International Journal of Medicine Research
www.medicinesjournal.com
ISSN: 2455-7404
Received: 20-12-2022, Accepted: 05-01-2023, Published: 21-01-2023
Volume 8, Issue 1, 2023, Page No. 1-6

Study of clinical profile of fever with thrombocytopenia in Mata Gujri Memorial Medical College in Kishanganj, Bihar

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Abstract
Background: Fever is a common manifestation of an illness. Thrombocytopenia is most frequent finding in febrile illness. Thrombocytopenia with fever narrows the differential diagnosis of clinical entity and helps in reaching the diagnosis of febrile illness. The present study is carried out to find the cause of thrombocytopenia with fever and to assess the clinical complication associated with severity of thrombocytopenia and fever.
Material and Method: This study was carried out in the department of general medicine Mata Gujri Memorial Medical College in Kishanganj, Bihar during the period of July 2021 to September 2022. Total 100 patients were enrolled in this study. Informed written consent was taken from patients. This is a hospital-based observational study.
Results: Dengue was the most common cause of febrile thrombocytopenia (50%) followed by malaria (23%). The other causes were viral fever (19%), scrub typhus (4%), mixed dengue and scrub typhus (2%), septicemia (2%). The patients were in the age group 16-80 years with 60 male and 40 females. Maximum patients (76%) were found to have thrombocytopenia in the range of 50,000-1,50,000/cumm, 16 cases had thrombocytopenia in the range of 20,000-50,000/cumm while 8 cases had thrombocytopenia in the range of <20,000cumm. bleeding manifestations were very rarely seen as present in 3 cases (3%) with petechiae as the commonest bleeding manifestation (2%). Severe thrombocytopenia was seen in dengue fever and falciparum malaria. Mortality was observed in 2 cases (2%) and multiorgan dysfunction was present in all those 2 cases.
Conclusion: Dengue is the commonest cause of febrile thrombocytopenia and the severity of thrombocytopenia was not associated with increased mortality but mortality was due to multiorgan dysfunction.

Keywords: dengue fever, malaria, scrub typhus, septicemia, thrombocytopenia

Introduction

Background

fever is most ancient health mark of disease which is defined as the elevation in the body temperature above the normal circadian range as result of change in thermoregulatory centre located in anterior hypothalamus. Morning temperature of >37.2 degree (98.9 F) or evening temperature >37.7 degree (99.9 F) would define fever [1]. Thrombocytopenia is defined as subnormal level of platelets in circulatory blood e.g.-counts below 1.5 lac/cumm [2]. A normal platelet count ranges from 1, 50,000-4, 50,000/cumm. Often the patients of thrombocytopenia are asymptomatic and thrombocytopenia becomes revealed on routine complete blood counts. Thrombocytopenia is results of various processes such as accelerated platelets destructions, deficient platelets production, abnormal distribution or pooling of platelets within the body and artifactual thrombocytopenia [3]. Thrombocytopenia due to decreased platelet production occurs in vitamin B12 and folate deficiency, leukemia, sepsis as result of bacterial and viral infection and hereditary disease. Thrombocytopenia due to increased destruction occurs in idiopathic thrombocytopenia purpura, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, disseminated intravascular coagulation, paroxysmal nocturnal hemoglobinuria, systemic lupus erythematosus, antiphospholipid syndrome, post-transfusion purpura and hypersplenism. Drugs causing thrombocytopenia are quinine, heparin, interferon, valproic acid, isotretinoin, and chemotherapy. Occasionally, there may be bruising, purpura, petechiae, gum bleeding, epistaxis, menorrhagia and rarely platelets count below 5,000/cumm predisposing the life-threatening bleeding in the central nervous system, from gastrointestinal and genitourinary tracts [4]. Infection is the commonest cause of thrombocytopenia and febrile thrombocytopenia is the thrombocytopenia associated with fever.

Fever is the common manifestation of the infection in most of case with few exceptions like chronic kidney disease, alcoholic, immune compromise host. Infectious diseases which commonly present with fever and thrombocytopenia are malaria, enteric fever, septicemia, Leptospira, rickettsial infections like scrub typhus, dengue and other viral infections including human immunodeficiency virus [15].

