with a poorer prognosis and more rapid progression to full-blown AIDS in spite of antiretroviral treatment.

A recent study showed that platelets have the ability to ‘engulf' the Human immunodeficiency virus and *Staphylococcus aureus* – perhaps another reason why thrombocytopenia is prone to a more rapid acceleration of disease. Severe thrombocytopenia also limits one’s treatment options, as many drugs cause bone marrow suppression and peripheral platelet consumption. HIV enters the megakaryocytes and platelets via the CXCR4 receptors. Once the virus is in the megakaryocyte it starts to cause havoc, as shown by the change in megakaryocyte morphology

Thrombocytopenia early on in HIV is mainly due to peripheral destruction, while later on in the advanced stage (AIDS) it is more likely to be due to decreased production. In fact, CD4 counts above 200 are associated with increased peripheral destruction while thrombocytopenia in CD4 counts of < 200 is associated with decreased platelet production.

In one study the authors found a 3-fold increase in megakaryocytes in patients with HIV. However, there was no increase in the mean platelet mass, suggesting the presence of dysmegakaryopoiesis. This suggests that thrombocytopenia in HIV is multifactorial because of:

• direct HIV infection of the megakaryocyte, causing apoptosis

• dysmegakaryopoiesis, abnormal and dysfunctional production of megakaryocytes and platelets

• peripheral destruction of platelets due to cross-reactivity of HIV Abs.

Who to treat

There are no standardized guidelines in the treatment of HIV-induced thrombocytopenia.

The generally accepted guideline is to treat when there are < 30 000 platelets or < 50 000 if the patient is on warfarin or a haemophiliac. One must still remember that thrombocytopenia correlates with a poorer outcome and accelerated HIV course and at least a 2- fold increase in mortality. In opposition

to this, treatment of thrombocytopenia is immunosuppressive in its nature and therefore should be given in conjunction with antiretrovirals. A platelet count of 50000 post-treatment is quite acceptable for protection against bleeding, but still does predict a poorer outcome with regards to mortality and morbidity.

Therefore thrombocytopenia occurs as a result of:

• increased peripheral destruction or

• increased peripheral sequestration or

• decreased production or

• a combination of the above.

Approach to management

Do a bone marrow biopsy, to asses megakaryocyte numbers and morphology. One can then easily exclude granulomas, Kaposi's sarcoma and lymphoma or even fibrosis in the marrow. Once the decision is made to treat, then the difficulty is deciding how to treat.

Steroids

A dose of 1 mg/kg/day prednisone should be started as a first-line therapy. Monitor the platelet counts regularly and be alert for opportunistic infections. If no response is seen within a 2-week period, one can try a higher dosage of 2 mg/kg/day. This is the dosage used in the HIV-negative cohort. These

patients should be monitored carefully and be on antiretrovirals. Patient should not stay on high-dosage therapy for more than a month. If no response or a nominal response is seen, it should be considered as treatment failure and alternative treatment given. Prednisone does not stimulate viral replication but does however accelerate the course of Kaposi's sarcoma.

Intravenous immunoglobulin

Intravenous immunoglobulin (IVIG) is effective in raising a patient's platelet counts. However, it is not cheap and results can be short lasting. It is not a cost-effective way of maintaining a platelet count and should only be used in chronic cases as a last resort. In the acute setting it is good for raising counts prior to a splenectomy or if patients have severe or uncontrollable haemorrhage. This would then be used in conjunction with platelet transfusions. The exact mechanisms of action are not entirely understood – suffice to say that excessive immunoglobulin (Ig) overwhelms the immune system and stimulates the suppressor B cells to suppress endogenous Ig production. The IVIG also blocks the Fc receptors in the spleen and macrophages, thereby limiting their platelet-destroying function. The dosage of the IVIG can differ from 0.5 g/kg to 2 g/kg either as a bolus but mostly given over 2 - 5 days. The cost and availability of IVIG are the most limiting factors.

Anti-D

The anti-rhesus globulin can also be used with varying success. This should not be used in patients who are Rh+ as it may cause haemolysis. It can however be used if the patient has a normal haemoglobin. Its effects, if there is going to be a response, are said to be longer lasting than IVIG.

Splenectomy

Splenectomy is the usual 2nd-line of therapy with the HIV-negative cohort.There were concerns initially that it would accelerate the course of HIV. This was before antiretroviral therapy was commonly available. At the moment, besides the concerns of infections from capsulated organisms and malaria, splenectomy may be a good alternative. The literature has shown splenectomy to attenuate immune reconstitution syndrome and has shown to produce patients with a higher CD4 and CD8 counts along with a slower progression to AIDS. Splenic irradiation is of no value in this situation.

Megestrol acetate

This drug was initially used to treat cachexia and anorexia in HIV. It is known to block the Fc receptors in macrophages. Trials have shown that megestrol acetate (MA) increases peripheral platelet counts and improves platelet survival. There were no improvements in body mass index (BMI), peripheral CD4

counts or viral loads. Danazol is still of value in idiopathic thrombocytopenic purpura, even in HIVinduced ITP.

Transfusions

Transfusions have a transient effect, they are expensive and should be limited to emergencies and during surgery. Normally they should be given with IVIG to have a longer lasting effect. Transfusions have other sideeffects e.g. transfusion reactions, infections and transfusion-related acute lung injury (TRALI). Multiple transfusions are known to decrease immunity and stimulate HIV-1 expression.

Novel therapies

These are still in experimental phases but include entities such as recombinant thrombopoietin, alpha interferon and IL-6, IL-3, AND IL-11.

THROMBOCYTOPENIA IN LEPTOSPIROSIS

Leptospirosis is a zoonosis with protean manifestations. The commonly identified complications of acute renal failure and jaundice have been widely described and reviewed in a considerable number of literatures. Severe cases of leptospirosis often presents not only with renal failure and jaundice, but

also with other organ involvement including myocarditis, aseptic meningitis, and hemorrhagic diathesis.

The hemorrhagic manifestations of leptospirosis occur in many ways. Pulmonary hemorrhage is a dreaded complication because it is associated with a high mortality rate. In 1984, an epidemic of pulmonary hemorrhagic fever occurred in Korea. Extensive investigations were undertaken to determine the cause, including clinical, pathological and epidemiological studies of all possible causative agents. The investigations finally came up with leptospirosis as the culprit.

In the year 1995, an outbreak of an acute febrile illness and pulmonary hemorrhage occurred during the period of October to November. More than 2000 persons were affected and at least 40 patients died from acute pulmonary hemorrhage and respiratory insufficiency. The initial considerations were dengue hemorrhagic fever and the hantavirus pulmonary syndrome, but serologic tests detected anti-leptospiral antibodies and immunohistochemical staining of tissues from fatal cases demonstrated leptospiral antigens present in various organs. Together with myocarditis, pulmonary hemorrhage and GI bleeding were identified as common complications leading to death.

Thrombocytopenia in leptospirosis has received little attention. Most studies on the pathogenesis of leptospirosis focused on renal failure and jaundice.

With the outbreaks of pulmonary hemorrhage in association with leptospirosis, our focus should shift to the mechanisms causing the bleeding diathesis in this particular disease. Thrombocytopenia is thought to be fleeting, mild and rare. However, reviews reported increasing prevalence of thrombocytopenia. Some authors postulated that this could possibly be attributed to

1) disseminated intravascular coagulation (DIC) or a toxin or cytotoxin mediated mechanism;

2) as a direct complication of leptospiral vasculitis as a general phenomenon of septicemia, or due to an undetected platelet antibody.

Whether either of these mechanisms is operating alone or in combination is uncertain and merits extensive investigation.

It is important for clinicians to be aware and to recognize the various ways in which leptospirosis can present. Although classically occurring as an acute febrile illness with renal failure and jaundice, the other less common manifestations may predominate. The changing pattern of the virulence of the disease could have been better explained by identifying the serovars involved. It has been speculated that a new strain of leptospires may be responsible for the more severe presentation in some patients. Our poor yield in culture studies for Leptospira, and the unavailability of specific antigens for the different serovars makes this difficult.

Thrombocytopenia can occur in mild to moderate to severe forms; majority of the platelet counts were between 20,000 and 80,000.Thrombocytopenia in leptospirosis was also associated with increased number of fatal complications. The presence of thrombocytopenia indicated a more severe form of leptospirosis.. Mortality rate was higher in the thrombocytopenic group compared to the nonthrombocytopenic group

THROMBOCYTOPENIA IN TYPHOID FEVER

The hematological changes are common in typhoid fever and these include anemia, leucopoenia, eosinophilia, thrombocytopenia and sub clinical disseminated intravascular coagulation. Thrombocytopenia is a common finding amongst patients presenting with typhoid fever as it causes reversible bone marrow suppression**.** Bone marrow suppression and hemophagocytosis are considered to be an important mechanism in producing hematological changes.[57]

Many cases of typhoid fever have peripheral blood cytopenias that were not concurrent bone marrow suppression, suggesting a peripheral mechanism responsible for the blood dyscrasia in those cases[58]. However, in other studies the patients suffering from typhoid fever with pancytopenia, bone marrow examination revealed extensive haemophagocytosis which possibly contributed to

the pancytopenia. The term haemophagocytosis describes the pathological finding of activated macrophages and engulfing erythrocytes, leucocytes, platelets, and their precursors cells.[59]

THROMBOCYTOPENIA IN SEPSIS :

Thrombocytopenia is a frequent finding in critical illness and is commonly employed in clinical trials of severe sepsis therapies as a **marker of hematologic organ dysfunction**.

In the ICU setting platelets <1,00,000/mm^3 are identified in 20-40% of patients. In a study of ICU patients sepsis was identified as a major risk factor for thrombocytopenia.

Mechanism:

Sepsis induced thrombocytopenia is multifactorial in origin.

1) In experimental models of sepsis platelets adhere to activated endothelium in multiple organs. Following adhesion the activated platelets may either dislodge and return to the circulation or release their granule contents and undergo irreversible aggregation with vicious metamorphosis.

2) Inflammatory mediators and bacterial products such as endotoxins can contribute to sepsis induced thrombocytopenia by enhancing platelet reactivity and adhesivity.

3) Phagocytosis of platelets by reticuloendothelial elements may also contribute to cytopenias in sepsis.

4) Immune mechanisms may contribute to sepsis-induced thrombocytopenia. Nonspecific platelet-associated antibodies can be detected in up to 30% of ICU patients. In these patients, nonpathogenic IgG presumably binds to bacterial products on the surface of platelets, to an altered platelet surface, or as immune complexes. A subset of patients with platelet-associated antibodies have autoantibodies directed against glycoprotein IIb/IIIa. These antibodies have been implicated in the pathogenesis of immune thrombocytopenic purpura and, although not proved, may play a role in mediating sepsis-induced thrombocytopenia.

Microscopy of bone marrow in patients with sepsis often demonstrated **hemophagocytic histiocytes**. In a prospective study of 50 patients with sepsis hemophagocytosis was identified in 32 patients (64%). This process appears to be a function of elevated levels of macrophage colony stimulated factors and is correlated with the presence and extent of multiorgan dysfunction. In some patientswith sepsis antibodies to specific antiplatet antigens such as GPIIb/IIIa and GP Ib/IX have been detected.

The acute phase response is often characterized by increased platelet counts (thrombocytosis). However, patients who are admitted to the ICU with or without underlying sepsis are more commonly diagnosed as thrombocytopenia. Thrombocytopenia occurs in up to 20% of medical ICU and 35% of surgical ICU admissions[61,62,63]. Sepsis is a clear risk factor for thrombocytopenia, with an estimated incidence of 35% to 59%[64,65]. In addition, there is an inverse relationship between the severity of sepsis and the platelet count.

In a prospective study of critically ill patients with thrombocytopenia only 34% had a diagnosis of DIC. Secondary consumptive thrombocytopenia and DIC represent an extreme in the continuum of hemostatic abnormalities. In addition to sepsis-related mechanisms, other causes of thrombocytopenia should be considered in the critically ill patient. For example, thrombocytopenia may occur as a complication of heparin therapy. Other types of drug induced thrombocytopenia are rare in the ICU setting. Dilutional thrombocytopenia may occur in patients with trauma or those who have undergone complicated surgery. Preexisting underlying disease, including cancer and immune thrombocytopenic purpura, may also contribute to a low platelet count. Given the inverse correlation between platelet count and mortality and the proposed association of platelet activation with tissue injury and organ dysfunction, the

development of thrombocytopenia in the patient with sepsis is best regarded as maladaptive.

Clinical Manifestations and Diagnosis

Thrombocytopenia is a common cause of bleeding in the ICU setting. Patients with thrombocytopenia may have petechiae, purpura, bruising, or bleeding. Thrombocytopenia is diagnosed on the basis of the complete blood cell count. A peripheral smear may show evidence of platelet clumping. If that is the case, the platelet count should be remeasured in blood withdrawn into a non-EDTA containing tube. If the thrombocytopenia is associated with consumptive coagulopathy, the DIC screen may be abnormal, and the peripheral smear may show schistocytes. Although patients with sepsis may have increased platelet-associated IgG, testing for this gives nonspecific results and does not help to guide therapy.

Prognosis

Thrombocytopenia is a predictor of mortality in patients in the ICU and in patients with severe sepsis[65,66]. The degree and duration of thrombocytopenia, as well as the net change in the platelet count, are important determinants of survival[67,68,69]. Interestingly, once the platelet count decreases

lower than 100 $x10^9$/L, mortality continues to increase, whereas the risk of bleeding does not increase.

Treatment

Patients with severe thrombocytopenia should be treated with platelet transfusions. Although guidelines for prophylactic transfusions in patients with chemotherapy-induced thrombocytopenia have been established, the threshold for transfusions for the thrombocytopenic patient with sepsis is not as clear. In the absence of confounding factors, patients should probably receive transfusions when the platelet count is less than 10000 – 150000/cumm. If the patient has concomitant coagulopathy (eg. liver disease), active bleeding, or platelet dysfunction (eg, uremia), the transfusion threshold should be increased.

MATERIALS AND METHODS:

Study group :

All new patients above 18 years with fever **(**temperature > 99.9 F) and thrombocytopenia (platelet count less than 1,50,000cells/ cu.mm) admitted to Government Royapettah hospital

Study design **:** Cross-Sectional study

Place of study **:** Government Royapettah Hospital

Duration of study **:** 6 months (March-August 2013)

This study protocol was approved by the Ethical committee for research studies of Government Kilpauk Medical College Hospital, Chennai.

Inclusion criteria :

- All new patients above 18 years with fever (temperature > 99.9 F) and thrombocytopenia (platelet count less than 1,50,000 cells/ cu.mm)

Exclusion criteria :

- Patients presenting with thrombocytopenia without fever
- Diagnosed cases of Thrombocytopenic purpura on treatment

- Patients with thrombocytopenia already diagnosed to have haematological disorder / malignancy , on treatment with chemotherapy and other immunosuppresants
- Diagnosed cases of platelet disorders and dysfunction
- Patients on treatment with antiplatelet drugs and other drugs causing thrombocytopenia
- Patients with cirrhosis and chronic liver disease

METHODOLOGY:

Once the patients are admitted with fever and those who have thrombocytopenia confirmed by complete blood count, a careful history will be recorded, general physical examination and detailed examination of various systems will be done. Routine investigations and specific investigations will be done as and when indicated. Details of history, general physical examination and laboratory and technical investigation reports will be noted down from time to time.

- **STUDY TOOLS-**

Questionnair

Case sheets of patients

Temperature charts

- **VARIABLES**

- **Age group** - four groups were made, below 20yrs, 20-40yrs ,40 – 60yrs and above 60 yrs
- **Sex** - male and female
- **Fever duration**
- **Chills and rigor**- if present or not
- **Joint pain**- recorded from the history
- **Head ache**- the duration and episodes of headache assessed, and considered present or absent
- **Vomiting**- the number of episodes of vomiting and number of days for which it persists are considered, 2-4 episodes for more than 2 days are considered as vomiting present. Rest as no vomiting

- **Myalgia**-those having muscle pain for more than 2 days, without any relief even with rest are considered as myalgia present

- **Organomegaly** – this includes both hepatomegaly and spleenomegaly, it is assessed by the clinical examination of the patient, the clinical records and the ultrasonogram results.

- **Bleeding –** any bleeding manifestation like purpura, petechiae, hematuria, malena, hematemesis was considered as positive
- **Anemia –** less than 10 gm hemoglobin were considered as having anemia
- **Thrombocytopenia**- A count below 1,50,000/cumm was considered to have thrombocytopenia
- **Creatinine –** a creatinine valve > 1 mg/dl was considered as renal involvement
- **ALT/AST –** values more than 40 IU/L was considered elevated for each
- **Serum bilirubin –** more than 1mg/dl was considered as hyperbilirubinemia
- **Peripheral smear study or QBC for malaria –** was considered diagnostic for malaria
- **Widal test or blood culture for Salmonella typhi -** was considered diagnostic for enteric fever
- **IgM dengue –** was considered diagnostic for dengue fever

- **IgM for leptospirosis or MAT –** was considered diagnostic for leptospirosis
- **ELISA/Western blot –** was taken as positive for HIV
- patients in whom the diagnosis could not be made even after all the above mentioned investigations were categorised as having unspecified viral fever.

Once the specific diagnosis was reached, patients were treated specifically and symptomatically. Data was collected by using pre-tested proforma meeting the objectives of the study. The data collected would be transferred in to a Master Chart, which was then subjected for statistical analysis.

Data collection:

The data of each patient was collected on a proforma specially designed for this study and which includes demographic details, clinical features, past medical history, clinical and Lab values which was analysed for statistical significance and correlation.

STATISTICAL ANALYSIS

Data was entered in Windows Excel format. Frequency tables and measures of central tendency (mean) and measures of dispersion (Standard Deviation) were calculated by using the statistical package SPSS- 20

OBSERVATION AND RESULTS

1.DISTRIBUTION OF THE PLATELET COUNT IN THE STUDY POPULATION

PLATELET COUNT	FREQUENCY	PERCENT
< 20000	3	3.0
20001-50000	10	10.0
50001-100000	54	54.0
100001-150000	33	33.0

Table 1. showing the distribution of platelet count in the study population

Among the 100 patients in the study group, the maximum number of patients (54%) had a platelet count between 50,000 to 100000.

