ORIGINAL RESEARCH ARTICLE

Evaluation of Clinical Profile of Fever with Thrombocytopenia in Patients Attending GIMSR, Visakhapatnam

Mudunuri Sitarama Lakshmi[1], Gandi Srinivasa Rao[2]

[1]Assistant Professor, Department of General Medicine, Gitam Institute of Medical Sciences and Research, Rushikonda, Visakhapatnam, [2]Assistant Professor, Department of General Medicine, Gitam Institute of Medical Sciences and Research, Rushikonda, Visakhapatnam, India

Corresponding author: Gandi Srinivasa Rao, Assistant Professor, Dept of General Medicine, Gitam Institute of Medical Sciences and Research, Rushikonda, Visakhapatnam, India

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ABSTRACT

Introduction: Fever has been recognized as a cardinal manifestation of disease since ancient times, as recorded by ancient scholars like Hippocrates. Infections like dengue, leptospirosis, malaria, typhoid, military TB, HIV, septicemia are some of the common causes of fever with thrombocytopenia. Study aimed to evaluate clinical profile of fever with thrombocytopenia in patients attending GIMSR, Visakhapatnam.

Material and Methods: Patients with fever with thrombocytopenia attending to (GIMSR) GITAMS Medical college during the period from July 2018 to June 2019 were studied. 100 patients presenting with fever with thrombocytopenia were taken up for study. Age and gender distribution, duration of fever, clinical features, platelet counts, bleeding manifestations, liver function tests and presence of various etiologies was studied.

Results: A total of 100 patients were studied. The patient age ranged from 14 years to 67 years and the mean age was 33.38 years (SD=14.19) and the male : female ratio was 1.44:1. The febrile illness with thrombocytopenia had maximum occurrence in the third (32%). The four diseases which contributed mainly to febrile thrombocytopenia in our study were acute viral fever (34%), Dengue (29%), Leptospirosis (13%) and Malaria (10%). The duration of fever ranged from 1-20 days with mean duration of 6.05 days and 92% of them had duration of < 10 days. Headache was the most common symptom other than fever in the present study. Derangement of LFT was also observed in most of the cases.

Conclusion: Febrile illness patients should be investigated for platelet count irrespective of bleeding manifestations. Strong probability of dengue fever or other common causes like viral fever and leptospirosis should be kept in mind in any case of fever and thrombocytopenia as decreased platelet count could be severe without external manifestation and could be an indicator of bad prognosis and require early platelet transfusion.

Keywords: Fever, Thrombocytopenia, Dengue Fever, Leptospirosis

INTRODUCTION

Fever has been recognized as a cardinal manifestation of disease since ancient times, as recorded by ancient scholars like Hippocrates.[1] Seen first as a disease but later recognized as an accompaniment to a variety of disease entities; fever is an easily noted and reliable marker of illness.[2]

Normal body temperature displays a diurnal pattern with lower values in the early morning hours and higher values in the afternoon. Normal ranges are between 36.5°C and 37.5°C (97.7°F and 99.5°F). Fever is superimposed on this pattern and thus temperatures are usually greatest in the afternoon and evening.

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

Many infections can have significant thrombocytopenia and Malaria is one such infection. It is endemic throughout most of the tropics and is common in India as well. WHO states that more than 207 million developed symptomatic malaria in 2012.[4]

Physicians use fever as a reliable guide to the presence of disease and the response of disease to therapy. It is in the diagnosis of febrile illness that the science and art of medicine come together.[5]

It is well known fact in medicine that one can diagnose a disease only when one is aware of the disease and looks for it. Thrombocytopenia was often missed, because it was not often looked for and the required investigation was not asked for. Now with increasing awareness of the association of thrombocytopenia with various illnesses especially with febrile illness, this entity is now viewed with due regards. Though thrombocytopenia is encountered in various diseases, it is fortunate that potentially fatal bleeding due to

thrombocytopenia is rare.[6]

The causes of thrombocytopenia are impaired platelet production, accelerated platelet destruction or dilution and/or splenic sequestration.[7]

Even though there is no absolute relation between platelet counts and bleeding, certain broad generalizations can be made, with counts less than 10,000/μl, bleeding is usual and may be severe.[8]

Thrombocytopenia correlates inversely with mortality and morbidity in various febrile illnesses, and serial monitoring of platelet counts has prognostic value. This highlights the importance of thrombocytopenia in various febrile disorders.[9]

Platelets play a central role in normal haemostasis and therefore also in thrombosis. Thrombocytopenia is characterized by bleeding most often from small vessels. This can manifest as petechiae over the skin, hemorrhages from mucosa of gastrointestinal and genitourinary tract. Intracranial haemorrhage is a dangerous consequence in thrombocytopenic patients.