Thrombocytopenia has relation with mortality and morbidity in various febrile illnesses such as dengue and thus serial monitoring of platelets count has prognostic significance. Hence a well-organized systemic approach is carried out with awareness of cause of fever that will shorten the number of investigation and bring out the diagnosis. Therefore, the present study was carried out to know the underlying etiology of febrile thrombocytopenia, the clinical profile of febrile thrombocytopenia and to assess the severity of thrombocytopenia in the various etiology of fever with thrombocytopenia and relationship between platelet count and severity of disease and prognosis.

Aim and objectives

To evaluate clinical profile of fever with thrombocytopenia and to identify the underlying etiology of febrile thrombocytopenia, to assess severity of thrombocytopenia in the various etiology of febrile thrombocytopenia and relationship between platelets counts and severity of disease and prognosis.

Material and Methods

This is hospital based observational study and the present study was conducted on 100 patients admitted in the department of general medicine of Mata Gujri Memorial Medical College in Kishanganj, Bihar during July 2021 to September 2022. The patients were selected as per protocol based on inclusion and exclusion criteria. Informed written consent was taken from the patients and ethical committee approval was obtained.

Inclusion criteria

1. All new patients of both sex with age >16 years were admitted with fever (temperature>99.9F) and found to have thrombocytopenia (i.e. counts<150.000/cumm).

Exclusion criteria

1. Patient with thrombocytopenia diagnosed as hematological disorder or malignancy on treatment with chemotherapy and other immunosuppressive drugs.
2. Patient on treatment with antiplatelets and other drugs causing thrombocytopenia.
3. Patient with known case of immune thrombocytopenia purpura on treatment.
4. Patient with cirrhosis of liver, chronic kidney disease, connective tissue disorder like SLE.

Methodology

All the cases during study period were included**,** once the patients were admitted with fever and found to have thrombocytopenia, careful history was recorded, general physical and systemic examination was done, routine investigation including complete blood counts, peripheral smear examination, kidney function test, liver function test, electrocardiography, and ultrasonography was done. The specific and special investigations were done as and when indicated. The temperature was measured orally by clinical thermometer after keeping the thermometer for 1 minute while asking the patient to take breath from nose. Complete blood counts were done Agappe analyzer, both thick and thin blood smear examined for malarial parasites as well as for total leukocyte counts, platelets count and any abnormal cells. Special investigation like NS1 antigen for dengue, IgM Elisa for dengue, IgM Elisa for scrub typhus, widal test, blood culture and sensitivity, body fluid analysis and bone marrow analysis were done as and needed. In whom final definitive diagnosis was reached, were treated for the disease and platelet count was repeated in severe thrombocytopenia, bleeding manifestations and at the time of discharge.

Results

Total 100 patients admitted in our hospital over a period of July 2021- September 2022 were studied. the study subjects were in age group 16-80 years with 60 males and 40 females (Figure 1).

Febrile thrombocytopenia was common in young and middle age group i.e. < 40 years (45%) with maximum number of patients in age group of 16-30 years. 30 patients were in the age group of 41-65 years and 25 patients were in age group of 66 years. (Figure 3).

Febrile thrombocytopenia was more commonly seen in season of July to September affecting 62 patients.19 patients were affected in October to December and 13 patients were affected in January to march and 6 patients were affected in April to June (Figure 4).

The commonest cause of febrile thrombocytopenia was dengue fever (50%) followed by malaria (23%). the other causes were in our study like viral fever (19%), scrub typhus (4%), mixed dengue and scrub typhus (2%), septicemia (2%) (Table 1). Viral fever was labeled in the patients whose definitive diagnosis was not made after investigations. The least common cause of febrile thrombocytopenia was septicemia (2%) in our study, out of 23 cases of malaria, p. vivax with 12(12%) cases was most common type followed by P. Falciparum with 7(7%) cases and least common type was mixed p. vivax and p. falcifarum with 4(4%) cases. Apart from fever which was present in all cases, the commonest clinical manifestation was myalgia (85%), followed by chills and rigor (78%). The least common clinical feature was rash (3%). Bleeding manifestation was present in 3(3%) cases. and petechiae were the most common bleeding manifestation seen in 2 (2%) cases followed by subconjunctival hemorrhage seen in 1(1%) case.