Platelet count less than 20000 were found in only three patients.

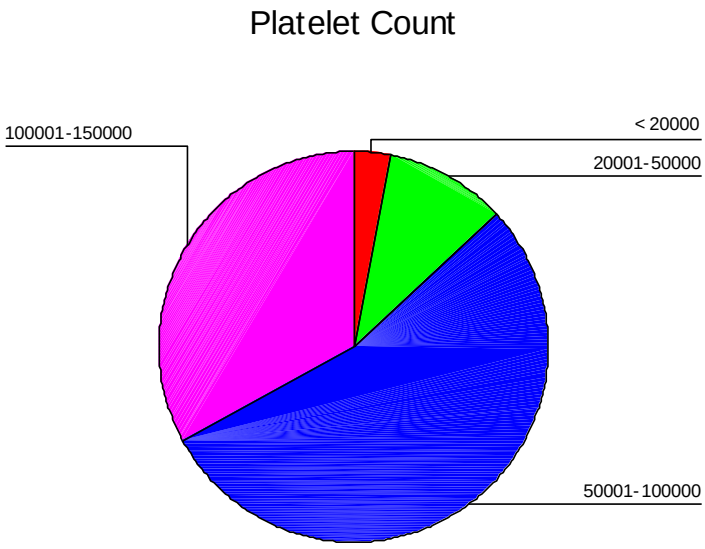


Fig.1. A pie diagram showing the distribution of platelet count in the study population

2.DISTRIBUTION OF THE STUDY POPULATION ACCORDING TO DIAGNOSIS AND PLATELET COUNT

DIAGNOSIS		PLATELET COUNT				TOTAL
		< 20000	20001-50000	50001-100000	100001-150000	
Malaria	Count	1	4	24	13	42
	% within Diagnosis	2.4%	9.5%	57.1%	31.0%	100.0%
Dengue	Count	1	3	14	9	27
	% within Diagnosis	3.7%	11.1%	51.9%	33.3%	100.0%
Typhoid	Count	0	0	5	1	6
	% within Diagnosis	.0%	.0%	83.3%	16.7%	100.0%
Leptospirosis	Count	0	0	2	3	5
	% within Diagnosis	.0%	.0%	40.0%	60.0%	100.0%
Sepsis	Count	0	2	1	0	3
	% within Diagnosis	.0%	66.7%	33.3%	.0%	100.0%
Unspecified viral fever	Count	0	1	8	7	16
	% within Diagnosis	.0%	6.3%	50.0%	43.8%	100.0%
HIV	Count	1	0	0	0	1
	% within Diagnosis	100.0%	.0%	.0%	.0%	100.0%

Table 2. showing the distribution of study population according to diagnosis and platelet count

Out of 100 patients, a definitive diagnosis was made in 84 patients.

Among them, the leading cause of febrile thrombocytopenia in this study was **MALARIA** (42 cases).

The second most common cause was **DENGUE FEVER** accounting for 27 cases.

It was followed by

UNSPECIFIED VIRAL FEVER (16 cases),
TYPHOID (6 cases),
LEPTOSPIROSIS (5 cases),
SEPSIS (3 cases), and
HIV (1 case) in that order.

Only three patients were having platelet counts less than 20,000 in this study. They were caused by malaria, dengue fever and HIV each.

The maximal frequency of platelet count in malaria, dengue, typhoid, sepsis and unspecified viral fever were in the range of **50000-100000 /cumm**.

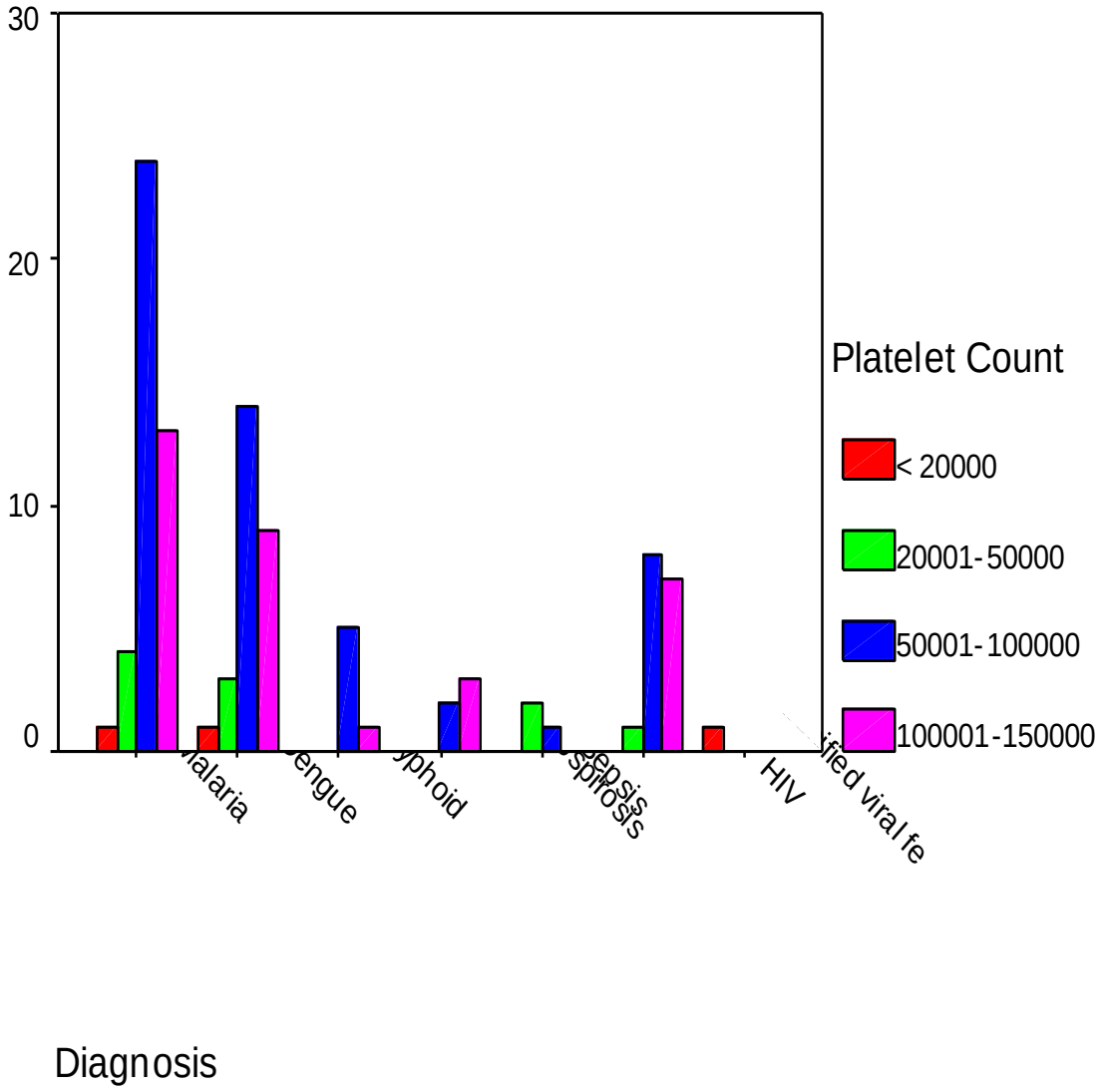


Fig. 2. showing the distribution of study population according to diagnosis and platelet count

3.DISTRIBUTION OF THE STUDY POPULATION ACCORDING TO THE BLEEDING MANIFESTATION

DIAGNOSIS		BLEEDING MANIFESTATION		TOTAL
		Yes	No	
Malaria	Count	5	37	42
	% within Diagnosis	11.9%	88.1%	100.0%
Dengue	Count	1	26	27
	% within Diagnosis	3.7%	96.3%	100.0%
Typhoid	Count	0	6	6
	% within Diagnosis	0%	100.0%	100.0%
Leptospirosis	Count	1	4	5
	% within Diagnosis	20.0%	80.0%	100.0%
Sepsis	Count	2	1	3
	% within Diagnosis	66.7%	33.3%	100.0%
Unspecified viral fever	Count	2	14	16
	% within Diagnosis	12.5%	87.5%	100.0%
HIV	Count	0	1	1
	% within Diagnosis	.0%	100.0%	100.0%
Total	Count	11	89	100
	% within Diagnosis	11.0%	89.0%	100.0%

Table 3. showing the distribution of study population according to bleeding manifestation

A total number of 11 patients had various bleeding manifestations out of the 100 study population.

5 out of 42 patients with malaria had shown bleeding manifestation (11.9%)

1 out of 27 patients with dengue fever had shown bleeding manifestation (3.7%)

2 out of 3 patients with sepsis had bleeding manifestations (66.7%)

1 out of 5 patients with leptospirosis had bleeding manifestation (20%)

In the unspecified viral fever group, 2 out of 16 patients had bleeding manifestation (12.5%)

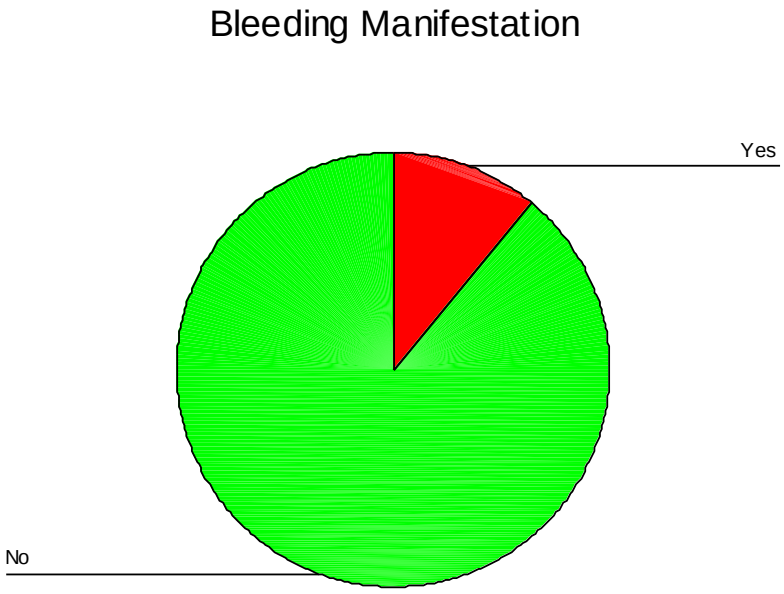


Fig.3.1. showing the distribution of study population according to bleeding manifestation

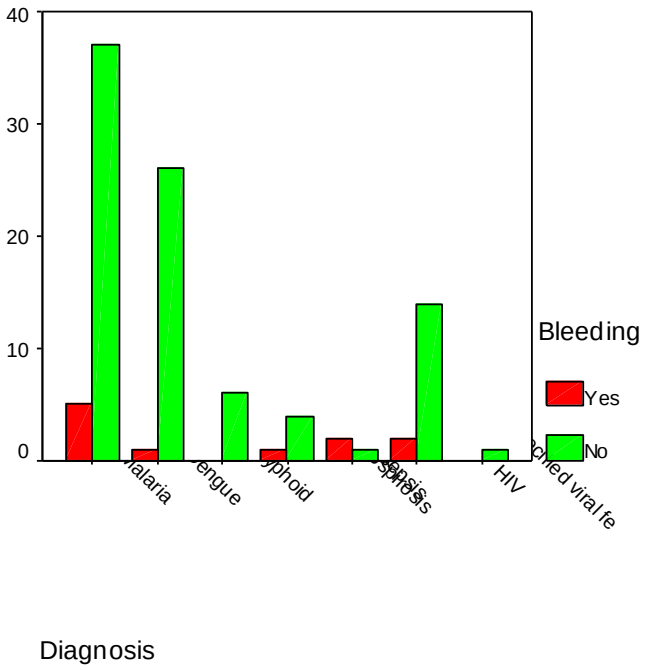


Fig.3.2. showing the distribution of study population according to bleeding manifestation

4.AGEWISE DISTRIBUTION OF STUDY POPULATION

DIAGNOSIS	AGE GROUP IN YEARS				TOTAL
	< 20	21-39	40-59	> 60	
Malaria	8	15	12	7	42
Dengue	2	13	11	1	27
Typhoid	3	3	0	0	6
Leptospirosis	2	1	1	1	5
Sepsis	0	0	3	0	3
Unspecified viral fever	3	5	4	4	16
HIV	0	0	0	1	1
Total	18	37	31	14	100

Table 4. showing age wise distribution of study population

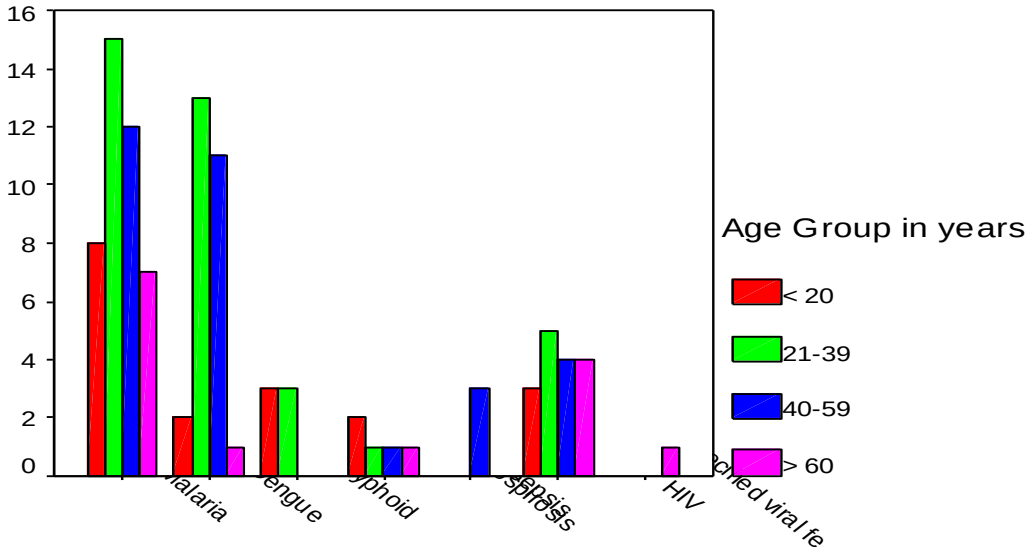


Fig. 4. showing age wise distribution of study population

5.DISTRIBUTION OF THE STUDY POPULATION ASSOCIATED WITH CHILLS AND RIGORS

DIAGNOSIS		CHILLS & RIGORS		TOTAL
		Yes	No	
Malaria	Count	32	10	42
	% within Diagnosis	76.2%	23.8%	100.0%
Dengu	Count	16	11	27
	% within Diagnosis	59.3%	40.7%	100.0%
Typhoid	Count	4	2	6
	% within Diagnosis	66.7%	33.3%	100.0%
Leptospirosis	Count	5	0	5
	% within Diagnosis	100.0%	.0%	100.0%
Sepsis	Count	0	3	3
	% within Diagnosis	.0%	100.0%	100.0%
Unspecified viral fever	Count	14	2	16
	% within Diagnosis	87.5%	12.5%	100.0%
HIV	Count	0	1	1
	% within Diagnosis	.0%	100.0%	100.0%
Total	Count	71	29	100
	% within Diagnosis	71.0%	29.0%	100.0%

Table 5. showing distribution of study population associated with chills and rigors

71 out of 100 patients had fever associated with chills and rigors.

32 out of this 71 patients were diagnosed with malaria.

16 patients with dengue fever, 4 patients with typhoid fever, 5 patients with leptospirosis and 14 patients with unspecified viral fever were having fever associated with chills and rigors.

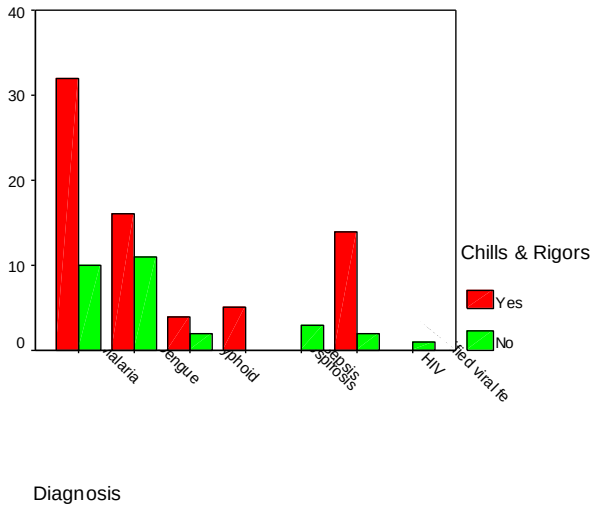


Fig.5. showing distribution of study population associated with chills and rigors

6.DISTRIBUTION OF THE STUDY POPULATION ASSOCIATED WITH HEADACHE

DIAGNOSIS		HEADACHE		TOTAL
		Yes	No	
Malaria	Count	29	13	42
	% within Diagnosis	69.0%	31.0%	100.0%
Dengue	Count	15	12	27
	% within Diagnosis	55.6%	44.4%	100.0%
Typhoid	Count	4	2	6
	% within Diagnosis	66.7%	33.3%	100.0%
Leptospirosis	Count	4	1	5
	% within Diagnosis	80.0%	20.0%	100.0%
Sepsis	Count	3	0	3
	% within Diagnosis	100.0%	.0%	100.0%
Unspecified viral fever	Count	14	2	16
	% within Diagnosis	87.5%	12.5%	100.0%
HIV	Count	1	0	1
	% within Diagnosis	100.0%	.0%	100.0%
Total	Count	70	30	100
	% within Diagnosis	70.0%	30.0%	100.0%

Table 6. showing distribution of study population associated with headache

70 out of 100 patients had fever associated with headache.

29 out of this 70 patients were diagnosed with malaria.

15 patients with dengue fever, 4 patients with typhoid fever, 4 patients with leptospirosis, 3 patients with sepsis and 14 patients with unspecified viral fever were having fever associated with headache.

