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A Study of Clinical Profile of Patients with Febrile Thrombocytopenia.

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ABSTRACT

Background: Febrile thrombocytopenia is one of the unrecognized complication which may be missed if platelet count is not done routinely. Increased awareness and early recognition of thrombocytopenia can avoid catastrophes like fatal bleed. The aim of study is to find clinical presentation of patients with febrile thrombocytopenia and find causes and complications associated with febrile thrombocytopenia. **Methods:** In the present study 107 patients who presented to Shri B. M. Patil Hospital with fever with thrombocytopenia who fulfil inclusion criteria are included in study, a detailed history general physical examination, investigations were performed and patients were treated symptomatically and specifically after diagnosis. **Results:** In the present study subjects were in the age group of 18-80 years. Youngest was 18 years old and oldest 80 years. In the present study out of 107 cases of fever with thrombocytopenia, 79 were males and 28 were females. Out of 107 patients of fever with thrombocytopenia, 102 had definitive diagnosis with Dengue 54 cases as the commonest cause, followed by Malaria which constituted 40 cases, Mixed infections 3 cases(Dengue fever with enteric fever, Vivax malaria, falciparum malaria), Acute Gastroenteritis 2 cases, Urinary tract infections 1 case, Leptospirosis 2 cases and Enteric fever 2 cases and Unknown causes accounted for 5 cases. In our study 61 patients had platelet count less than 60,000 cells/cumm, whereas 46 had above 60,000 cells/cumm. Common range of platelet count was from 41,000 – 60,000 cells/cumm in 27 cases.Of 107 patients 104 of them recovered and 3 expired with mortality of 2.8% with All 3 patients had MODS. **Conclusion:** In all cases of Febrile thrombocytopenia, thrombocytopenia led to various bleeding manifestations and influenced the clinical profile of these illnesses. Petechiae were the most common bleeding manifestation. The spectrum varied from mild self-limiting disease to severe fatal disease. This highlights the need for rapid diagnosis and appropriate management of patients to prevent complications.

Keywords: Platelet Count, Thrombocytopenia.

INTRODUCTION

Fever is such a common manifestation of infectious illness that it is not surprising to find accurate descriptions of the febrile patients in early-recorded history. Normal body temperature is 37.0 °C or 98.6 °F. The normal range is quite wide, being affected by site of measurement, diurnal variation, heavy exercise, hormonal and menstrual status, individual variation, and environmental factors. A patient's body temperature is often estimated by measurements taken in the mouth for reasons of convenience, but oral temperatures can be affected by mouth-breathing, by the respiratory rate, and by recent drinking of hot or cold liquids.[1]

"Febrile thrombocytopenia is one of the common complications which may be missed if platelet count is not done routinely. Increased awareness and early recognition of thrombocytopenia can avoid catastrophes like fatal bleed. Thrombocytopenia has an inverse relation to mortality and morbidity is various febrile illness, serial monitoring of platelet counts has prognostic value. This highlights the importance of thrombocytopenia in various febrile disorders. As the fever course is prolonged and fever with thrombocytopenia narrows the differential diagnosis of the clinical entity.[2]

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 and thus treatment. Hence, a need for study to know the causes and complications and varied manifestations thrombocytopenia of infective etiology.

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Aims and objectives of the study

- To study the clinical presentation of febrile thrombocytopenia.
- To identify the cause of febrile thrombocytopenia.

- To study the complications in relation to febrile thrombocytopenia.

MATERIALS AND METHODS

Method of Collection of Data:

Inclusion Criteria:

1. Patients with platelet count less than 1,50,000 cells / cumm.
2. Patients more than 18 years of age.
3. History of fever for less than 2 weeks. Fever defined as oral A.M. temperature of >37.2°C (>98.9°F) or a P.M. temperature >37.7°C (>99.9°F).

Exclusion criteria:

1. Patients less than 18 years of age.
2. Patients with chronic diseases like malignancy ,haematopoic disorder.
3. Patients with drug induced thrombocytopenia. Idiopathic thrombocytopenic purpura.