In our study, 8 patients had platelet count<20,000/cumm, 16 patients in range of 20,000-50,000/cumm and 76 patients had platelet counts >50,000/cumm, Severe thrombocytopenia was seen in most case of dengue fever and viral fever followed by falciparum. Moderate thrombocytopenia was seen more common in p.vivax and mixed malaria. Mild thrombocytopenia was seen in all cases of scrub typhus and septicemia also had mild thrombocytopenia in our study (Table 2). Maximum bleeding manifestations were seen with platelet count <20,000/cumm. No bleeding manifestation was observed with platelet count >100000/cumm (Figure 5). In our study, lowest platelet counts were 3,000/cumm. Platelet counts were repeated in patient with severe thrombocytopenia and bleeding manifestations. Definitive increase in platelet count was noted after the underlying cause was treated. Out of 100 patients, 98 patients had good recovery. 2 patients had expired (Figure 6). Mortality was seen in 2 cases, which was due to multiorgan dysfunction caused by septicemia and complicated malaria which was present in all those cases.

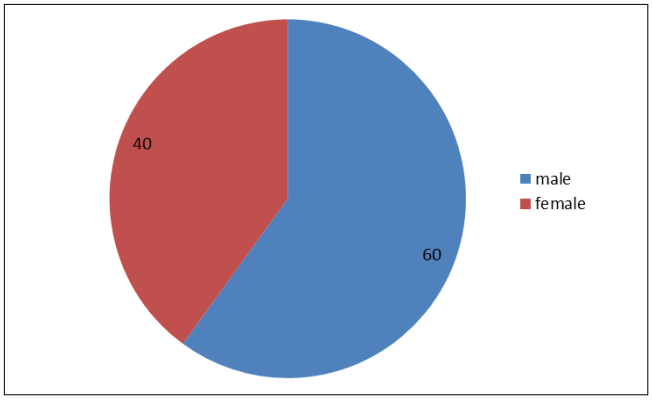

Fig 1: Sex wise distribution of febrile thrombocytopenia.

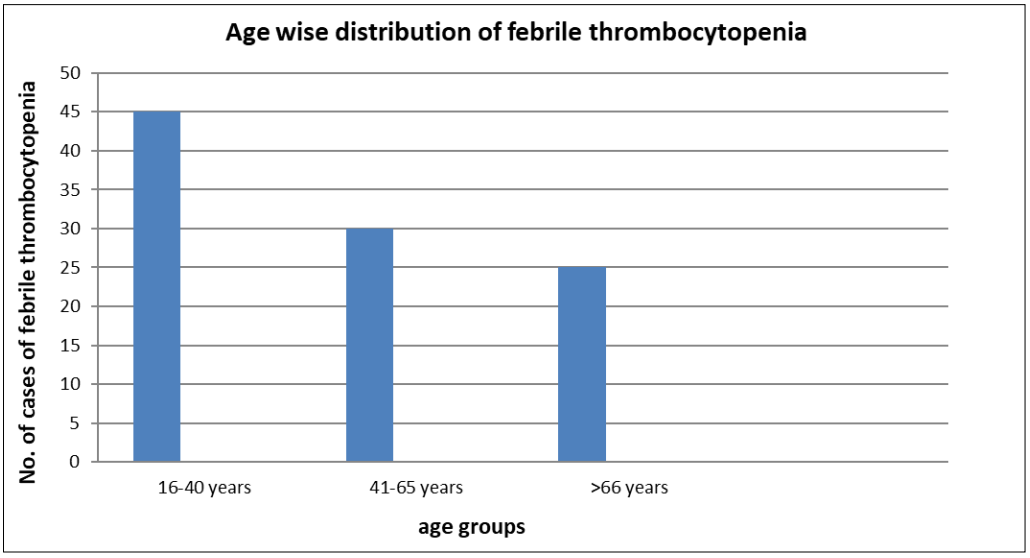

Fig 2: Age wise distribution of febrile thrombocytopenia.