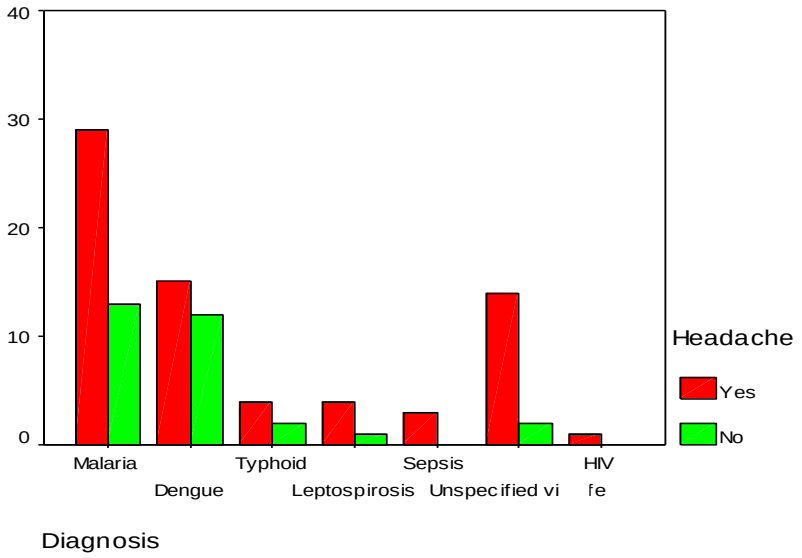


Fig.6. showing distribution of study population associated with headache

7.DISTRIBUTION OF THE STUDY POPULATION ASSOCIATED WITH GENERAL EXAMINATION FINDINGS

DIAGNOSIS		GENERAL EXAMINATION			TOTAL
		NORMAL	ANEMIA	JAUNDICE	
Malaria	Count	34	4	4	42
	% within Diagnosis	81.0%	9.5%	9.5%	100.0%
Dengue	Count	25	2	0	27
	% within Diagnosis	92.6%	7.4%	.0%	100.0%
Typhoid	Count	5	1	0	6
	% within Diagnosis	83.3%	16.7%	.0%	100.0%
Leptospirosis	Count	2	0	3	5
	% within Diagnosis	40.0%	.0%	60.0%	100.0%
Sepsis	Count	0	1	2	3
	% within Diagnosis	.0%	33.3%	66.7%	100.0%
Unspecified viral fever	Count	13	3	0	16
	% within Diagnosis	81.3%	18.8%	.0%	100.0%
HIV	Count	0	1	0	1
	% within Diagnosis	.0%	100.0%	.0%	100.0%
Total	Count	79	12	9	100
	% within Diagnosis	79.0%	12.0%	9.0%	100.0%

Table 7. showing distribution of study population associated with general examination findings

12 % of the total patients had anemia and 9% of them had jaundice overall.

4 out of 42 patients with malaria had anemia and jaundice on examination (9.5%).

2 out of 27 patients with dengue fever were found to be anemic (7.4%). None had jaundice.

33% of patients with sepsis had anemia and 67 % had jaundice.

8.DISTRIBUTION OF THE STUDY POPULATION ASSOCIATED WITH JOINTPAIN

DIAGNOSIS		JOINT PAIN		TOTAL
		Yes	No	
Malaria	Count	8	34	42
	% within Diagnosis	19.0%	81.0%	100.0%
Dengue	Count	19	8	27
	% within Diagnosis	70.4%	29.6%	100.0%
Typhoid	Count	0	6	6
	% within Diagnosis	.0%	100.0%	100.0%
Leptospirosis	Count	1	4	5
	% within Diagnosis	20.0%	80.0%	100.0%
Sepsis	Count	0	3	3
	% within Diagnosis	.0%	100.0%	100.0%
Unspecified viral fever	Count	10	6	16
	% within Diagnosis	62.5%	37.5%	100.0%
HIV	Count	0	1	1
	% within Diagnosis	.0%	100.0%	100.0%
Total	Count	38	62	100
	% within Diagnosis	38.0%	62.0%	100.0%

Table 8. showing distribution of study population associated with joint pain

38% of the total study population presented with joint pain.

19 % of patients with malaria had joint pain whereas 70.4% of patients with dengue fever had joint pain.

62.5% of patients with unspecified viral fever had joint pain.

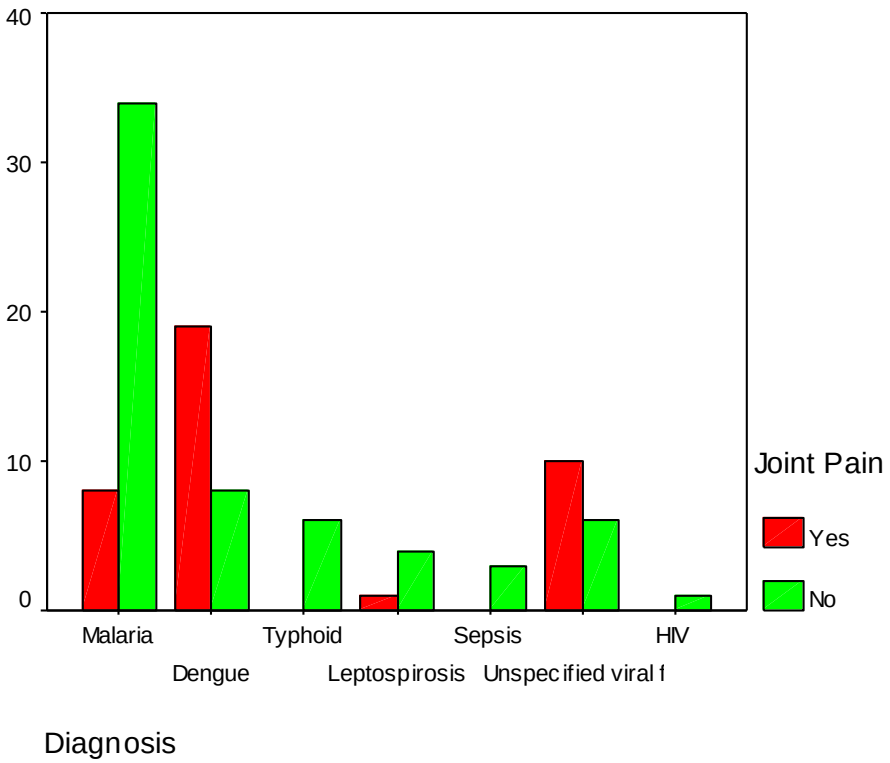


Fig. 8. showing distribution of study population associated with joint pain

9.DISTRIBUTION OF THE STUDY POPULATION ASSOCIATED WITH NAUSEA AND VOMITING

DIAGNOSIS		NAUSEA,VOMIT		TOTAL
		Yes	No	
Malaria	Count	27	15	42
	% within Diagnosis	64.3%	35.7%	100.0%
Dengue	Count	11	16	27
	% within Diagnosis	40.7%	59.3%	100.0%
Typhoid	Count	3	3	6
	% within Diagnosis	50.0%	50.0%	100.0%
Leptospirosis	Count	4	1	5
	% within Diagnosis	80.0%	20.0%	100.0%
Sepsis	Count	3	0	3
	% within Diagnosis	100.0%	.0%	100.0%
Unspecified viral fever	Count	6	10	16
	% within Diagnosis	37.5%	62.5%	100.0%
HIV	Count	0	1	1
	% within Diagnosis	.0%	100.0%	100.0%
Total	Count	54	46	100
	% within Diagnosis	54.0%	46.0%	100.0%

Table 9. showing distribution of study population associated with nausea and vomiting

54 out of 100 patients had nausea and vomiting as one of the complaint in presenting illness.

27 patients with malaria and 11 patients with dengue fever had nausea and vomiting.

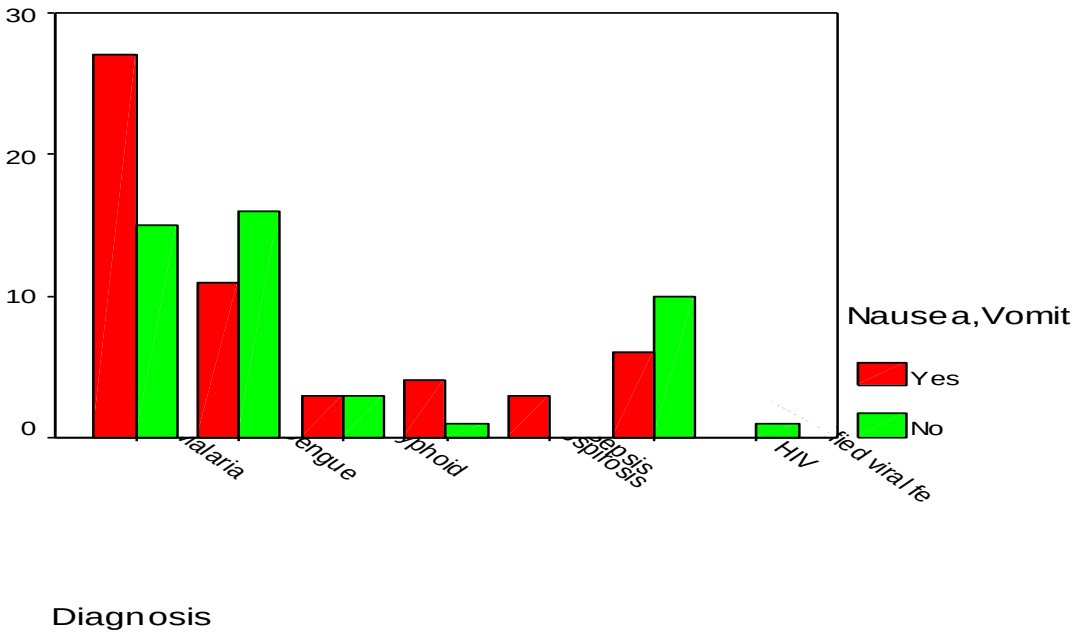


Fig. 9. showing distribution of study population associated with nausea and vomiting

10.DISTRIBUTION OF THE STUDY POPULATION ASSOCIATED WITH ALTERED SENSORIUM

DIAGNOSIS		ALTERED SENSORIUM		TOTAL
		Yes	No	
Malaria	Count	3	39	42
	% within Diagnosis	7.1%	92.9%	100.0%
Dengue	Count	1	26	27
	% within Diagnosis	3.7%	96.3%	100.0%
Typhoid	Count	0	6	6
	% within Diagnosis	.0%	100.0%	100.0%
Leptospirosis	Count	0	5	5
	% within Diagnosis	.0%	100.0%	100.0%
Sepsis	Count	2	1	3
	% within Diagnosis	66.7%	33.3%	100.0%
Unspecified viral fever	Count	2	14	16
	% within Diagnosis	12.5%	87.5%	100.0%
HIV	Count	0	1	1
	% within Diagnosis	.0%	100.0%	100.0%
Total	Count	8	92	100
	% within Diagnosis	8.0%	92.0%	100.0%

Table 10. showing distribution of study population associated with altered sensorium

8 of the patients presented with altered sensorium in the study group.

Out of which 3 of them had malaria, 2 had septicemia, 2 had unspecified viral fever and 1 was diagnosed with dengue fever.

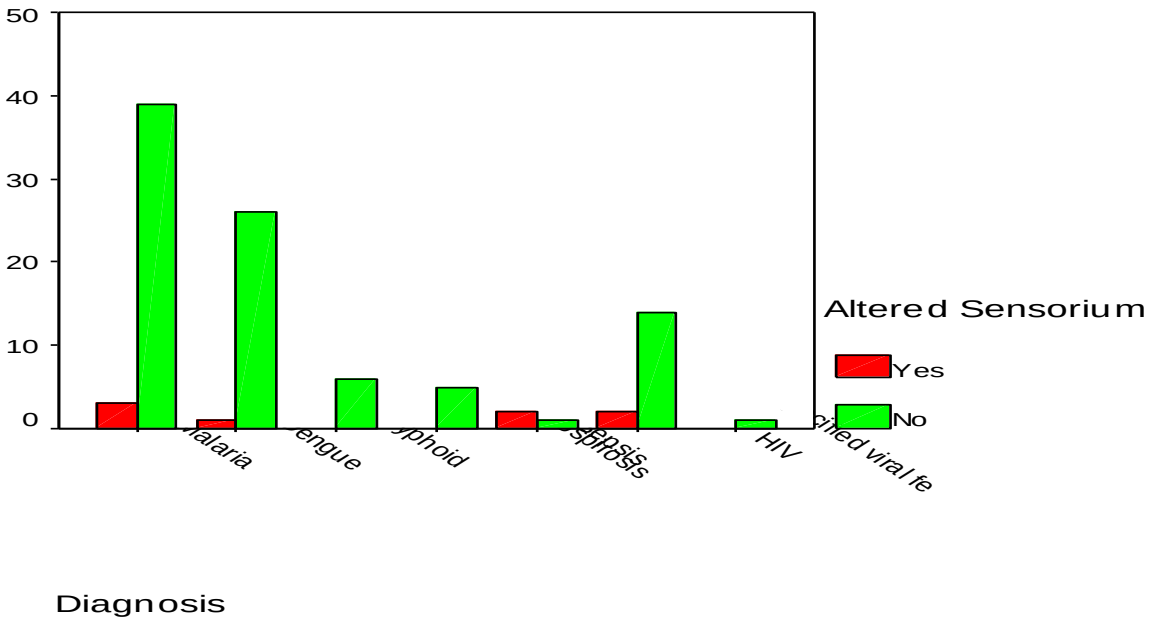


Fig. 10. showing distribution of study population associated with altered sensorium

11.DISTRIBUTION OF THE STUDY POPULATION ASSOCIATED WITH HEPATOMEGALY AND SPLENOMEGALY

DIAGNOSIS		HEPATOMEGALY		TOTAL
		Yes	No	
Malaria	Count	12	30	42
	% within Diagnosis	28.6%	71.4%	100.0%
Dengue	Count	1	26	27
	% within Diagnosis	3.7%	96.3%	100.0%
Typhoid	Count	4	2	6
	% within Diagnosis	66.7%	33.3%	100.0%
Leptospirosis	Count	5	0	5
	% within Diagnosis	100.0%	.0%	100.0%
Sepsis	Count	1	2	3
	% within Diagnosis	33.3%	66.7%	100.0%
Unspecified viral fever	Count	2	14	16
	% within Diagnosis	12.5%	87.5%	100.0%
HIV	Count	1	0	1
	% within Diagnosis	100.0%	.0%	100.0%
Total	Count	26	74	100
	% within Diagnosis	26.0%	74.0%	100.0%

Table 11. showing distribution of study population associated with hepatomegaly

26 patients in the total study group had hepatomegaly.

Out of 26 patients with hepatomegaly, 12 pateints had malaria, 5 patients had leptospirosis, 4 patients had typhoid fever, 2 patients had unspecified viral fever, 1 patient had dengue fever and 1 had HIV infection.

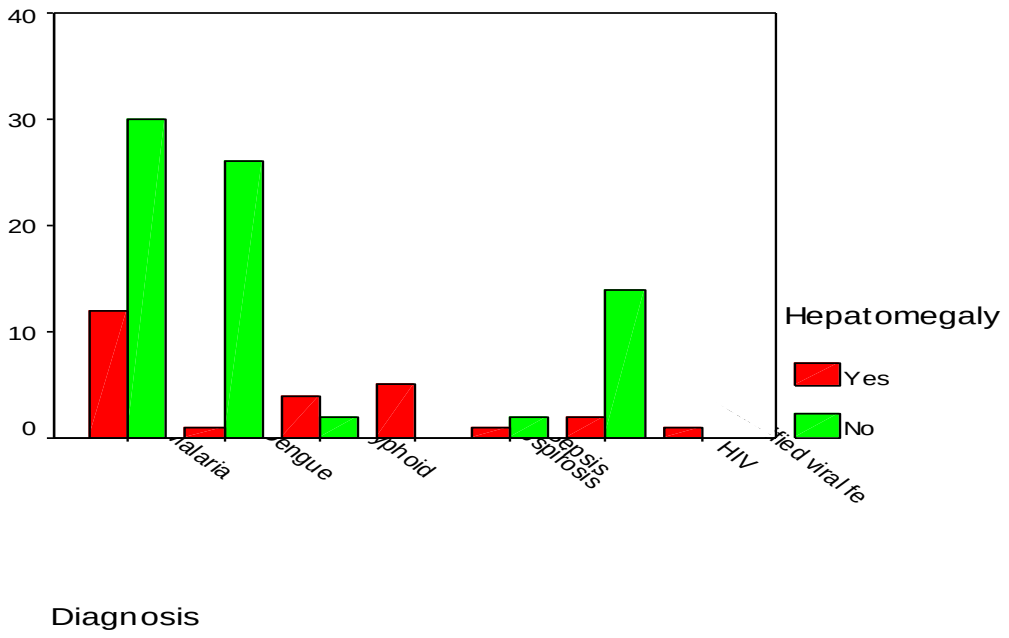


Fig. 11. showing distribution of study population associated with hepatomegaly

45 out of 100 study population had splenomegaly.

29 out of 49 patients with splenomegaly had malaria.

4 patients with typhoid fever and 4 patients with leptospirosis had leptospirosis.

12.DISTRIBUTION OF THE STUDY POPULATION ASSOCIATED WITH ASCITES

DIAGNOSIS		ASCITES		TOTAL
		Yes	No	
Malaria	Count	3	39	42
	% within Diagnosis	7.1%	92.9%	100.0%
Dengue	Count	0	27	27
	% within Diagnosis	.0%	100.0%	100.0%
Typhoid	Count	0	6	6
	% within Diagnosis	.0%	100.0%	100.0%
Leptospirosis	Count	2	3	5
	% within Diagnosis	40.0%	60.0%	100.0%
Sepsis	Count	2	1	3
	% within Diagnosis	66.7%	33.3%	100.0%
Unspecified viral fever	Count	0	16	16
	% within Diagnosis	.0%	100.0%	100.0%
HIV	Count	0	1	1
	% within Diagnosis	.0%	100.0%	100.0%
Total	Count	7	93	100
	% within Diagnosis	7.0%	93.0%	100.0%

Table 12. showing distribution of study population associated with ascites

7 patients in the study group had ascites. Out of which 3 patients had malaria, 2 had leptospirosis and 2 had sepsis as their etiology.