Thrombocytopenia is defined as platelet count <1,50,000/μL. This is due to decreased production, increased destruction (immunogenic and non-immunogenic), and increased sequestration in spleen. Of these, infections is one of the commonest cause of thrombocytopenia.[10,11]

Infections like dengue, leptospirosis, malaria, typhoid, military TB, HIV, septicemia are some of the common causes of fever with thrombocytopenia.

Therefore a well organized systematic approach that is carried out with an awareness of causes of fever with thrombocytopenia narrows the differential diagnosis of the clinical entity and brings out diagnosis.

Study aimed to evaluate clinical profile of fever with thrombocytopenia in patients attending GIMSR, Visakhapatnam.

MATERIAL AND METHODS

Before stating the study, permission was taken from the Institutional Ethical Committee and Informed consent was taken from all patients included in the study.

Patients with fever with thrombocytopenia attending GIMSR Medical College during period of one year from July 2018 to June 2019 were taken into the study. 100 patients, selected by Simple random sampling, presenting with fever with thrombocytopenia were taken up for the study.

Inclusion criteria
Age from 14-70 years
Both genders
The patients presenting with fever < 2 weeks duration
Patients admitted with fever and found to have thrombocytopenia, that is platelet count < 1.5 lakhs were included in the study

Exclusion criteria
Age below 14 years and above 70 years
Patients with prolonged fever > 2 weeks duration
Patients with fever and no thrombocytopenia
Patients with thrombocytopenia without fever
Once the patients with fever and thrombocytopenia were admitted, a careful history was recorded, and general physical examination and detailed examination of various systems was done. Routine investigation were done. The specific and special investigations were done as and when indicated. In those patients where a final definite diagnosis was reached, were treated for the disease and platelet counts were repeated. Details of history, general physical examination and laboratory investigation reports were noted down from time to time.

The diagnostic work up of patients with fever and thrombocytopenia was done including battery of investigations such as biochemical tests, hemograms, peripheral smear examination, QBC for Malarial parasite, WIDAL test, for dengue fever, IgM ELISA was done, Leptospiral antibodies test. Also Blood cultures were done in some cases.

RESULTS

The present study includes 100 patients who were admitted for acute febrile illness with thrombocytopenia in GIMSR, Visakhapatnam, between July 2018 to June 2019.

Males were more commonly involved than females in all age groups in the present study. The male: female ratio was 1.44:1 (table-1).

The patient age ranged from 14 years to 67 years and the mean age was 33.38 years (SD= 14.19years). The febrile illness with thrombocytopenia had maximum occurrence in the age group of third decade (32%) followed by second decade (23%) and was evenly distributed in the fourth and sixth decades having19% and 16% patients respectively.

were Acute viral fever (34%), Dengue (29%), Leptospirosis (13%) and Malaria (10%). Acute febrile illness with thrombocytopenia due to above causes occurred maximum in second and third decades (table-2).

The duration of fever in the present study ranged from 1-20 days with mean duration of 6.05 days (SD=3 days). In 92% of the cases the duration was < 10 days.

Headache was the most common symptom other than fever (32%) in the present study. Other prominent symptoms in the descending order of frequency were myalgia (31%), vomiting (27%), joint pain (10%) pain abdomen (6%) and altered sensorium in (1%) cases (table-3).

Hepatosplenomegaly contributed to major signs in the present study (21-24%). Petechiae and conjunctival hemorrhage were seen in 20% cases, followed by jaundice (17%) cases.

In the present study platelet count varied from 10,000 to 1 lakh/cumm. The platelet count for the patients with bleeding episodes ranged from 18000 to 40000/cumm in the present study (table-4).

Age (in years)	Males (n=59)	Females (n=41)	Total (%)
14-20	4	9	13
21-30	20	12	32
31-40	10	9	19
41-50	7	1	8
51-60	8	8	16
61-70	0	2	2
Total	49	41	100 (100%)
Table-1: Age and gender distribution in present study			

Age (in years)	Dengue	Viral fever	Leptospirosis	Malaria
14-20	7	10	2	3
21-30	9	16	4	3
31-40	7	4	2	3
41-50	3	0	4	1
51-60	2	4	1	0
61-70	1	0	0	0
Total	29 (29%)	34 (34%)	13 (13%)	10 (10%)

Table-2: Age distribution for various etiologies

Days	Number of days	Percent (%)
1-5	55	55%
6-10	37	37%
11-15	6	6%
>15	2	2%
Total	100	100%