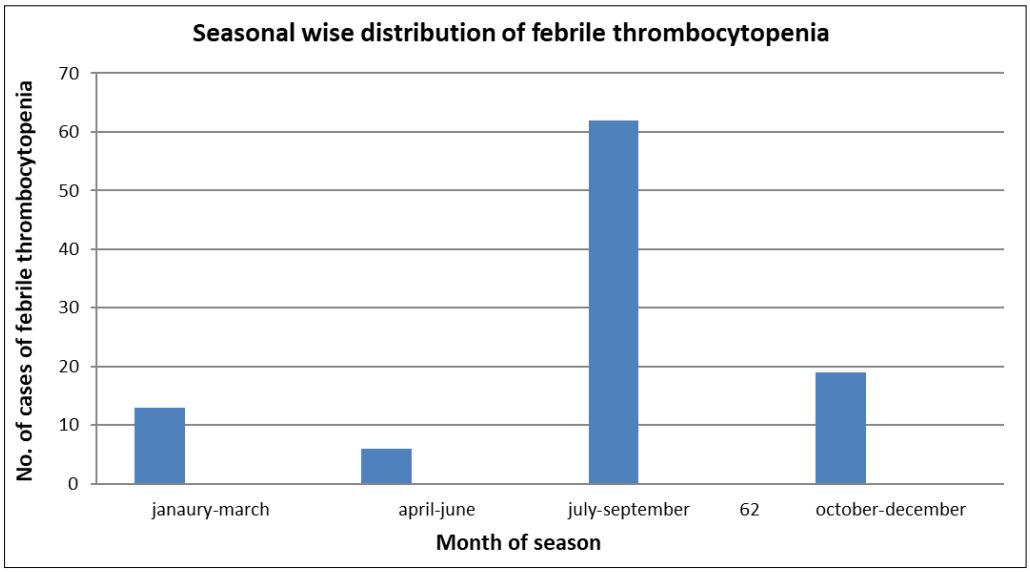

Fig 3: Seasonal wise distribution of febrile thrombocytopenia.

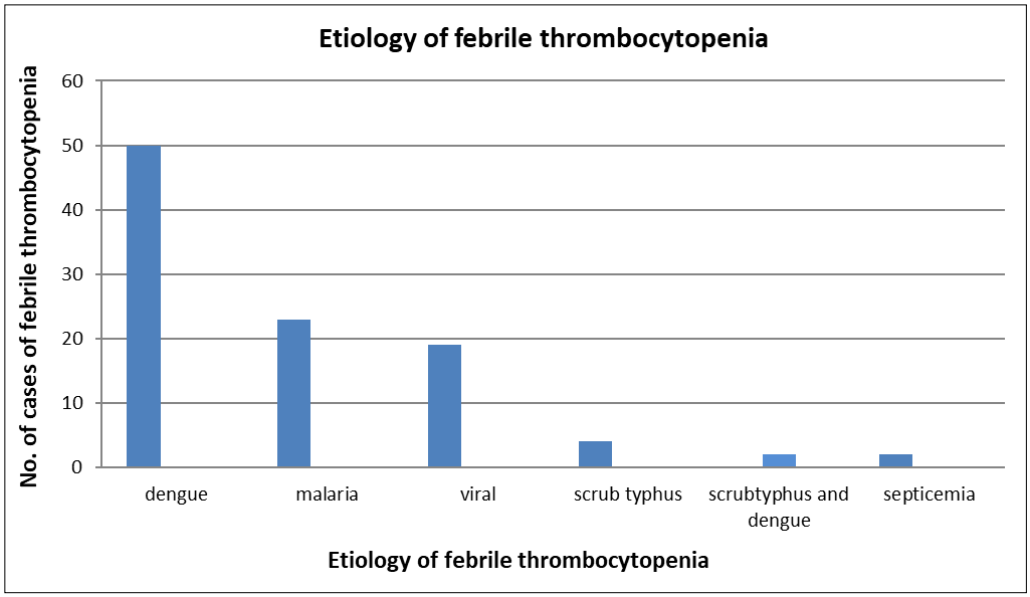

Fig 4: Etiology of febrile thrombocytopenia.

Table 1: Clinical manifestations of febrile thrombocytopenia.

Clinical symptoms/signs	Number of case
fever	100
Chills and rigor	78
headache	69
body ache	65
myalgia	85
Joint pain	35
vomiting	51
Abdomen pain	32
Loose motion	23
Cough and dyspnoea	12
Rash and bleeding	3
hypotension	15
tachycardia	15
pallor	14
jaundice	2
Abnormal renal function test	2
Abnormal liver function test	2

Table 2: Platelet count distribution according to different etiology.