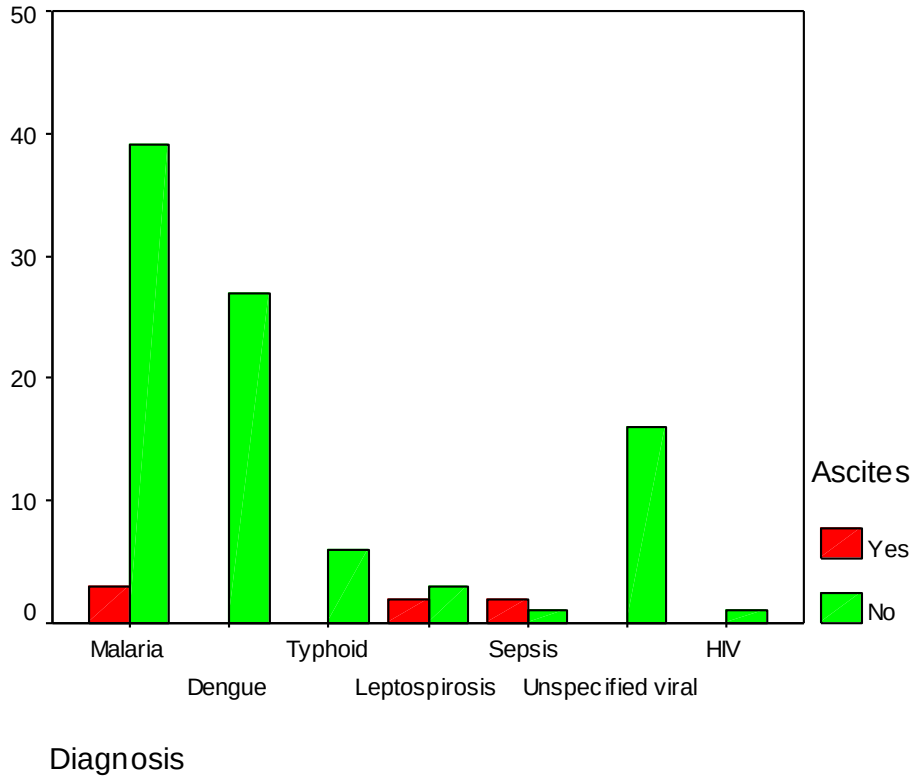


Fig. 12. showing distribution of study population associated with ascites

13 .DISTRIBUTION OF THE STUDY POPULATION ASSOCIATED WITH ANEMIA

DIAGNOSIS		HB (G%)		TOTAL
		<= 10	> 10	
Malaria	Count	11	31	42
	% within Diagnosis	26.2%	73.8%	100.0%
Dengue	Count	6	21	27
	% within Diagnosis	22.2%	77.8%	100.0%
Typhoid	Count	1	5	6
	% within Diagnosis	16.7%	83.3%	100.0%
Leptospirosis	Count	3	2	5
	% within Diagnosis	60.0%	40.0%	100.0%
Sepsis	Count	2	1	3
	% within Diagnosis	66.7%	33.3%	100.0%
Unspecified viral fever	Count	4	12	16
	% within Diagnosis	25.0%	75.0%	100.0%
HIV	Count	1	0	1
	% within Diagnosis	100.0%	.0%	100.0%
Total	Count	28	72	100
	% within Diagnosis	28.0%	72.0%	100.0%

Table 13. showing distribution of study population associated with anemia

28 patients out of the entire study group presented with anemia.

Out of the 28 people, 11 had malaria as their diagnosis

6 patients with dengue fever presented with anemia.

4 patients with unspecified viral fever, 3 patients with leptospirosis, 2 patients with sepsis, 1 patient with HIV and 1 patient with typhoid presented with anemia.

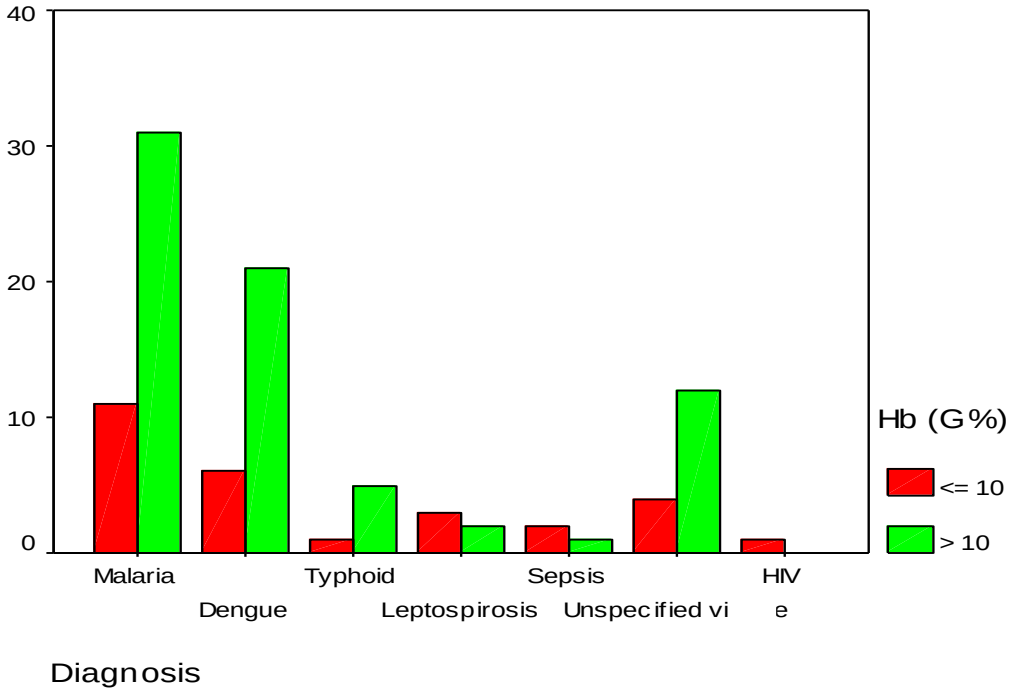


Fig. 13. showing distribution of study population associated with anemia

14 .DISTRIBUTION OF THE STUDY POPULATION ASSOCIATED WITH LEUKOCYTOSIS

DIAGNOSIS		TLC		TOTAL
		< 11000	> 11000	
Malaria	Count	35	7	42
	% within Diagnosis	83.3%	16.7%	100.0%
Dengue	Count	27	0	27
	% within Diagnosis	100.0%	.0%	100.0%
Typhoid	Count	3	3	6
	% within Diagnosis	50.0%	50.0%	100.0%
Leptospirosis	Count	2	3	5
	% within Diagnosis	40.0%	60.0%	100.0%
Sepsis	Count	0	3	3
	% within Diagnosis	.0%	100.0%	100.0%
Unspecified viral fever	Count	15	1	16
	% within Diagnosis	93.8%	6.3%	100.0%
HIV	Count	1	0	1
	% within Diagnosis	100.0%	.0%	100.0%
Total	Count	83	17	100
	% within Diagnosis	83.0%	17.0%	100.0%

Table 14. showing distribution of study population associated with leukocytosis

17 patients out of study population had leukocytosis in this study.

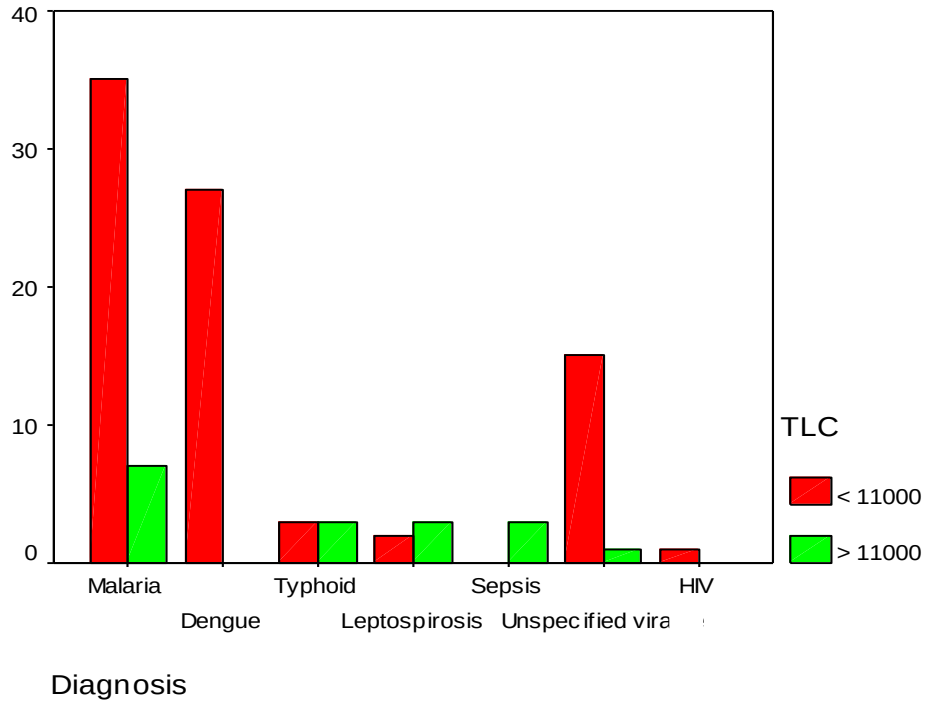


Fig .14.. showing distribution of study population associated with leukocytosis

15 .DISTRIBUTION OF THE STUDY POPULATION ASSOCIATED WITH ELEVATED CREATININE

DIAGNOSIS		CREATININE(MG/DL)		TOTAL
		< 1	> 1	
Malaria	Count	38	4	42
	% within Diagnosis	90.5%	9.5%	100.0%
Dengue	Count	27	0	27
	% within Diagnosis	100.0%	.0%	100.0%
Typhoid	Count	5	1	6
	% within Diagnosis	83.3%	16.7%	100.0%
Leptospirosis	Count	4	1	5
	% within Diagnosis	80.0%	20.0%	100.0%
Sepsis	Count	0	3	3
	% within Diagnosis	.0%	100.0%	100.0%
Unspecified viral fever	Count	15	1	16
	% within Diagnosis	93.8%	6.3%	100.0%
HIV	Count	1	0	1
	% within Diagnosis	100.0%	.0%	100.0%
Total	Count	90	10	100
	% within Diagnosis	90.0%	10.0%	100.0%

Table 15. showing distribution of study population associated with elevated creatinine

10 patients out of the entire study group had elevated creatinine.

Malaria accounted for 4 of the cases.

Elevated creatinine was found in 3 patients with sepsis. 1 patient of typhoid fever, leptospirosis and unspecified viral fever had elevated creatinine each.

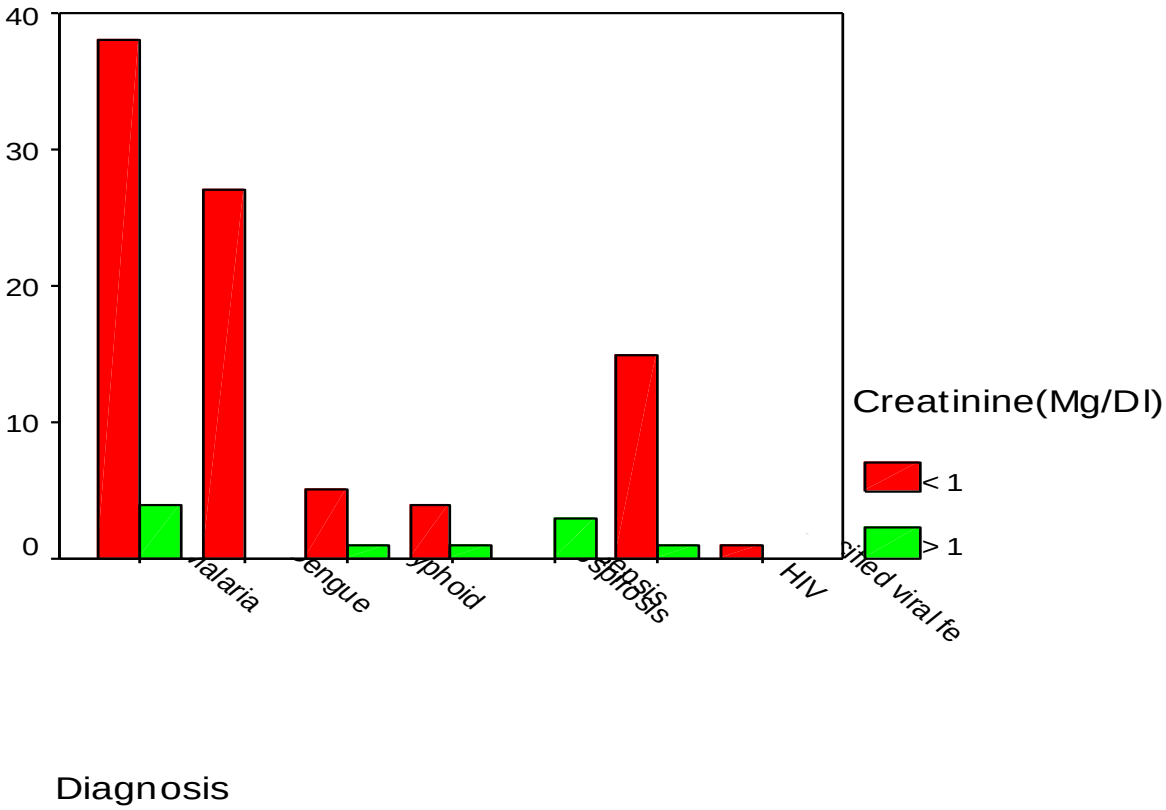


Fig. 15. showing distribution of study population associated with elevated creatinine

16 .DISTRIBUTION OF THE STUDY POPULATION ASSOCIATED WITH HYPERBILIRUBINEMIA

DIAGNOSIS		SERUM BILIRUBIN(MG/DL)		TOTAL
		< 1	> 1	
Malaria	Count	38	4	42
	% within Diagnosis	90.5%	9.5%	100.0%
Dengue	Count	27	0	27
	% within Diagnosis	100.0%	.0%	100.0%
Typhoid	Count	5	1	6
	% within Diagnosis	83.3%	16.7%	100.0%
Leptospirosis	Count	3	2	5
	% within Diagnosis	60.0%	40.0%	100.0%
Sepsis	Count	0	3	3
	% within Diagnosis	.0%	100.0%	100.0%
Unspecified viral fever	Count	16	0	16
	% within Diagnosis	100.0%	.0%	100.0%
HIV	Count	1	0	1
	% within Diagnosis	100.0%	.0%	100.0%
Total	Count	90	10	100
	% within Diagnosis	90.0%	10.0%	100.0%

Table 16. showing distribution of study population associated with serum bilirubin

10 patients out of the entire study population presented with jaundice.

Out of the 10 patients having jaundice, 4 were diagnosed as having malaria, 3 were diagnosed as having sepsis.

2 patients with leptospirosis had presented with jaundice and 1 patient with typhoid fever had jaundice.

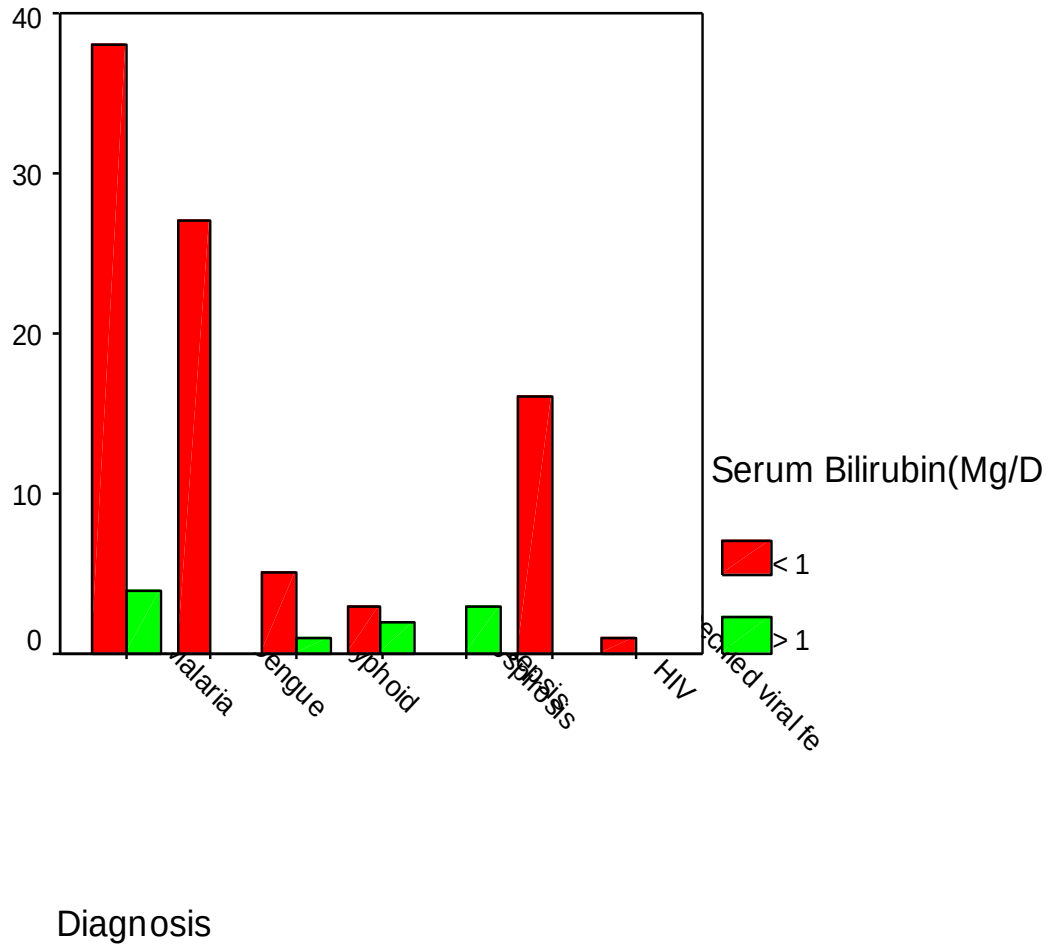


Fig.16. showing distribution of study population associated with serum bilirubin

17 .DISTRIBUTION OF THE STUDY POPULATION ASSOCIATED WITH ELEVATED ALT LEVELS

DIAGNOSIS		ALT (IU/L)		TOTAL
		< 40	> 40	
Malaria	Count	33	9	42
	% within Diagnosis	78.6%	21.4%	100.0%
Dengue	Count	24	3	27
	% within Diagnosis	88.9%	11.1%	100.0%
Typhoid	Count	3	3	6
	% within Diagnosis	50.0%	50.0%	100.0%
Leptospirosis	Count	3	2	5
	% within Diagnosis	60.0%	40.0%	100.0%
Sepsis	Count	0	3	3
	% within Diagnosis	.0%	100.0%	100.0%
Unspecified viral fever	Count	14	2	16
	% within Diagnosis	87.5%	12.5%	100.0%
HIV	Count	0	1	1
	% within Alt (Iu/L)	.0%	4.3%	1.0%
Total	Count	77	23	100
	% within Diagnosis	77.0%	23.0%	100.0%

Table 17. showing distribution of study population associated with serum ALT

23 patients out of the study group had ALT > 40 IU/L.