Statistical Method

Data will be analyzed using

1. Mean SD
2. T test
3. Chi-square test

RESULTS

A total number of 107 patients admitted over a period of two years from December 2016 to June 2018 in BLDE (Deemed to be University) SHRI. B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTER were studied.

In the present study subjects were in the age group of 18-80 years. Youngest was 18 years old and oldest 80 years. In the present study out of 107 cases of fever with thrombocytopenia, 79 were males and 28 were females. Out of 107 patients of fever with thrombocytopenia, 102 had definitive diagnosis with Dengue 54 cases as the commonest cause, followed by Malaria which constituted 40 cases, Mixed infections 3 cases (Dengue fever withenteric fever, Vivax malaria falciparum malaria), Acute Gastroenteritis 2 cases, Urinary tract infections 1 case, Leptospirosis 2 cases and Enteric fever 2 cases and Unknown causes accounted for 5 cases. Out of 40 Malaria cases, Vivax Malaria constituted 31 cases, with 5 cases of Falciparum malaria and 4 cases of Mixed Malaria (Vivax and falciparum both).

The 3 Mixed infections included Dengue fever with Enteric fever, Vivax malaria and Falciparum malaria. In our study 61 patients had platelet count less than 60,000 cells/cumm, whereas 46 had above 60,000 cells/cumm. Common range of platelet count was from 41,000 – 60,000 cells/cumm in 27 cases. Bleeding manifestations were present in 52 patients and there were no clinical manifestations of thrombocytopenia in 55 patients.

Out of 52 patients with bleeding manifestation 43 patients (82.7%) had petechiae, bleeding gums in 25 patients (48%). Malena was present in 12 patients (23%), epistaxis in 4(7.7%).

Of 107 patients 104 of them recovered and 3 expired with mortality of 2.8% with All 3 patients had MODS.

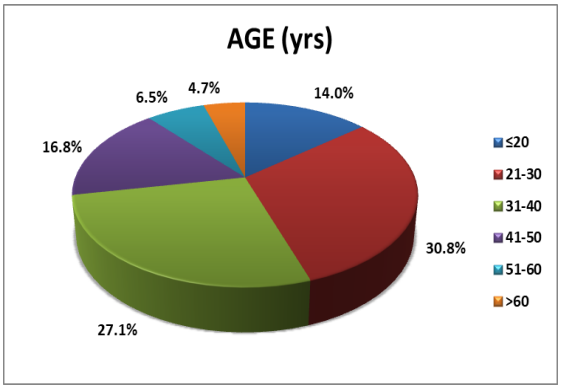

Figure 1: Age Distribution

Highest number of cases seen in the age group of 21 - 40 years is 62 cases (57.9%) followed by 41 – 60 years in 25 cases (23.3%).youngest was 18 yrs old whereas eldest was 80 years old. Mean age was 33.69 years

Table 1: clinical presentation of patients studied (n=107)

Symptoms	N	%
Chills	98	91.6
Rigors	62	57.9
Cough	15	14
Headache	25	23.4
Jaundice	7	6.5

98 patients presented with chills, of which 62 had rigors. 25 patients had headache followed by 15 patients with complains of cough and 7 with jaundice.

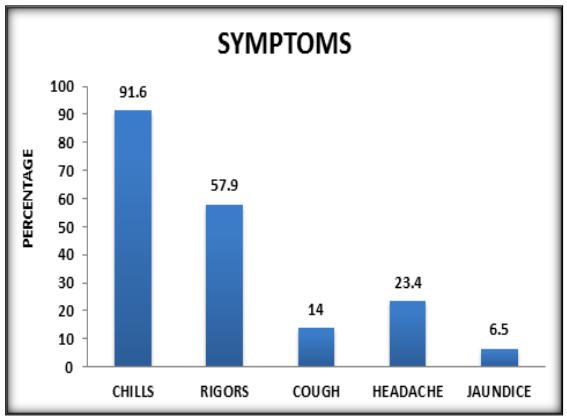

Figure 2: Clinical Presentation of Patients Studied (N=107)

Table 2: Bleeding Symptoms of Patients Studied (N=107)

Bleeding symptoms	N	%
Rash	43	40.2
Itching	36	33.6
Gums	25	23.4
Malena	12	11.2
Hematemesis	1	0.9
Others	11	10.2

Among Bleeding manifestations, 43 presented with petechial rash, 25 with bleeding gums, 12 with malena, 1 with hematemesis.