Platelet count	Dengue (n=50)	P.F (n=7)	P.V (n=12)	P.V+P.F (n=4)	Viral (n=19)	Scrub typhus (n=4)	Septicemia (n=2)	Scrub typhus + dengue (n=2)	Total (n=100)
<20,000/cumm	3	1	1	0	3	0	0	0	8
20,000-50,000/cumm	1	2	5	2	6	0	0	0	16
50,000-100,000/cumm	20	3	6	2	8	3	0	0	42
100,000-150,000/cumm	26	1	0	0	2	1	2	2	34

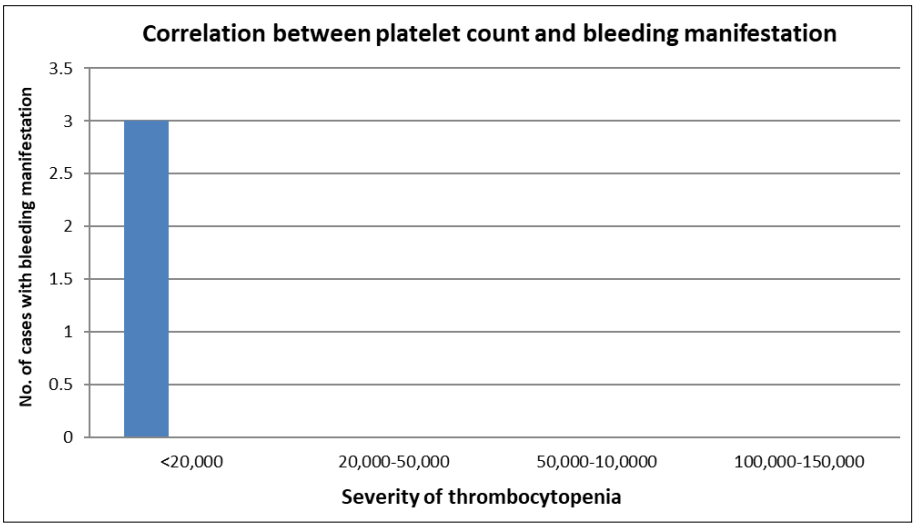

Fig 5: Correlation between platelet count and bleeding manifestation.

Figure 5: Shows new information in relation between bleeding manifestation and severity of thrombocytopenia.

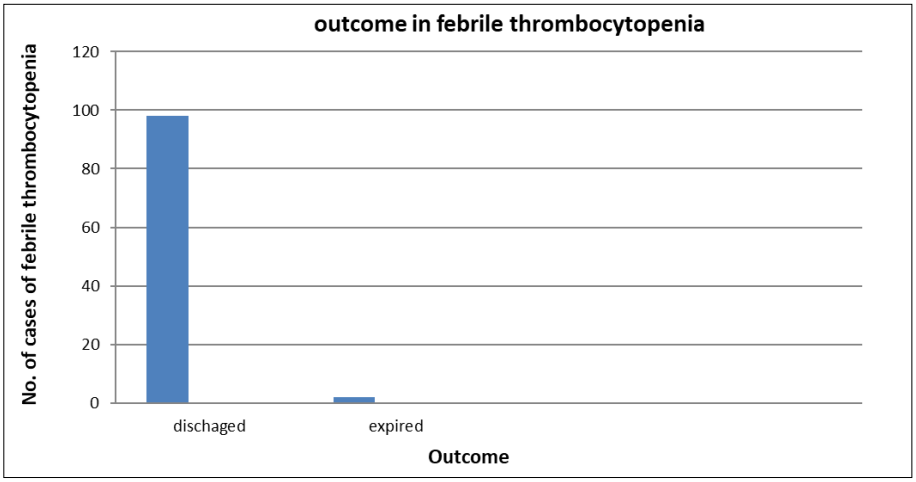

Fig 6: Outcome in febrile thrombocytopenia.