9 patients with malaria and 3 patients with dengue, typhoid and sepsis each had elevated ALT.

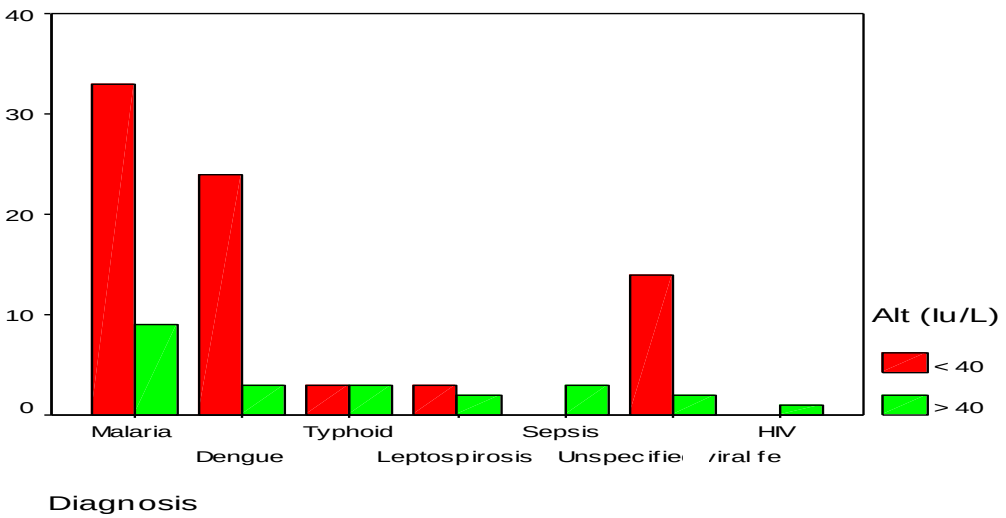


Table 17. showing distribution of study population associated with serum ALT

18 .DISTRIBUTION OF THE STUDY POPULATION ASSOCIATED WITH ELEVATED AST LEVELS

DIAGNOSIS		AST (IU/L)		TOTAL
		< 40	> 40	
Malaria	Count	33	9	42
	% within Diagnosis	78.6%	21.4%	100.0%
Dengue	Count	23	4	27
	% within Diagnosis	85.2%	14.8%	100.0%
Typhoid	Count	2	4	6
	% within Diagnosis	33.3%	66.7%	100.0%
Leptospirosis	Count	3	2	5
	% within Diagnosis	60.0%	40.0%	100.0%
Sepsis	Count	1	2	3
	% within Diagnosis	33.3%	66.7%	100.0%
Unspecified viral fever	Count	15	1	16
	% within Diagnosis	93.8%	6.3%	100.0%
HIV	Count	0	1	1
	% within Diagnosis	.0%	100.0%	100.0%
Total	Count	77	23	100
	% within Diagnosis	77.0%	23.0%	100.0%

Table 18. showing distribution of study population associated with serum AST

23 patients out of the study group had AST > 40 IU/L.

9 patients with malaria and 4 patients with dengue and typhoid each had elevated AST. 2 patients with leptospirosis and 2 patients with sepsis had AST >40IU/L.

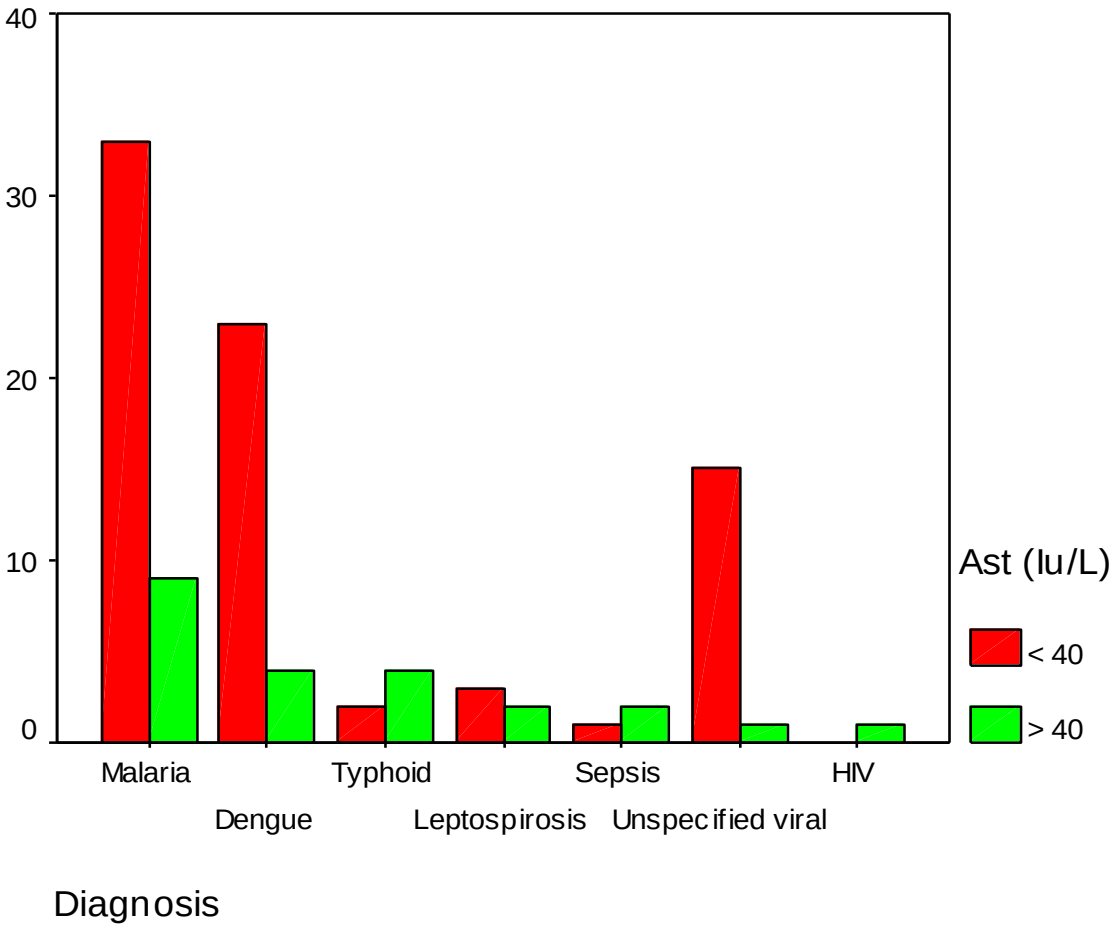


Fig. 18. showing distribution of study population associated with serum AST

19 .DISTRIBUTION OF THE STUDY POPULATION BASED ON THE REQUIREMENT OF BLOOD TRANSFUSION

DIAGNOSIS		BLOOD TRANSFUSION			TOTAL
		No transfusion	Fresh blood	Whole blood, platelets	
Malaria	Count	40	1	1	42
	% within Diagnosis	95.2%	2.4%	2.4%	100.0%
Dengue	Count	26	1	0	27
	% within Diagnosis	96.3%	3.7%	.0%	100.0%
Typhoid	Count	6	0	0	6
	% within Diagnosis	100.0%	.0%	.0%	100.0%
Leptospirosis	Count	3	2	0	5
	% within Diagnosis	60.0%	40.0%	.0%	100.0%
Sepsis	Count	0	2	1	3
	% within Diagnosis	.0%	66.7%	33.3%	100.0%
Unspecified viral fever	Count	15	1	0	16
	% within Diagnosis	93.8%	6.3%	.0%	100.0%
HIV	Count	1	0	0	1
	% within Diagnosis	100.0%	.0%	.0%	100.0%
Total	Count	91	7	2	100
	% within Diagnosis	91.0%	7.0%	2.0%	100.0%

Table 19. showing distribution of study population according to need for blood transfusion

A total of 9 patients had received transfusion of blood products.

7 patients had received fresh whole blood alone and 2 of them had been transfused both fresh whole blood and platelets.

The two patients who had received platelet transfusion were having sepsis and malaria.

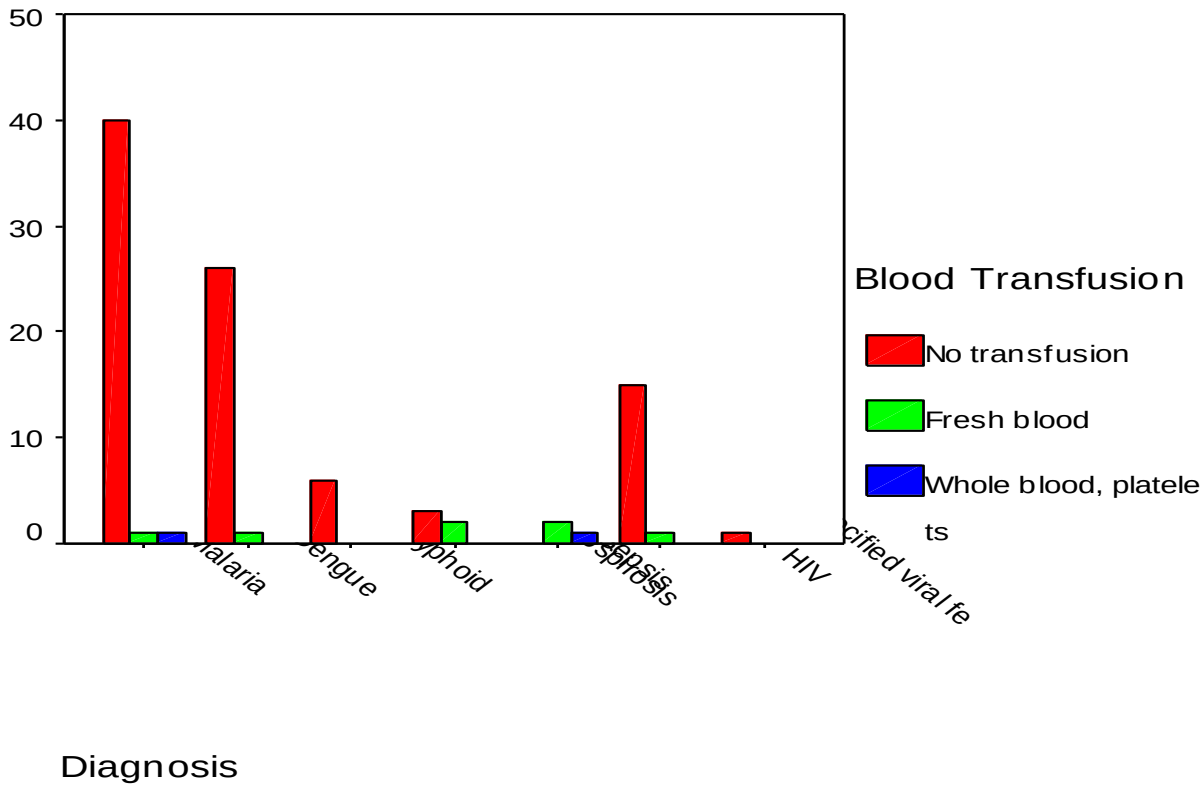


Fig. 19. showing distribution of study population according to need for blood transfusion

20. MEAN PLATELET COUNT IN THE STUDY POPULATION

	NO. OF CASES	MEAN PLATELET COUNT	STD. DEVIATION
Malaria	42	87928.57	29008.319
Dengue	27	85770.37	30635.460
Typhoid	6	91166.67	11617.516
Leptospirosis	5	112000.00	18694.919
Sepsis	3	49333.33	25006.666
Unspecified viral fever	16	101562.50	24668.384
HIV	1	8100.00	.

Table 20. showing distribution of study population with mean platelet count and etiology

The mean platelet count of patients with malaria was 87,929 ± 29,008 /cu.mm

The mean platelet count of patients with dengue was 85,770 ± 30635/cu.mm

The mean platelet count of patients with typhoid fever was 91167 ±11618/cu.mm

The mean platelet count of patients with leptospirosis was 112000 ± 18695/cu.mm

The mean platelet count of patients with sepsis was 49333 ± 25007/cu.mm

The mean platelet count of patients with unspecified viral fever was 101562 ± 24668/cu.mm

The mean platelet count of patients with HIV was 8100/cu.mm

21. DISTRIBUTION OF THE STUDY POPULATION BASED ON THE THE GENDER

	FREQUENCY	PERCENT
Male	59	59.0
Female	41	41.0
Total	100	100.0

Table 21. showing distribution of study population according to age

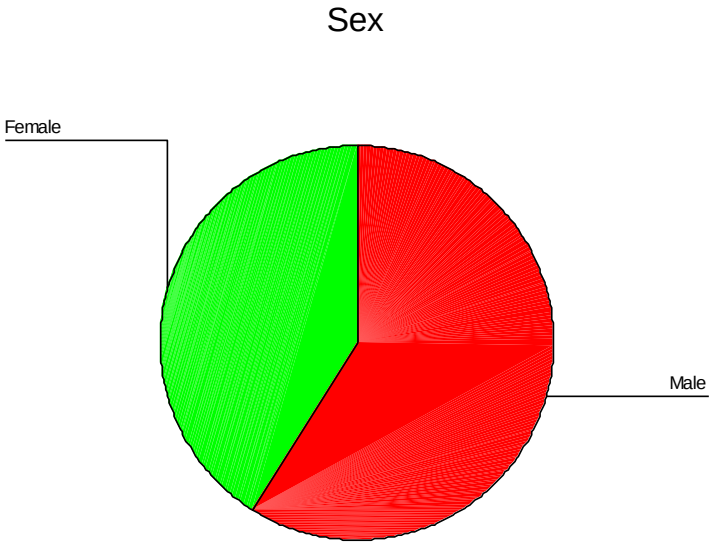


Fig. 21. showing distribution of study population according to age

22. DISTRIBUTION OF THE STUDY POPULATION BASED ON DEFINITE DIAGNOSIS

	FREQUENCY	PERCENT
Specified	84	84.0
Unspecified viral fever	16	16.0
Total	100	100.0

Table 22. showing distribution of study population based on definite diagnosis

A definitive diagnosis was made in 84 patients out of the 100 patients in the study group.

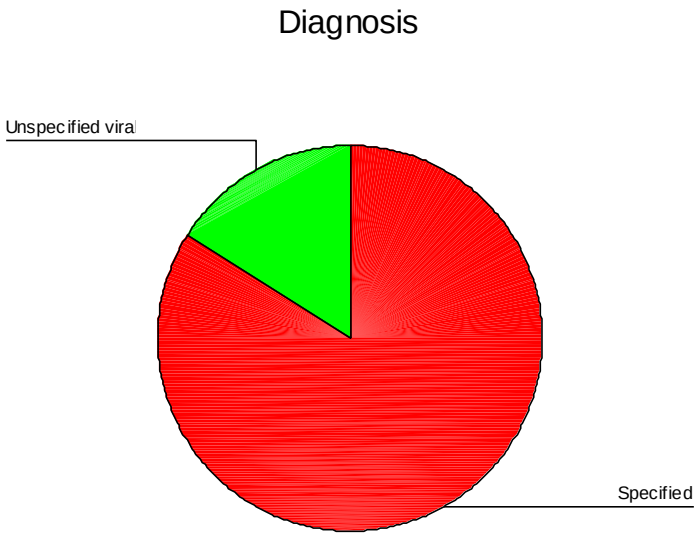


Fig. 22. showing distribution of study population based on definite diagnosis

23. DISTRIBUTION OF THE STUDY POPULATION BASED ON THE SPECIES OF MALARIAL PARASITE

	FREQUENCY	PERCENT
Total malaria		
Vivax	29	29.0
Falciparum	13	13.0

Table 23. showing distribution of study population based the species of malarial parasite

Out of 42 patients with malaria, 29 of them were plasmodium vivax positive and 13 of them were having plasmodium falciparum infection.

24. DISTRIBUTION OF THE STUDY POPULATION BASED ON THE MEAN PLATELET COUNT IN MALARIA

	N	MEAN	STD. DEVIATION
Vivax	28	92464.29	25611.748
Falciparum	14	75384.62	32745.327
Total	100	88969.00	29839.157

Table 24. showing distribution of study population based on the mean platelet count in malaria

The mean platelet count of patients with vivax malaria was 92,464 ± 25,612/cu.mm

The mean platelet count of patients with falciparum malaria was 75384 ± 32,745/cu.mm

25) DISTRIBUTION OF PATIENTS WITH BLEEDING MANIFESTATION

NO.	ETIOLOGY	PLATELET COUNT Cells/cumm
1	Malaria	46000
2	Sepsis	32000
3	Malaria	56000
4	Leptospirosis	88000
5	Unspecified viral fever	130000
6	Malaria	12000
7	Sepsis	38000
8	Dengue fever	42000
9	Unspecified viral fever	98000
10	Malaria	97000
11	Malaria	71000

Table 25. showing distribution of study population based on bleeding manifestation

Among patients who had bleeding manifestation (11 patients), 5 patients had malaria, 1 patient had dengue fever, 2 patients had sepsis, 1 patient had leptospirosis and 2 patients had unspecified viral fever.