Table-3: Duration of fever at the time of presentation

Platelet count/cumm	No. of patients	Percent (%)
10001-20000	5	5%
20001-40000	20	20%
40001-60000	18	18%
60001-80000	27	27%
80001-100000	30	30%
Total	100	100%

Table-4: Platelet count in present study

Platelet count	Dengue	Viral fever	Leptospirosis	Malaria
10000-20000	5	1	0	0
20000-40000	13	5	1	0
40000-60000	4	4	6	0
60000-80000	3	16	3	4
80000-100000	4	8	3	6
Total (86)	29	34	13	10

Table-5: Platelet count in different etiologies

Site of bleeding	<20000	20000- 40000	40000-60000	60000-80000	80000-100000
Petechiae	5	10	0	1	0
Gum bleeding	2	3	0	1	0
Conjunctival haemorrhage	0	1	2	0	1
Petechiae+gum bleeding	2	2	0	1	0
Petechiae+epistaxis	0	1	0	0	0
Malena	0	1	0	0	0
Petechiae+conjunctival Hg	0	1	0	0	0

Table-6: Bleeding manifestation and platelet count

LFT	Viral fever			Dengue			Leptospirosis			Malaria		
	Total Bilirubin	SGOT	SGPT	Total Bilirubin	SGOT	SGPT	Total Bilirubin	SGOT	SGPT	Total Bilirubin	SGOT	SGPT
Normal	25	21	23	12	10	9	3	2	2	7	7	8
Abnormal	9	13	11	17	19	20	10	11	11	3	3	2

Table-7: Liver function tests in different etiologies

Etiology	Nair et al[14]	Lakum et al[6]	Dash et al[13]	Raiker et al[12]	Present study
Dengue	13.8%	35.4%	20%	52%	29%
Malaria	9.2%	46.8%	45%	45%	10%
Enteric fever	14.7%	4.6%	10%	3%	1%
Leptospirosis	-	-	2%	-	13%
Septicaemia	26.6%	7.8%	21%	-	13%
Viral Fever	18.3%	-	-	-	34%
Table-8: Comparison of etiology of fever with thrombocytopenia in various studies					

Total platelet count varied according to the etiology. Dengue fever caused severe thrombocytopenia. Out of 29 cases of dengue fever 17.24% had platelet count <20000, 44.83% had platelet count in the range of 20001-40000/cumm. Of 34 cases of Viral fever, 2.94% had severe thrombocytopenia <20000/cumm, 14.71% had counts in the range of 2000-40000, 82.35% had platelet counts of >40000/cumm. In Leptospirosis 7.69% of patient had platelets in the range of 2000-40000, 92.31% of patients had plateletcount of >40000/cumm. In Malaria none had <40,000/cumm. This showed that severe thrombocytopenia occurred more in patients with dengue fever in the present study (table-5).

Out of 100 patients of fever with thrombocytopenia, other viral fevers (34%) was the commonest cause followed by dengue fever (29%), leptospirosis (13%), septicemia (13%), malaria (10%) and enteric fever (1%) in the present study.

Bleeding manifestation in the form of petechiae was a common manifestation of thrombocytopenia. Petechiae with and without gum bleeding/epistaxis/conjunctival hemorrhage occurred in 16% of patients in the present study. The gum bleeding alone happened in 1% of patients, conjunctival hemorrhage alone in 3% of patients and Malaena in 1% patients was encountered.

There was no relation between platelet count and bleeding manifestation and maximum number of bleeding episodes occurred when the platelet count was in the range of 20000-40000/cumm. The majority of the patients in our study had total leukocyte count in the range of 2000 to 4000/cumm (40%) as expected in viral fever (table-6).

Abnormal total bilirubin levels were seen in 26.47% cases. Abnormal SGOT was seen in 38.24% and abnormal SGPT was seen in 32.35% cases in viral fevers.

Dengue fever casesand Leptospirosis cases also showed high or deranged LFT in considerable number of cases (table-7).

DISCUSSION

The present study included 100 patients of fever with thrombocytopenia in which males were more affected than females; 59% were males and 41% were females and the ratio was 1.44:1.

Comparative studies based on age distribution

In the present study, the maximum prevalence of fever with thrombocytopenia was in the age group of 21-30 years with 32% patients. The least number of patients were in ≥60 year age group with only 2% accounting for it. In the study by Raiker et al[12] they also observed maximum number of cases to be in the age range of 12 - 30 years accounting for 66% of cases and least prevalence was observed in > 60 years age group accounting for 10% of cases. Age distribution in both studies

is well correlated. In both the studies maximum prevalence was seen in younger age group and least prevalence was seen in older age group.