Discussion

Febrile thrombocytopenia is a common clinical condition and is caused by infectious and noninfectious disease. total of 100 cases of febrile thrombocytopenia admitted over period of one year in our hospital were studied. The affected populations were in the age group of 16-80 years with 60 male and 40 female, with maximum number affected in age group of 16-30 years. Similar results were seen in study by Kumar P *et a*l [4]. Febrile thrombocytopenia was more prevalent in the month of July to September in our study, this was because of high incidence of dengue and malaria in this region during that period. In our study the commonest etiology of febrile thrombocytopenia was dengue fever accounts for 50(50%) case followed by malaria (23%), viral fever (19%), scrub typhus (4%), scrub typhus+ dengue (2%), septicemia (2%).in previous study by Gandhi AA *et al* [5] found malaria as the commonest cause for febrile thrombocytopenia, this difference might be due to seasonal and regional variation of the febrile illness. Malaria and dengue fever are predominantly present in rainy season because there can be clustering of these cases in this season. In our study myalgia was the most common clinical feature apart from fever and myalgia was predominantly present in dengue fever, viral fever, scrub typhus and Leptospira. Similar results were observed in study by Tong Seng Fahet *et al* [7]. i.e. myalgia being the commonest clinical feature. In the present study, bleeding manifestation were very rarely seen as present in only 3(3%) cases, with petechiae as common manifestation followed by subconjunctival bleed. In study by Nair PS *et al* [6]. Bleeding manifestation observed in 41.3% cases with petechiae and gastrointestinal bleed as most common bleeding manifestation. In our study no patient found to have gastrointestinal bleed which were present in the above-described study. In our study, mild thrombocytopenia was most commonly seen in 76 (76%) cases. In study by Nair PS *et al* [6] it was 56.8%. Platelet counts in the range of 20,000-50,000/cumm was seen in 16(16%) cases. severe thrombocytopenia i.e. count <20,000/cumm observed in 8(8%) cases. It was 25.7% in study by Nair PS *et al* [6]. Present study as compared to 13.39% cases in study by Gandhi AA *et al* [5], distribution of platelet counts correlates with the above-mentioned study. In our study, severe thrombocytopenia was present in dengue fever followed by falciparum malaria while moderate thrombocytopenia was common in viral fever, P. vivax and mixed malaria. Scrub typhus and septicemia had mild thrombocytopenia. in study by Gandhi AA *et al* [5] severe thrombocytopenia was seen in falciparum malaria while moderate thrombocytopenia was common in vivax malaria. And thus from these study it is evident that moderate thrombocytopenia is a feature of vivax malaria and severe thrombocytopenia is commonly seen in falciparum malaria. Thrombocytopenia in malaria is probably due to increased splenic sequestration, immune-mediated destruction and shortened platelet survival and consumption by disseminated intravascular coagulation [8]. Along, with quantitative defects, qualitative defects have also been documented, which are platelet hyperactivity due to aggravating agent like immune complexes and damage of endothelial cells followed by platelet hypoactivity. Which returns to normal in 1-2 weeks. Thrombocytopenia along with acute febrile syndrome is having 100% sensitivity, 70% specificity, 100% negative predictive value and 86% positive predictive value in malarial diagnosis [13]. Another study had reported 60% sensitivity and 88% specificity of thrombocytopenia for malaria diagnosis in acute febrile patients [14]. So we observed in our study, thrombocytopenia is commonly mild in febrile thrombocytopenia. In our study, severe thrombocytopenia was seen in 8(8%) cases while moderate thrombocytopenia was seen in 16(16%) cases. our results are similar with Gandhi AA *et al* [5]. Dengue is the most common arbovirus disease worldwide and occurs in tropical countries. Thrombocytopenia is an important finding and has got predictive and recovery parameter of dengue fever. There are two mechanisms of thrombocytopenia in dengue fever are impaired thrombocytosis as results of invasion of megakaryocytic by virus and peripheral platelet destruction [9, 12]. In our study we found 4 cases of scrub typhus with mild thrombocytopenia. In study by Venkategowda PM *et al* [10]. In India, scrub typhus was found in the subhimalayan region and southern India like tamilnadu and karala. High degree of clinical suspicion is necessary as the classical eschar is found in only few cases of scrub typhus and the disease remains undiagnosed due to non specific clinical presentation and limited diagnostic resources. Recently there are reported cases of scrub typhus in other part of the country. Also, early clinical suspicion and prompt institution of treatment reduce the development of the life threatening complication in scrub typhus. In our study, we also found 2 cases of mixed infection with scrub typhus and dengue and 2 cases of septicemia. There is no previous study, in which scrub typhus with dengue found. The etiology of thrombocytopenia in sepsis is multifactorial. It is commonly associated with disseminated intravascular coagulation and caused by spleen destruction of immune coated platelet, platelet adherence to damaged vascular surface and direct platelet toxicity caused by microorganism [15]. In our study, we did not find any cases of enteric fever as possible cause of febrile thrombocytopenia. In previous studies, Leptospira also is important cause of thrombocytopenia. But in our study, we are unable to include Leptospira as cause of thrombocytopenia because of lack of diagnostic facility for Leptospira in our institute. In our study, mortality was seen in only 2 cases but mortality was not related to the severity of thrombocytopenia. In our study, multiorgan dysfunction due to septicemia and complicated malaria seen in all those 2 cases. The similar results were observed in study by Lohitashwa *et al* [11].