26) DISTRIBUTION OF PATIENTS WITH PLATELETS <20,000/CU.MM

NO.	ETIOLOGY	PLATELET COUNT	BLEEDING
1	Malaria	12000	YES
2	Dengue	12800	NO
3	HIV	18000	NO

Table 26. showing distribution of patients with platelets <20,000/cumm

DISCUSSION

THE INDIAN STUDY:

This study was conducted by **Nair PS, Jain A, Khanduri U, Kumar V** in New Delhi for a period of one and half years. A total of 109 patients (76 males and 33 females) were admitted under Department of Medicine, St. Stephen's Hospital from March 2002 to June 2003 and having the criteria similar to our study.

In their study, Septicemia [29 pts (26.6 %)] was the leading cause of fever-associated thrombocytopenia. Second common cause was typhoid fever followed by dengue fever [16 pts (14.7 %)], megaloblastic anemia, malaria and hematological malignancy in that order. Out of 109 patients 45 patients had thrombocytopenic signs accounting for 41.3%. Out of 45 patients spontaneous bleeding was seen in 31 patients. Out of 109 patients 62 patients (56.8 %) had platelet count between 50000- 100000, followed by 28 patients (25.7%) had count between 20000 – 50000.

THE SRILANKAN STUDY :

A retrospective study and analysis of patients admitted to a general medical unit with fever and thrombocytopenia as the primary reason for admission to the University Medical Unit, National Hospital of Sri Lanka over a period of 2 months (May 1, 2009 to the June 30, 2009) was done by Shiyana Ibrahim et al.

Overall, 27% of patients had a platelet count below 50×10^{9}/L while three patients were found to have a count below 10×10^{9}/L on admission. The mean platelet count at admission was 85.52 (range, 6–150) $\times10^{9}$/L.

The lowest platelet count and highest hematocrit were seen on day 5. Bleeding manifestations were seen in 9(36%) of the 25 patients with a platelet count below 50×10^{9}/ L. Bleeding manifestations were significantly more likely with lower platelet counts ($P<0.008$).

However, there was no correlation between initial platelet counts and age, use of intravenous fluids, or length of hospital stay.

THE COMPARISION BETWEEN VARIOUS STUDIES

DISEASE CATEGORY	NAIR STUDY		PRESENT STUDY	
	NO. OF CASES	PERCENTAGE	NO. OF CASES	PERCENTAGE
Septicemia	29	26..6	3	3
Enteric fever	16	14.7	6	6
Dengue fever	15	13.8	27	27
Hematological conditions	17	15.6	-	-
Malaria	10	9.2	42	42
Others	20	18.3	22	22

In Nair's study, the leading cause for fever with thrombocytopenia was septicemia. In our study the leading cause of febrile thrombocytopenia was malaria. Septicemia accounted for only 3% of cases in our study.

In Nair's study, the 2nd leading cause for fever with thrombocytopenia was typhoid fever(among infections). In our study the 2nd leading cause of febrile thrombocytopenia was dengue fever. Typhoid fever accounted for only 6% of cases in our study.

Dengue fever accounted for 13.8% of cases in Nair's study wheras 27% of patients had dengue fever in our study. This could be due to seasonal and regional variations.

Patients in whom diagnosis could not be made was 20 patients (18.3%) in Nair's study whereas in our study it was 16 patients (16%).

BLEEDING MANIFESTATION	**NAIR STUDY**		**PRESENT STUDY**	
	NO. OF CASES	**PERCENTAGE**	**NO. OF CASES**	**PERCENTAGE**
Present	45	41.3	11	11
Absent	64	58.7	89	89

In Nair's study, 41.3% had presented with bleeding manifestations wheras in our study only 11% of patients had bleeding manifestations.

distribution of platelet count in thousands	**NAIR STUDY**		**PRESENT STUDY**	
	NO. OF CASES	**PERCENTAGE**	**NO. OF CASES**	**PERCENTAGE**
< 20000	19	17.5	3	3.0
20001-50000	28	25.7	10	10.0
50001-100000	62	56.8	54	54.0
100001-150000	-	-	33	33.0

In Nair's study 17.5 % of patients presented with platelet count less than 20000/cu.mm whereas in our study 3 patients had platelet count less than 20000/cu.mm.

In Nair's study 25.7 of patients presented with platelet count 20001-50000/cu.mm whereas in our study 10 patients had platelet count 20001-50000 /cu.mm.

In our study, a total of 9 patients had received transfusion of blood products. 7 patients had received fresh whole blood alone and 2 of them had been transfused both fresh whole blood and platelets.The two patients who had received platelet transfusion were having sepsis and malaria.

CONCLUSION

1) Infections are one of the most common causes of thrombocytopenia. The leading cause of fever with thrombocytopenia in our study was Malaria.

2) In malarial infection, the most common species was Plasmodium vivax followed by Plasmodium falciparum.

3) Dengue fever was the second commonest cause of febrile thrombocytopenia

4) There is no direct correlation between the severity of thrombocytopenia and the bleeding manifestation.

4) Bleeding manifestation was present only in 11% of patients in the study. So in majority of patients, the thrombocytopenia was transient and asymptomatic.

5) Prophylactic platelet transfusion may not be required in all cases of severe thrombocytopenia. It may be restricted to selected patients with bleeding manifestation or platelets <10,000/cumm which may indicate bone marrow compromise.

6) Most of the patients in our study did not require platelet or blood transfusion and the platelet count significantly increased after the treatment of the underlying infection.

BIBLIOGRAPHY

1) S. N. Wickramasinghe and S. H. Abdalla, "Blood and bone marrow changes in malaria," *Bailliere's Best Practice and Research in Clinical Haematology*, vol. 13, no. 2, pp. 277–299, 2000.

2) V. D'Acremont, P. Landry, I. Mueller, A. P´ecoud, and B. Genton, "Clinical and laboratory predictors of imported malaria in an outpatient setting: an aid to medical decision making in returning travelers with fever," *American Journal of Tropical Medicine and Hygiene*, vol. 66, no. 5, pp. 481–486, 2002.

3) Lathia TB, Joshi R 2004. Can hematological parameters discriminate malaria from nonmalarious acute febrile illness in the tropics? *Indian J Med Sci 58*: 239 244.

4)Patel U, Gandhi G, Friedman S, Niranjan S 2004. Thrombocytopenia in malaria. *J Natl Med Assoc 96*: 1212-1214.

5) Beale PJ, Cormack JD, Oldrey TB 1972. Thrombocytopenia in malaria with immunoglobulin (IgM) changes. *BMJ 1*: 345-349.

6) Kochar DK, Das A, Kochar A, Middha S, Acharya J, Tanwar GS, Gupta A, Pakalapati D, Garg S, Saxena V, Subudhi AK, Boopathi PA, Sirohi P, Kochar SK

2010. Thrombocytopenia in *Plasmodium falciparum*, *Plasmodium vivax* and mixed infection malaria: a study from Bikaner (Northwestern India). *Platelets 21*: 623-627.

7) Dennis LH, Eichelberger JW, Inman MM, Conrad ME 1967. Depletion of coagulation factors in drug-resistant *Plasmodium falciparum* malaria. *Blood 29*: 713-721.

8) Marques HO, Alexandre MAA, Oliveira VM, Marreira L, Lacerda MVG, Alecrim MGC, Morelli VM, Lourenço DM 2005. Hemostatic changes in patients with malaria. Annals of the XX Congress of the International Society on Thrombosis and Hemostasis, Sydney (Australia). *J Thromb Haemost 3* (Suppl. I): 1452.

9) Engwerda CR, Beattie L, Amante FH 2005. The importance of the spleen in malaria. *Trends Parasitol 21*: 75-80.

10) Skudowitz RB, Katz J, Lurie A, Levin J, Metz J 1973. Mechanisms of thrombocytopenia in malignant tertian malaria. *BMJ 2*: 515-518.

11) Menendez C, Fleming AF, Alonso PL 2000. Malaria-related anaemia. *Parasitol Today 16*: 469-476.

12) Beale PJ, Cormack JD, Oldrey TB 1972. Thrombocytopenia in malaria with immunoglobulin (IgM) changes. *BMJ 1*: 345-349.

13) Kreil A, Wenisch C, Brittenham G, Looareesuwan S, Peck-Radosavljevic M 2000. Thrombopoietin in *Plasmodium falciparum* malaria. *Br J Haematol 109*: 534-536.

14) Lacerda MVG 2007. *Manifestações clínicas e patogênese da plaquetopenia na malária*, PhD Thesis, Universidade de Brasília, 439 pp.

15) Maina RN, Walsh D, Gaddy C, Hongo G, Waitumbi J, Otieno L, Jones D, Ogutu BR 2010. Impact of *Plasmodium falciparum* infection on haematological parameters in children living in Western Kenya. *Malar J 9* (Suppl. 3): S4.

16) Kelton JG, Keystone J, Moore J, Denomme G, Tozman E, Glynn M, Neame PB, Gauldie J, Jensen J 1983. Immune-mediated thrombocytopenia of malaria. *J Clin Invest 71*: 832-836.

17) Lacerda MVG 2007. *Manifestações clínicas e patogênese da plaquetopenia na malária*, PhD Thesis, Universidade de Brasília, 439 pp.

18) Silva SBR 2009. *Avaliação da frequência e dos fatores associados à plaquetopenia causada pelo* Plasmodium vivax, MSc Thesis, Universidade Federal do Mato Grosso, 64 pp.

19) Essien EM, Ebhota MI 1981. Platelet hypersensitivity in acute malaria (*Plasmodium falciparum*) infection in man. *Thromb Haemost 46*: 547-549

20)Gerardin P, Rogier C, Ka AS, Jouvencel P, Brousse V, Imbert P 2002. Prognostic value of thrombocytopenia in African children with falciparum malaria. *Am J Trop Med Hyg 66*: 686-691.

21) Rogier C, Gerardin P, Imbert P 2004. Thrombocytopenia is predictive of lethality in severe childhood falciparum malaria. *Arch Dis Child 89*: 795-796.

22) Alexandre MA, Ferreira CO, Siqueira AM, Magalhaes BL, Mourao MPG, Lacerda MVG, Alecrim MGC 2010. Severe *Plasmodium vivax* malaria, Brazilian Amazon. *Emerg Infect Dis 16*: 1611-1614

23) Grynberg P, Fernandes Fontes CJ, Braga EM 2007. Association between particular polymorphic residues on apical membrane antigen 1 (AMA-1) and platelet levels in patients with vivax malaria. *Clin Microbiol Infect 13*: 1089-1094.

24) Silva SBR 2009. *Avaliação da frequência e dos fatores associados à plaquetopenia causada pelo* Plasmodium vivax, MSc Thesis, Universidade Federal do Mato Grosso, 64 pp.

25) Rebulla P 2001. Revisitation of the clinical indications for the transfusion of platelet concentrates. *Rev Clin Exp Hematol 5*: 288-310.

26) Lacerda MVG, Cavalcante TB, Silva AC, Macêdo VO 2006. Avaliação das indicações de transfusão de concentrado de plaquetas. Anais do XLII Congresso da

Sociedade Brasileira de Medicina Tropical, Teresina. *Rev Soc Bras Med Trop 39* (Suppl. I): 104.

27) Schlossberg HR, Herman JH 2003. Platelet dosing. *Transfus Apher Sci 28*: 221-226.

28) de Paula LV, Klafke A, Bordin R, Pereira JPM, Job FM 1993. Avaliação da eficácia das transfusões de concentrados de plaquetas nos Serviços de Hematologia e Hemoterapia do Hospital de Clínicas de Porto Alegre. *Bol Soc Bras Hematol Hemoter 15*: 9-13.

29) Franchini M 2005. Pathophysiology, diagnosis and treatment of disseminated intravascular coagulation: an update. *Clin Lab 51*: 633-639.

30) Blajchman MA 2003. Substitutes and alternatives to platelet transfusions in thrombocytopenic patients. *J Thromb Haemost 1*: 1637-1641.

31) Lacerda MV, Alexandre MA, Santos PD, Arcanjo AR, Alecrim WD, Alecrim MGC 2004. Idiopathic thrombocytopenic purpura due to vivax malaria in the Brazilian Amazon. *Acta Trop 90*: 187-190.

32) Lacerda MVG 2007. *Manifestações clínicas e patogênese da plaquetopenia na malária*, PhD Thesis, Universidade de Brasília, 439 pp.

33) Warrell DA, Looareesuwan S, Warrell MJ, Kasemsarn P, Intaraprasert R, Bunnag D, Harinasuta T 1982. Dexamethasone proves deleterious in cerebral malaria. A double-blind trial in 100 comatose patients. *N Engl J Med 306*: 313-319

34) Hoffman SL, Rustama D, Punjabi NH, Surampaet B, Sanjaya B, Dimpudus AJ, McKee KT, Jr., Paleologo FP, Campbell JR, Marwoto H 1988. High-dose dexamethasone in quinine-treated patients with cerebral malaria: a double-blind, placebo-controlled trial. *J Infect Dis 158*: 325-331.

35) Muniz-Junqueira MI, Silva FO, de Paula Júnior MR, Tosta CE 2005. Thalidomide influences the function of macrophages and increases the survival of *Plasmodium berghei*-infected CBA mice. *Acta Trop 94*: 128-138.

36) Mohanty S, Patel DK, Pati SS, Mishra SK 2006. Adjuvant therapy in cerebral malaria. *Indian J Med Res 124*: 245-260.

37) Muniz-Junqueira MI 2007. Immunomodulatory therapy associated to anti-parasite drugs as a way to prevent severe forms of malaria. *Curr Clin Pharmacol 2*: 59-73.

38) Onlamoon, N. et al. (2010) Dengue virus-induced hemorrhage in a nonhuman primate model. Blood 115, 1823–1834

39)Nakao, S. et al. (1989) Dengue virus, a flavivirus, propagates in human bone marrow progenitors and hematopoietic cell lines. Blood 74, 1235– 1240

40) Noisakran, S. et al. (2009) Detection ofdengue virus in platelets isolated from dengue patients. Southeast Asian J. Trop. Med. Public Health 40, 253–262

41) Saito, M. et al. (2004) Association of increased platelet-associated immunoglobulins with thrombocytopenia and the severity of disease in secondary dengue virus infections. Clin. Exp. Immunol. 138, 299–303

42) de Araujo, J.M. et al. (2009) A retrospective survey of dengue virus infection in fatal cases from an epidemic in Brazil. J. Virol. Methods 155, 34–38

43) La Russa, V.F. and Innis, B.L. (2008) Mechanisms of dengue virus-induced bone marrow suppression. Baillibres Clin. Haematol. 8, 249–270

44) Nakao, S. et al. (1989) Dengue virus, a flavivirus, propagates in human bone marrow progenitors and hematopoietic cell lines. Blood 74, 1235– 1240

45) Murgue, B. et al. (1997) Dengue virus inhibits human hematopoietic progenitor growth in vitro. J. Infect. Dis. 175, 1497–1501

46) Basu, A. et al. (2008) Dengue 2 virus inhibits in vitro megakaryocytic colony formation and induces apoptosis in thrombopoietin-inducible megakaryocytic differentiation from cord blood CD34+ cells. FEMS Immunol. Med. Microbiol. 53, 46–51

47) Rothwell, S.W. et al. (1996) Dengue-2 virus infection of human bone marrow: characterization of dengue-2 antigen-positive stromal cells. Am. J. Trop. Med. Hyg. 54, 503–510

48) La Russa, V.F. and Innis, B.L. (2008) Mechanisms of dengue virus-induced bone marrow suppression. Baillibres Clin. Haematol. 8, 249–270

49) Lin, C.F. et al. (2006) Autoimmune pathogenesis in dengue virus infection. Viral Immunol. 19, 127–132

50) Rothwell, S.W. et al. (1996) Dengue-2 virus infection of human bone marrow: characterization of dengue-2 antigen-positive stromal cells. Am. J. Trop. Med. Hyg. 54, 503–510

51) Lin, C.F. et al. (2001) Generation of IgM anti-platelet autoantibody in dengue patients. J. Med. Virol. 63, 143–149

52) Sun, D.S. et al. (2007) Antiplatelet autoantibodies elicited by dengue virus non-structural protein 1 cause thrombocytopenia and mortality in mice. J.Thromb. Haemost. 5, 2291–2299

53) Falconar, A.K. (2007) Antibody responses are generated to immunodominant ELK/KLE-type motifs on the nonstructural-1 glycoprotein during live dengue virus infections in mice and humans: implications for diagnosis, pathogenesis, and vaccine design. Clin. Vaccine Immunol. 14, 493–504

54) Saito, M. et al. (2004) Association of increased platelet-associated immunoglobulins with thrombocytopenia and the severity of disease in secondary dengue virus infections. Clin. Exp. Immunol. 138, 299–303

55) Suharti, C. et al. (2002) The role of cytokines in activation of coagulation and fibrinolysis in dengue shock syndrome. Thromb. Haemost. 87, 42–46

56) de Castro, R.A. et al. (2007) Thrombocytopenia associated with dengue hemorrhagic fever responds to intravenous administration of anti-D (Rh(0)-D) immune globulin. Am. J. Trop. Med. Hyg. 76, 737–742

57) Khosla SN, Anad A, Singh U. Hematological profile in Typhoid fever. Tropical Doctor 1995;25:156-8.

58) Joseph James, Tarun Kumar Dutta AND S. Jayanthi**.** Correlation of Clinical and Hematologic Profiles with Bone Marrow Responses in Typhoid Fever. Am. J. Trop. Med. Hyg 1997; 57: 313-6.