Comparative studies based on gender distribution

In the present study, males were 59 (59%) and females were 41 (41%) and male to female ratio was 1.44: 1. In a study of fever with thrombocytopenia by Dash et al[13] male to female ratio was 1.5:1. In Raiker et al[12] study this ratio was 2.7:1 and in the study by Lakum N et al[6] it was 1.85:1.

Comparative studies based on clinical signs and symptoms

In the present study, fever was seen in 100% of the cases. Other than fever, headache was the most common symptom seen in 32 (32%) cases, followed by myalgias (31%), vomiting (27%), pain abdomen (6%), bleeding manifestations (3%), and altered sensorium (1%) cases. In the study by Lakum N et al[6] fever was the presenting complaint in all cases, weakness in 40% of cases, weight loss in 10% of cases and bleeding was the presenting complaint in 10% of cases.

In the present study, most commonly detected signs were splenomegaly (24%), hepatomegaly (21%), jaundice (17%), and petechiae (16%). Other signs included pallor (7%) and conjunctival hemorrhage (4%). In the study by Lakum N et al[6] most common finding was pallor and was seen in 70% of cases, followed by splenomegaly in 45% of cases, hepatomegaly in 35% of cases and lymphadenopathy was seen in 10% of cases. Table 8 shows comparison of etiology of fever with thrombocytopenia in various studies.

Comparative studies based on platelet count

In ourstudy, platelet count of ≤40000/cumm was seen in 20% of patients and 18% of patients had platelet count of 40000-60000/cumm. 27% patients had platelet count of 60000-80000/cumm and 30% of patients had platelet count in the range of 80000 to 100000/cumm. In the present study 20% of patients had platelet count between 20,000-40,000/cumm and 75% had platelet count above 40,000/cumm. In the study by Dash et al[13] majority of patients (26%) had platelet count in the range of 61000 – 80000/cu.mm, followed by 25% (21000 – 40000/cu.mm), 19% in the range of 81000-100000/cu.mm, 17% of cases in the range of 0- 20000/cu.mm, 13% of cases in the range of 41000 – 60000/cumm. Results of this study correlate well with the above study. In both the studies, majority of patients were in the range of 61000 – 80000/cu.mm.

In the study by Raikar et al[12] no correlation was seen between the platelet count and bleeding manifestations. In the study by Dash et al[13] bleeding manifestations in the form of petechiae and purpura were seen in 35% of cases and spontaneous bleeding was seen in 18% of the cases.

Liver Function Tests in different etiologies

The total bilirubin level was abnormal in 26.47% of viral fever cases, 58.62% of dengue fever cases and 76.92% of leptospirosis cases and 30% of malaria cases in the present study. The abnormal SGOT was seen in 38.24% of viral fever cases, 65.52% of enteric cases, 84.62% of leptospirosis and 30% of malaria cases in the present study. The abnormal SGPT was seen 32.35% of viral fever cases, 68.97% of dengue fever cases, 84.62% of leptospirosis and 20% of malaria cases in the present study. This shows that abnormal liver function test was more prevalent in leptospirosis and dengue fever because of dengue hepatitis and hepatitis in leptospirosis.

Out of 100 cases, 8 cases died. Four deaths were due to septicaemia accounting for 50% of cases. Two cases died due to dengue shock syndrome contributing to 25% of deaths, and two cases died due to malaria contributing to 25% of deaths. In the study by Dash et al[13] 22 cases died. Septicaemia contributed to 77% of cases. Dengue contributed to 5% of cases and malaria contributed to 18% of cases. So in all the studies septicaemia, dengue, malaria were causes of mortality. In septicaemia, cause of mortality was DIC and multiorgan dysfunction. In Dengue, deaths were due to dengue shock syndrome. In malaria deaths were due to DIC and multiorgan dysfunction.

So strong probability of dengue fever or other common causes like malaria, enteric fever, septicaemia and leptospirosis should be kept in mind in any case of fever and thrombocytopenia to start empirical therapy before final diagnosis is reached so that high mortality can be prevented.

CONCLUSION

Febrile illness patients should be investigated for platelet count irrespective of the bleeding manifestations. Strong probability of dengue fever or other common causes like viral fever and leptospirosis should be kept in mind in any case of fever and thrombocytopenia as decreased platelet count could be severe without external manifestations and could be an indicator of bad prognosis if not treated early with platelet transfusion.

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