Conclusion

Febrile thrombocytopenia is an important clinical condition commonly caused by infection. In our study, the commonest etiology of febrile thrombocytopenia was dengue fever. Thrombocytopenia due to infectious disease shows seasonal variation most commonly seen during rainy and winter season mostly in month of July to September. mortality in febrile thrombocytopenia is not directly associated with degree of thrombocytopenia but it is due to multiorgan dysfunction caused by septicemia and complicated malaria and thrombocytopenia is usually mild in febrile thrombocytopenia and majority case of febrile thrombocytopenia were asymptomatic but rarely there were evidence of life threatening bleeding in central nervous system, gastrointestinal and genitourinary system even death. Hence serial monitoring of platelet count is required and has predictive and recovery parameter in dengue fever. chance of bleeding manifestation increase with platelet

count below 20,000/cumm. So platelet count should be asked in all cases with fever. Treatment of underlying condition will lead to rapid improvement in platelet count with complete clinical recovery. This study helps in correlating the clinical features, laboratory values to determine possible cause of thrombocytopenia plus helping in the diagnosis and management of these patients. Also similar studies will help in finding changing trends of locally prevalent infectious disease and finding some new emerging disease not prevalent in the particular region.

References

1. Wood TE. The fever Pattern as a diagnostic Aid: In Fever: Basic mechanism and management.(ed Mackowiack P.A), New York, Lippincott-Raven Publishers, Philadelphia, 1997, 215-235.
2. Handian RI. Bleeding and Thrombosis. Chapter 62, In: Harrison principals of internal medicine, 15th Ed, Edt. Braunwald et al, USA: McGraw Hill,2001:1:358.
3. Firkin, Chesterman, Penangtion Rush. Edt., Hemorrhagic disorder; Capillary and platelet defect Chapter 14, In: Degruchys Clinical hematology in Medical Practice, 5th Ed; Oxford Blackwell science, 1989, 360.
4. Kumar P, Chandra K. A Clinical Study of Febrile Thrombocytopenia: A Hospital based Retrospective study. Indian Journal of Clinical Practice,2014:24(10):952-57.
5. Gandhi AA, Akholkar PJ.Clinical and Laboratory Evaluation of Patient with Febrile Thrombocytopenia. NJMR,2015:5(1):43-46.
6. Nair PS,Jain A, Khanduri U, Kumar V.A Study of fever associated with thrombocytopenia JAPI,51:1173.
7. Tong SengFah, Noorazah Abdul Aziz, Chin Gekliew, KLhairani Omar. Clinical features of Acute Febrile Thrombocytopenia among Patients attending primary Care Clinics. Malaysian Family Physician,2006:1:16-18.
8. Makkar RP Mukhopadhyay S, Monga A, Monga A, Gupta AK.Plasmodium vivax malaria presenting with thrombocytopenia. Braz J Infect Dis,2002:6:263-5.
9. ME Yeolekar, Munjal YP, Sharma SK, Agrawal AK, Gupta P. LKamath SA, Nadkar SA, Singal RK, Sundar S, Verma S, Pangtey GS, Prakash A Shah SN editors API Textbook of Medicine 9th edition Japyee brothers 2012 Chapter 42 Dengue:1158.
10. Venkategowda PM, Rao SM, Mutkule DP, Rao MU et al,Scrub Typhus: Clinical spectrum and outcome. Indian J Crit Care Med 2015Shirley PApr,19(4):208-213.
11. Lohitashwa SB, Vishwanath BM, Srinivas G.Clinical and Lab Profile of Fever with Thrombocytopenia. Abstract Free paper Oral Presentation-APICON, 2008 available at: http://www.japiorg/march 2009/oral presentation.
12. Jayashree K, Manasa GC, Pallavi P, Manjunath GV, Evaluation of platelets as predictive parametersin dengue Fever. Indian J Hematol Blood Transfus,2011:27(3):127-30.
13. Patel U, Gandhi G, Friedman S, Niranjan S, Thrombocytopenia in malaria.J Natl Med Assoc,2004:96(9):1212-4
14. Lathia TB, Joshi R. Can hematological parameters discriminate malaria from non malarious acute febrile illness in the tropics? Indian J Med Sci,2004:58(6):239-44.
15. Lee GR, Foerster J, Lukens J Paraskevas F, Greer JP, Rodgers GM, Shirley Parker Levine-Miscellaneous causes of thrombocytopenia. In: Wintrobe's Clinical Haematology.Vol.2, 10th edition, Lipincott Williams Philadelphia, 1999, 1623-9.