59) Henter JI, Arico M, Egeler RM et al. A treatment protocol for hemophagocytic lymphohistiocytosis. Med Peddiatr Oncol 1997; 28:342-7

60) Stephan F, Cheffi MA, Kaplan C, et al. Autoantibodies against platelet glycoproteins in critically ill patients with thrombocytopenia. *Am J Med*. 2000;108:554-560.

61) Baughman RP, Lower EE, Flessa HC, Tollerud DJ. Thrombocytopenia in the intensive care unit. *Chest*. 1993;104:1243-1247.

62). Stephan F, Hollande J, Richard O, Cheffi A, Maier-Redelsperger M, Flahault A. Thrombocytopenia in a surgical ICU. *Chest*. 1999;115:1363-1370.

63)Akca S, Haji-Michael P, de Mendonca A, Suter P, Levi M, Vincent JL. Time course of platelet counts in critically ill patients. *Crit Care Med*. 2002;30:753-756.

64) Low levels of protein C are associated with poor outcome in severe sepsis. *Chest*. 2001;120:915-922.

65). Brun-Buisson C, Doyon F, Carlet J, et al, French ICU Group for Severe Sepsis. Incidence, risk factors, and outcome of severe sepsis and septic shock in adults: a multicenter prospective study in intensive care units. *JAMA*. 1995;274:968-974.

66) Vanderschueren S, De Weerdt A, Malbrain M, et al. Thrombocytopenia and prognosis in intensive care. *Crit Care Med*. 2000;28: 1871-1876

67) Vanderschueren S, De Weerdt A, Malbrain M, et al. Thrombocytopenia and prognosis in intensive care. *Crit Care Med*. 2000;28: 1871-1876.

104. Martinez MA, Pena JM, Fernandez A, et al. Time course and prognostic significance of hemostatic changes in sepsis: relation to tumor necrosis factor-alpha. *Crit Care Med*. 1999;27:1303-1308.

68) Akca S, Haji-Michael P, de Mendonca A, Suter P, Levi M, Vincent JL. Time course of platelet counts in critically ill patients. *Crit Care Med*. 2002;30:753-756.

ABBREVIATIONS:

TNF – Tumor Necrosis Factor

IVIG – Intra Venous Immunoglobulin

ALT – Alanine aminotransferase

AST – Aspartate aminotransferase

QBC – Quantitative Buffy Coat

RBS –Random Blood Sugar

BT – Bleeding Time

P.Smear MP/MF – Peripheral smear for malarial parasite/microfilaria

PROFORMA

NAME :

AGE :

MARITAL STATUS :

DOA :

DOD :

Occupation :

CHIEF COMPLAINTS :

PRESENTING COMPLAINTS :

1. CHILLS & RIGORS	
2. MYALGIA	
3. RASHES	
4. JOINT PAIN/ 5. SWELLING	
6. ORAL ULCERS	
7. PETECHIAE,	
8. PURPURA	
9. ECCHYMOSES	
10. GUM BLEEDING	
11. EPISTAXIS	
12. HEMOPTYSIS	
13. HE1MATEMESIS	
14. HEMATURIA	
15. MALENA	
16. MENORRHAGIA	
17. VOMITING	
18. DIARRHEA	
19. COUGH	
20. BREATHLESSNESS	
21. PALPITATION,CHEST PAIN	
22. ABDOMINAL PAIN	
23. PERIODICITY OF FEVER	

24. CALF PAIN	
25. HEADACHE	
26. SEIZURES	
27. SORE THROAT	

PAST HISTORY :

1. MALARIA	
2. TYPHOID	
3. BLEEDING DISORDERS	
4. LIVER DISEASE	
5. DIABETES	
6. HYPERTENSION	
7. LIVER DISEASE	
8. TUBERCULOSIS	
9. DENGUE	
10.D YSLIPIDEMIA	

PERSONAL / DRUG HISTORY :

HISTORY	
ASPIRIN/CLOPIDOGREL	
SMOKERS	
ALCOHOLICS	

ON EXAMINATION:

EXAMINATION	
ANEMIA	
ICTERUS	
CYANOSIS	
CLUBBING	
PEDAL EDEMA	
LYMPHANEDOPATHY	
SUBCONJUNCTIVAL HEMORRHAGE	
PETECHIAE/PURPURA/ECCHYMOSIS	
EPISTAXIS/GUM BLEED	
ORAL ULCERS	
ARTHRALGIA/ ARTHRITIS	
RASH	
TACHYCARDIA	
BRADYCARDIA	
HYPERTENSION	
HYPOTENSION	
TACHYPNEA	
CVS INVOLVEMENT	
RS INVOLVEMENT	
CNS INVOLVEMENT	
HEPATOMEGALY	
SPLENOMEGALY	
ASCITES	
FUNDAL INVOLVEMENT	

INVESTIGATIONS :

DATE							DATE			
Blood Sugar							Hb			
Blood Urea							TC			
S. creatinine							DC			
Serum Na							ESR			
Serum K							PLATELETS			
Serum HCO3							BT,CT			
Serum Cl							Peri.smear			

DATE				DATE			DATE	
S.bilirubin				Urine sugar			S. Cholesterol	
Indirect bilirubin				Urine protein			S. TGL	
Direct bilirubin				Urine deposits			S.LDL	
TOTAL PROTEIN				Urine spot PCR			S.HDL	
ALT/AST				URINE C/S			BLOOD C/S	
SAP								
ALP								

DATE		DATE	
SMEAR - MP,MF		USG ABDOMEN	
WIDAL			
MSAT		CT	
LEPTOSPIROSIS IG			
HIV		XRAY	
Anti-HCV			

s.no	name	age	sex	duration of fever	chills & rigors	nausea,vomit	joint pain	headache	bleeding	altered sensorium	PICKLE	bleeding manifestation	splenomegaly	hepatomegaly	ascites	CVS	RS	CNS	Hb (g%)	TLC	platelet count	ESR	RBS (mg/dl)	urea(mg/dl)	creatinine(mg/dl)	serum bilirubin(mg/dl)	ALT/AST (IU/L)	s.albumin (g/dl)	BT	P.Smear MP/MF/QBC	Widal	IgM dengue	Igm lepto/MAT	HIV	Blood c/s	urine c/o	diagnosis	treatment	blood/platelet transfusion	platelet count at discharge
1	sameer	19	M	3	Y	N	N	N	N	N	N	N	N	N	N	normal	normal	normal	11	11300	96,000	22	112	18	0.9	1	194/88	4.2	-	vivax	-	-	-	-	-	-	malaria	chloroquine		1880000
2	arif	21	M	4	Y	N	N	N	N	N	N	N	N	Y	N	normal	normal	normal	10	9000	28,000	14	98	22	0.8	1	124/32	4.8	-	-	-	+	-	-	-	dengue	symptomatic		1100000
3	saravanan	55	M	7	N	Y	Y	Y	N	N	N	N	N	N	N	normal	normal	normal	11.3	4500	42000	10	87	56	1	1	120/28	5.2	-	vivax	-	-	-	-	-	-	malaria	chloroquine		1250000
4	kannaiah	61	M	3	Y	N	Y	Y	N	N	P	N	Y	N	N	normal	normal	normal	9.8	7600	350000	4	172	21	0.6	1	128/66	5.9	-	-	-	-	-	-	-	unspecified viral fever	symptomatic		1100000
5	vijaya	45	F	4	Y	Y	Y	Y	N	N	P	N	Y	N	Y	normal	normal	normal	11.3	4800	490000	6	94	22	0.8	1	122/44	5.7	-	falciparum	-	-	-	-	-	-	malaria	artesunate		940000
6	jayakumari	47	F	6	Y	N	N	N	N	N	N	N	Y	N	N	normal	normal	normal	10.8	5500	1120000	4	114	18	0.9	1	166/52	6	-	vivax	-	-	-	-	-	-	malaria	chloroquine		1460000
7	raikumar	18	M	9	Y	Y	N	Y	Y	N	P,I	Y	Y	Y	N	normal	normal	normal	8.9	9800	490000	8	78	67	1.1	3	65/234	5	+	falciparum	-	-	-	-	-	-	malaria	artesunate		1780000
8	anitha	35	F	6	Y	N	Y	Y	N	N	N	N	N	N	N	normal	normal	normal	12	6500	1280000	6	122	24	0.9	1	144/66	5.8	-	-	-	+	-	-	-	dengue	symptomatic		1100000
9	gnanamoorthy	55	M	3	N	Y	N	Y	Y	Y	P,I	Y	Y	N	Y	normal	crepts	drowsy	7.8	16500	320000	44	196	74	1.9	5	44/251	3.2	+	-	-	-	-	-	E	E	sepsis	ceftriaxone, Metronidazole	fresh blood	-
10	murugan	45	M	5	N	Y	Y	Y	Y	N	N	N	N	N	N	normal	normal	normal	10.2	9700	1200000	8	98	28	0.7	1	126/22	5.5	-	-	-	+	-	-	-	-	dengue	symptomatic		2180000
11	suresh	24	M	9	N	Y	N	Y	N	N	N	N	Y	Y	N	normal	normal	normal	11.4	4300	960000	24	116	42	1.1	1	188/64	4.6	-	-	+	-	-	-	S	-	typhoid	ceftriaxone		1900000
12	pachiaiapan	40	M	5	Y	Y	N	Y	N	N	N	N	N	N	N	normal	normal	normal	12	4900	900000	7	134	34	0.8	1	145/36	4.8	-	vivax	-	-	-	-	-	-	malaria	chloroquine		1700000
13	karupayee	60	F	2	Y	Y	N	N	N	N	N	N	Y	N	N	normal	normal	normal	13	5500	780000	11	115	22	0.8	1	123/22	4.2	-	vivax	-	-	-	-	-	-	malaria	chloroquine		1900000
14	krishnamma	40	F	6	N	Y	Y	Y	N	Y	N	N	N	N	N	normal	normal	normal	11	6600	940000	11	98	18	0.4	1	136/32	5	-	-	-	-	-	-	-	-	unspecified viral fever	symptomatic		2100000
15	sebastin	20	M	3	N	Y	N	Y	Y	N	Y	Y	Y	N	N	normal	normal	normal	12	5800	560000	8	78	22	0.7	1	146/36	4.8	-	falciparum	-	-	-	-	-	-	malaria	artesunate		1300000
16	masilamani	24	M	4	Y	Y	N	N	Y	Y	N	N	N	N	N	normal	normal	normal	10	7600	490000	55	126	24	0.6	1	124/16	3.9	+	vivax	-	-	-	-	-	-	malaria	chloroquine		1500000
17	karthik	30	M	5	N	N	N	N	N	N	N	N	Y	Y	N	normal	normal	normal	12	12000	760000	12	113	26	0.6	1	188/64	5.1	-	-	+	-	-	-	-	-	typhoid	ceftriaxone		1900000
18	devendra prasa	43	M	6	Y	Y	Y	Y	Y	N	N	P	N	Y	N	normal	normal	normal	8.9	10500	1240000	11	88	21	0.7	1	136/20	4.5	-	-	-	-	-	-	-	-	unspecified viral fever	symptomatic		2440000
19	karthikeyan	20	M	9	Y	Y	Y	Y	Y	Y	N	P,I	Y	Y	Y	normal	normal	normal	7.8	15800	880000	14	89	32	0.7	4	224/28	3.8	+	-	-	+	-	-	-	-	leptospirosis	ceftriaxone	fresh blood	2220000
20	abdul nasar	38	M	4	N	N	Y	Y	N	N	N	N	N	N	N	normal	normal	normal	12	5100	940000	10	121	23	1	1	124/15	4.9	-	-	-	+	-	-	-	-	dengue	symptomatic		2100000

sl.no	name	age	sex	duration of fever	chills & rigors	nausea,vomit	joint pain	headache	bleeding	altered sensorium	PICKLE	bleeding manifestation	epistenomegaly	hepatomegaly	ascites	CVS	RS	CNS	hb (g%)	TLC	platelet count	ESR	RBS (mg/dl)	urea(mg/dl)	creatinine(mg/dl)	serum bilirubin(mg/dl)	ALT/AST (IU/L)	S.albumin (g/dl)	BT	P.Smear MP/MF/QBC	Widal	IgM dengue	Igm lepto/MAT	HIV	Blood o/s	urine o/c	diagnosis	treatment	blood/platelet transfusion	platelet count at discharge
21	kalanidhi	35	M	3	Y	Y	Y	N	N	N	N	N	N	N	N	normal	normal	normal	11	12100	788000	6	112	32	0.6	1	33/24	5	-	falciparum	-	-	-	-	-	malaria	chloroquine		1900000
22	rajendran	60	M	4	Y	Y	Y	Y	N	N	N	N	N	N	N	normal	normal	normal	10.8	78800	1260000	111	92	24	0.7	1	22/18	4.4	-	-	-	+	-	-	-	dengue	symptomatic		2100000
23	mohamed rizw	21	M	6	Y	N	Y	N	N	N	N	N	N	N	N	normal	normal	normal	11.4	5560	1100000	10	72	33	0.6	1	18/14	5.8	-	-	-	+	-	-	-	dengue	symptomatic		2300000
24	ajith kumar	16	M	3	N	N	Y	Y	N	N	N	N	N	N	N	normal	normal	normal	12	87100	820000	165	114	23	0.5	1	22/20	5.1	-	-	-	+	-	-	-	dengue	symptomatic		1600000
25	mohamed	40	M	4	Y	Y	Y	Y	Y	N	P	N	Y	N	N	normal	normal	normal	7.8	12000	660000	6	121	21	0.6	1	34/36	5.4	+	vivax	-	-	-	-	-	malaria	chloroquine		1100000
26	jesina	16	F	5	Y	N	Y	Y	N	N	N	N	Y	Y	N	normal	normal	normal	10.2	13500	910000	165	89	32	0.9	1	213/12	5.9	+	-	+	-	-	-	-	typhoid	ceftriaxone		2100000
27	rambagadur	23	M	2	Y	Y	Y	Y	Y	Y	N	Y	N	N	N	normal	normal	normal	11	90000	1300000	12	87	22	0.6	1	18/22	5	+	-	-	-	-	-	-	unspecified viral fever	symptomatic		2400000
28	sivagami	45	F	3	Y	N	N	N	N	N	N	N	N	N	N	normal	normal	normal	12	76800	1210000	5	110	30	0.5	1	16/21	6	-	vivax	-	-	-	-	-	malaria	chloroquine		2300000
29	kala	35	F	11	Y	Y	N	Y	Y	Y	PJ	Y	Y	N	Y	normal	normal	normal	6	17000	120000	295	102	102	4.3	6	533/44	3.8	+	falciparum	-	-	-	-	-	malaria	artesunate, lumefantrine	whole blood, platelet	-
30	nagaraj	23	M	10	Y	Y	N	Y	N	N	N	N	N	N	N	normal	normal	normal	12	56600	780000	12	103	22	0.8	1	16/18	4.7	-	-	-	+	-	-	-	dengue	symptomatic		2100000
31	rani	28	F	5	N	Y	Y	Y	N	N	N	N	N	N	N	normal	normal	normal	10.6	7100	820000	14	86	21	0.7	1	28/20	5.8	-	-	-	+	-	-	-	dengue	symptomatic		2220000
32	srinivasan	61	M	4	Y	Y	Y	Y	N	N	N	N	N	N	N	normal	normal	normal	11.9	10500	1200000	5	78	20	0.6	1	22/21	6	-	-	-	-	-	-	-	unspecified viral fever	symptomatic		2600000
33	hameed	45	M	6	Y	Y	Y	Y	N	N	P	N	N	N	N	normal	normal	normal	8	67100	680000	4	88	32	0.9	1	33/28	5.9	-	-	-	+	-	-	-	dengue	symptomatic		1900000
34	saravanan	25	M	7	y	y	Y	N	N	N	N	N	Y	Y	N	normal	normal	normal	11	77100	550000	8	67	23	0.9	1	20/14	5	-	vivax	-	-	-	-	-	malaria	chloroquine		1100000
35	Jayalakshmi	30	F	5	Y	Y	N	Y	Y	Y	N	N	Y	N	N	normal	normal	normal	10	64400	1260000	7	74	20	6	1	21/18	4.9	+	vivax	-	-	-	-	-	malaria	chloroquine		2800000
36	meena	21	F	5	Y	Y	Y	N	Y	N	N	N	N	N	N	normal	normal	normal	12	77100	830000	3	85	66	1	1	22/44	6	-	-	+	-	-	-	-	typhoid	ceftriaxone		1300000
37	prabhakaran	23	M	3	Y	Y	N	N	N	N	N	N	N	N	N	normal	normal	normal	12	88800	1100000	5	94	22	0.8	1	40/32	4.9	-	-	-	+	-	-	-	dengue	symptomatic		2900000
38	meenatchi	58	F	4	N	Y	N	Y	N	Y	Y	Y	N	Y	Y	normal	crepts	drowsy	11	222000	380000	17	194	57	1.9	3	388/26	4	+	-	-	-	-	-	K	-	sepsis	cefoperazone	whole blood, platelet	9400000
39	kiran josy	27	M	2	Y	N	N	Y	N	N	N	N	N	N	N	normal	normal	normal	10	70000	1200000	12	112	28	0.7	1	42/34	5.1	-	-	-	-	-	-	-	unspecified viral fever	symptomatic		1900000
40	priyanka	16	F	5	N	N	N	Y	N	N	N	N	N	N	N	normal	normal	normal	11	55800	780000	10	76	22	0.6	1	22/20	5	-	-	-	-	-	-	-	unspecified viral fever	symptomatic		1400000

sl.no	name	age	sex	duration of fever	chills & rigors	nausea,vomit	joint pain	headache	bleeding	altered sensorium	PICKLE	bleeding manifestation	splenomegaly	hepatomegaly	ascites	CVS	RS	CNS	hb (g%)	TLC	platelet count	ESR	RBS (mg/dl)	urea(mg/dl)	creatinine(mg/dl)	serum bilirubin(mg/dl)	ALT/AST (IU/L)	⍵.albumin (g/dl)	BT	P.Smear MP/MF/QBC	Widal	IgM dengue	Igm lepto/MAT	HIV	Blood o/s	urine o/c	diagnosis	treatment	blood/platelet transfusion	platelet count at discharge
40	priyanka	16	F	5	N	N	Y	N	N	N	N	N	N	N	N	normal	normal	normal	11	55500	798000	10	76	22	0.6	1	22/220	5	-	-	-	-	-	-	-	unspecified viral feve	symptomatic		1400000
41	bala	21	M	6	Y	Y	N	Y	N	N	N	N	N	N	N	normal	normal	normal	12	56800	1200000	4	888	23	0.8	1	24/20	5.8	-	-	+	-	-	-	-	dengue	symptomatic		1900000
42	dinesh	54	M	4	N	N	Y	Y	N	N	N	N	N	Y	N	normal	normal	normal	12	65500	688000	5	886	22	1	1	34/46	6	-	falciparum	-	-	-	-	-	malaria	chloroquine		1600000
43	chandra	48	F	6	Y	Y	N	N	N	N	A	N	Y	N	N	normal	normal	normal	8	45500	739000	6	788	300	0.7	1	20/88	5	-	vivax	-	-	-	-	-	malaria	chloroquine		2100000
44	lakshmi	36	F	5	Y	N	Y	Y	N	N	N	N	N	N	N	normal	normal	normal	11	49800	1250000	4	96	28	0.9	1	28/24	4.2	-	-	-	-	-	-	-	unspecified viral feve	symptomatic		2300000
45	amsa	30	F	3	N	Y	N	Y	N	N	N	N	Y	N	N	normal	normal	normal	12	110000	760000	4	98	24	0.6	1	21/12	5.1	-	vivax	-	-	-	-	-	malaria	chloroquine		1300000
46	suriya	16	M	4	Y	N	N	Y	N	N	N	N	Y	Y	N	normal	normal	normal	10	120000	1100000	6	116	32	0.8	1	18/16	5	-	-	+	-	-	-	-	typhoid	ceftriaxone		1900000
47	soman	45	F	5	Y	Y	Y	N	N	N	N	N	N	N	N	normal	normal	normal	10.5	105500	489000	8	102	26	0.9	1	28/10	5.3	-	-	+	-	-	-	-	dengue	symptomatic		1200000
48	yamuna	16	F	7	Y	N	N	Y	N	N	N	N	Y	N	N	normal	normal	normal	12.6	77100	1200000	6	886	22	0.5	1	26/28	5.6	-	vivax	-	-	-	-	-	malaria	chloroquine		2100000
49	lakshmi	30	F	8	N	N	N	Y	N	N	N	N	N	N	N	normal	normal	normal	10.8	110000	910000	5	120	27	0.9	1	30/28	6	-	falciparum	-	-	-	-	-	malaria	chloroquine		1700000
50	mariammal	55	F	4	Y	Y	N	Y	Y	N	AJ	N	Y	Y	N	normal	ehfusio	normal	8	120000	960000	4	102	66	1.4	3	76/66	5	-	-	-	+	-	-	-	leptospirosis	ceftriaxone		1600000
51	subramani	42	M	4	Y	Y	N	Y	N	N	N	N	N	Y	N	normal	normal	normal	12	1050000	760000	5	112	28	0.6	1	23/18	4.7	-	vivax	-	-	-	-	-	malaria	chloroquine		1200000
52	narkunam	42	M	5	N	Y	Y	Y	N	N	N	N	N	N	N	normal	normal	normal	11	45500	988000	4	108	22	0.5	1	30/28	5	-	-	-	-	-	-	-	unspecified viral feve	symptomatic		1700000
53	arun kumar	20	M	6	Y	N	Y	Y	N	N	N	N	N	N	N	normal	normal	normal	10.8	54400	1260000	5	96	23	0.7	1	22/14	5.2	-	-	-	-	-	-	-	unspecified viral feve	symptomatic		1900000
54	dhanasekar	43	M	7	N	Y	N	Y	N	N	N	N	N	N	N	normal	normal	normal	11	78800	850000	6	78	28	0.8	1	20/22	5.9	-	-	+	-	-	-	-	dengue	symptomatic		1600000
55	kavitha	15	F	6	Y	N	N	Y	N	N	N	N	Y	Y	N	normal	normal	normal	11.5	88800	988000	4	112	300	0.6	1	28/24	4.8	-	vivax	-	-	-	-	-	malaria	chloroquine		2200000
56	sridevi	27	F	5	Y	Y	N	N	Y	N	N	N	Y	Y	N	normal	normal	normal	10.5	67700	1230000	6	87	28	0.8	1	34/40	5	+	-	-	+	-	-	-	leptospirosis	ceftriaxone		1800000
57	abirami	30	F	3	Y	Y	N	N	N	N	N	N	Y	N	N	normal	normal	normal	12	83000	670000	5	103	300	0.9	1	27/26	4.4	-	falciparum	-	-	-	-	-	malaria	chloroquine		1200000
58	markendeyan	40	M	8	N	Y	N	Y	N	N	N	N	N	N	N	normal	normal	normal	10	56600	1200000	4	98	26	0.8	1	34/30	5.4	-	vivax	-	-	-	-	-	malaria	chloroquine		1200000
59	meenatchi	51	F	5	N	Y	Y	N	Y	Y	A	Y	N	N	N	normal	normal	normal	6.5	66800	420000	5	88	22	0.7	1	22/24	6	+	-	-	+	-	-	-	dengue	symptomatic	fresh whole blood	6900000
60	bharadhan	20	M	4	Y	Y	N	N	N	N	N	N	N	N	N	normal	normal	normal	12	59800	980000	8	78	25	0.9	1	30/32	5.8	-	vivax	-	-	-	-	-	malaria	chloroquine		1600000

sl.no	name	age	sex	duration of fever	chills & rigors	nausea,vomit	joint pain	bleeding	altered sensorium	PICKLE	bleeding manifestation	splenomegaly	hepatomegaly	ascites	CVS	RS	CNS	hb (g%)	TLC	platelet count	ESR	RBS (mg/dl)	urea(mg/dl)	creatinine(mg/dl)	serum bilirubin(mg/dl)	ALT/AST (IU/L)	S.albumin (g/dl)	BT	P.Smear MP/MF/QBC	Widal	IgM dengue	IgM lepto/MAT	HIV	Blood c/s	urine c/o	diagnosis	treatment	blood/platelet transfusion	platelet count at discharge
61	jeyaraj	60	M	5	Y	N	N	Y	N	N	A	N	N	N	normal	normal	normal	13	7800	180000	6	98	21	0.6	1	24/26	6	-	-	-	-	-	-	-	unspecified viral fever	symptomatic		2100000
62	elavarasi	18	F	5	Y	N	N	N	N	N	A	N	N	N	normal	normal	normal	11	6500	910000	10	101	23	0.7	1	30/28	5.2	-	-	+	-	-	-	-	typhoid	ceftriaxone		1900000
63	kannan	60	M	4	Y	N	N	Y	N	N	N	N	N	Y	normal	normal	normal	10.5	10500	1230000	4	138	58	0.5	1	30/22	5	-	-	-	+	-	-	-	leptospirosis	ceftriaxone		1800000
64	dhanapal	37	M	5	Y	N	N	Y	N	N	N	N	Y	Y	normal	normal	normal	11.5	8700	980000	8	96	26	0.4	1	24/22	6.2	-	falciparum	+	+	-	-	-	-	malaria	chloroquine		1300000
65	aiith	45	M	3	Y	N	N	Y	N	N	N	N	N	N	normal	normal	normal	9.5	9900	760000	6	108	22	0.8	1	22/28	5.4	-	vivax	-	-	-	-	-	-	malaria	chloroquine		1600000
66	mahaver	60	M	4	N	N	Y	N	N	N	A	N	Y	Y	normal	normal	normal	8.8	3900	180000	4	112	46	0.6	1	92/114	5	-	-	-	-	-	+	-	HIV	HAART		1300000
67	parveen	45	F	5	N	N	Y	N	N	N	N	N	N	N	normal	normal	normal	11	4500	640000	6	98	26	0.7	1	54/66	4.9	-	-	-	+	-	-	-	dengue	chloroquine		1600000
68	parvathy	27	F	6	Y	N	Y	N	N	N	N	N	Y	N	normal	normal	normal	12	6500	1100000	6	96	28	0.6	1	34/54	4.8	-	vivax	-	-	-	-	-	-	malaria	chloroquine		1700000
69	ravi	43	M	3	N	Y	Y	N	N	N	N	N	N	N	normal	normal	normal	10.5	9800	1220000	8	115	32	0.9	1	26/24	6	-	-	-	+	-	-	-	dengue	symptomatic		2200000
70	santhosh	75	M	2	Y	N	N	Y	N	N	A	Y	N	y	normal	normal	normal	7	12000	980000	6	124	25	0.6	1	22/26	5	+	-	-	-	-	-	-	unspecified viral fever	symptomatic	fresh whole blood	-
71	suganthi	23	F	6	N	N	N	N	N	N	N	N	Y	Y	normal	normal	normal	11	7700	590000	7	98	28	0.8	1	18/22	5.7	-	vivax	-	-	-	-	-	-	malaria	chloroquine		1100000
72	keerthika	20	F	5	Y	Y	N	Y	N	N	A,J	N	Y	Y	normal	normal	normal	6	11800	1300000	4	98	32	0.6	1	29/20	5	+	-	-	-	-	+	-	-	leptospirosis	ceftriaxone	fresh whole blood	2600000
73	kumaresan	19	M	7	Y	N	Y	N	N	N	N	N	N	N	normal	normal	normal	10	5500	950000	6	120	45	0.8	1	40/34	4.5	-	-	-	+	-	-	-	dengue	symptomatic		1400000
74	praveen kuma	63	M	4	Y	Y	N	Y	N	N	N	N	Y	N	normal	normal	normal	11	6600	1400000	4	76	22	0.7	1	22/32	4.8	-	falciparum	-	-	-	-	-	-	malaria	chloroquine		2300000
75	ravishankar	53	M	5	Y	N	Y	N	N	N	N	N	N	N	normal	normal	normal	12	7400	760000	8	112	26	0.9	1	24/46	5	-	-	-	+	-	-	-	dengue	symptomatic		1500000
76	lakshmi	38	F	3	Y	Y	N	Y	Y	N	P	N	Y	N	normal	normal	normal	10.5	10800	980000	5	98	34	0.6	1	34/42	5.4	-	vivax	-	-	-	-	-	-	malaria	chloroquine		1400000
77	aarthi	20	F	6	Y	N	Y	N	N	N	N	N	N	N	normal	normal	normal	11.5	9800	870000	6	108	28	0.9	1	32/24	5.8	-	-	-	-	-	-	-	unspecified viral fever	symptomatic		1400000
78	muhaned ilias	57	M	5	N	N	Y	Y	Y	N	N	N	Y	N	normal	normal	normal	11.2	7600	122800	12	119	26	0.8	1	28/18	5.1	-	-	-	+	-	-	-	dengue	symptomatic		1600000
79	valarmathi	43	F	3	N	Y	Y	N	N	N	N	N	N	N	normal	normal	normal	10	9800	1220000	8	101	30	1	1	16/28	4.9	-	-	-	+	-	-	-	dengue	symptomatic		2100000
80	selvadurai	60	M	5	Y	y	N	y	Y	Y	A,J	y	y	y	Y	normal	normal	normal	7	11600	970000	10	76	77	1.8	3	42/36	6	-	falciparum	-	-	-	-	-	-	malaria	artesunate	fresh whole blood	2220000

s.no	name	age	sex	duration of fever	chills & rigors	nausea,vomit	joint pain	mesalgone	bleeding	altered sensorium	PICKLE	bleeding manifestation	splenomegaly	hepatomegaly	ascites	CVS	RS	CNS	Hb (g%)	TLC	platelet count	ESR	RBS (mg/dl)	urea(mg/dl)	creatinine(mg/dl)	serum bilirubin(mg/dl)	ALT/AST (IU/L)	S.albumin (g/dl)	BT	P.Smear MP/MF/QBC	Widal	IgM dengue	Igm lepto/MAT	HIV	Blood c/s	urine c/o	diagnosis	treatment	blood/platelet transfusion	platelet count at discharge
80	selvadurai	60	M	5	Y	y	N	y	Y	Y	A,J	y	y	y	Y	normal	normal	normal	7	11600	970000	10	76	77	1.8	3	142/36	6	-	falciparum	-	-	-	-	-	malaria	artesunate	fresh whole blood	2200000
81	selvi	56	F	3	Y	Y	N	Y	N	N	N	N	N	N	N	normal	normal	normal	10.8	9800	1240000	8	98	24	0.9	1	126/32	5.2	-	-	-	-	-	-	malaria	chloroquine		2400000
82	ravikumar	34	M	2	Y	N	N	Y	N	Y	N	N	N	N	N	normal	normal	normal	11	8700	860000	6	102	22	0.6	1	124/26	5.8	-	-	-	-	-	-	dengue	symptomatic		1600000
83	deepak	23	M	3	N	Y	N	Y	N	Y	N	N	N	Y	N	normal	normal	normal	10.5	7600	940000	4	78	46	0.8	1	134/34	6	-	vivax	-	-	-	-	-	malaria	chloroquine		1800000
84	ramassamy	60	M	6	Y	Y	N	Y	N	Y	N	N	N	N	N	normal	normal	normal	12	5900	1200000	6	97	26	0.9	1	122/26	5	-	vivax	-	-	-	-	-	malaria	chloroquine		1900000
85	kalaimani	35	F	4	Y	Y	N	N	N	N	N	N	N	N	N	normal	normal	normal	10	9400	670000	10	110	22	0.7	1	134/46	6	-	-	-	+	-	-	-	dengue	symptomatic		1700000
86	kannan	45	M	8	Y	Y	N	Y	N	Y	N	N	N	N	N	normal	normal	normal	11.5	7900	1100000	4	86	28	0.9	1	126/38	6.2	-	falciparum	-	-	-	-	-	malaria	artesunate		1600000
87	ramkumar	54	M	5	N	Y	N	Y	N	Y	N	N	A	N	Y	normal	crepts	normal	7	13500	780000	8	112	74	2	1	146/34	4.9	+	-	-	-	-	-	-	sepsis	cefotaxim	fresh whole blood	-
88	praveena	24	F	4	Y	N	N	Y	N	Y	N	N	N	N	Y	normal	normal	normal	12	5600	880000	4	85	24	0.9	1	124/28	5.2	-	-	-	-	-	-	E	E,K	unspecified viral fever	symptomatic		1500000
89	chitra	65	F	4	N	N	N	N	N	N	N	N	N	Y	Y	normal	normal	normal	11	7100	1200000	6	98	48	1	1	146/24	5	-	vivax	-	-	-	-	-	malaria	chloroquine		2400000
90	rekha	34	F	3	Y	N	N	Y	N	Y	N	N	N	N	N	normal	normal	normal	10.5	6800	1160000	5	112	24	0.7	1	126/30	4.6	-	-	-	+	-	-	-	dengue	symptomatic		1800000
91	padmavathi	33	F	7	Y	N	N	Y	N	Y	N	N	N	N	N	normal	normal	normal	12	6400	940000	4	85	26	0.6	1	128/28	5	-	-	-	+	-	-	-	dengue	symptomatic		1600000
92	roshini	25	F	6	Y	Y	N	N	N	N	N	N	N	A	N	normal	normal	normal	11	8100	860000	6	98	26	7	1	126/34	5.6	-	-	-	-	-	-	-	unspecified viral fever	symptomatic		1300000
93	prabu	33	M	4	Y	Y	N	Y	N	Y	N	N	N	N	Y	normal	normal	normal	11.2	7400	680000	8	78	34	0.8	1	128/22	4.6	-	vivax	-	-	-	-	-	malaria	chloroquine		1400000
94	bradadhraj	66	M	6	Y	Y	N	N	N	N	N	A,J	Y	Y	Y	normal	normal	normal	7.5	13000	710000	10	106	76	1	5	434/44	4.8	-	falciparum	-	-	-	-	-	malaria	artesunate		1100000
95	leela	54	F	3	Y	N	Y	Y	Y	N	N	N	N	N	N	normal	normal	normal	12.2	7800	530000	8	156	24	0.7	1	152/34	5.2	-	-	-	+	-	-	-	dengue	symptomatic		1000000
96	karthiknaraya	35	M	5	Y	N	N	Y	N	Y	N	N	N	Y	N	normal	normal	normal	10	4500	1380000	6	175	27	0.8	1	134/54	6	-	vivax	-	-	-	-	-	malaria	chloroquine		2700000
97	sriram	46	M	6	N	Y	Y	Y	Y	Y	N	N	N	Y	Y	normal	normal	normal	12.5	9800	1160000	5	130	25	0.6	1	128/22	5.1	-	vivax	-	-	-	-	-	malaria	chloroquine		1500000
98	kumaran	46	M	7	Y	Y	Y	Y	Y	N	N	N	N	N	N	normal	normal	normal	11.8	5400	980000	6	106	28	0.7	1	120/40	4.6	-	-	-	-	-	-	-	unspecified viral fever	symptomatic		1600000
99	balu	26	M	8	N	N	Y	N	N	N	N	N	N	N	N	normal	normal	normal	10.2	6700	870000	7	98	30	0.8	1	138/32	5	-	-	-	-	-	-	-	dengue	symptomatic		1600000
100	kannathal	64	F	2	Y	N	N	Y	N	N	N	N	N	N	N	normal	normal	normal	12	7100	950000	8	86	32	0.9	1	146/28	4.8	-	vivax	-	-	-	-	-	malaria	chloroquine		1800000

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Ref.No.2318/ME-1/Ethics/2012 Dt:04.04.2013
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "A Study on clinical study of fever with thrombocytopenia with special reference to infective etiology and complications admitted to Govt. Royapettah Hospital, Chennai" – For Project Work submitted by Dr.M.Manoj, MD (GM), PG Student, Govt. Royapettah Hospital, Chennai-14.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

GOVT. KILPAUK MEDICAL COLLEGE
29 MAY 2013
Kilpauk, Chennai-10.

29/5/13.

CHAIRMAN,
Ethical Committee
Govt.Kilpauk Medical College,Chennai

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