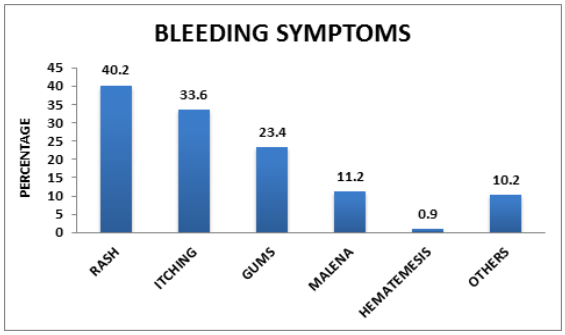

Figure 3: bleeding symptoms of patients studied (n=107)

Table 3: correlation of bleeding manifestations with platelet counts

Platelet count	Rash	Itching	Gums	Malena	Hematemesis	Others	Total
≤20000	3	2	1	0	0	1	12
21000-40000	12	7	9	4	0	2	19
41000-60000	13	13	8	4	0	5	30
61000-80000	6	4	4	2	1	1	16
81000-100000	4	4	2	1	0	1	17
>100000	5	6	1	1	0	1	13
Total	43	36	25	12	1	11	107

Table 4: correlation with serious complications

Diagnosis	Complications	Mods
AGE	1	0
DEN	4	1
ENT	1	1
FM	4	1
LEPTO	1	1
MM	1	0
UTI	1	0
VIR	5	3
VM	15	2
Total	33	9

Table 5: distribution of complications

Complications	N	%
AKI	7	6.6
ARDS	6	5.6
HEMOPERITONEUM	1	0.9
HEMOPTYSIS	1	0.9
HEP	6	5.6
MODS	9	8.4
PNEUMONIA	1	0.9
SDH	1	0.9
Total	32	29.9

DISCUSSION

A total number of 107 patients admitted over a period of two years from December 2016 to June 2018 in Shri. B. M.Patil Medical College, Hospitaland Research Center were studied.

In the present study, subjects were in the age group of 18-80 years, youngest being 18 years old and the eldest 80 years. The mean Age was 34.7 years which was similar in comparison to studies by Majumdar R et al, Riaz MM et al and SahuS et al,[40-42] The most common age group involved was from 18 to 40 years of age including of 72% of patients. This was similar to a study conducted in Kolkata in 2012 by Majumdar R et al.[40] Splitting the age group further, 57 cases from our study had an age group range from 21 to 40 years (53.77%). This was in contrast to a study conducted by Dash et al in 2010 in Andhra Pradesh which had majority as 26% cases ranging in age group 61 to 80 years. The difference in age group probably was due to different admission and treatment policies in different medical institutions.[43]

In the present study out of 107 cases of fever with thrombocytopenia, 79 were males and 28 were females depicting a male preponderance. This correlated with various studies conducted by Dash H S et al,[43] Debarati Gupta et al,[44] Emmanuel Bhaskar et al,[45] and many others.[46] Majority of cases in our study were admitted in rainy and early winter season among which 20 cases were admitted in the month of June. Malaria cases had a surge in rainy season similar to a study conducted in Bhavnagar in 2013 by Raikar S R et al,[50] whereas Dengue fever had onset in rainy season with post monsoon surge similar in pattern to a study in Lucknow done by Karoli R et al.[47]

Fever associated with chills (91.6%) and rigors (57.9%) were the most common symptoms of patients whereas bleeding manifestations were present in 52 patients (49%). This presentation was comparable to studies carried out by Emmanuel Bhaskaret al,[45] Gregory C J et al,[46] Karoli R et al,[47] and Umm-e-Asma, FarhaTaufiq, Wajihullah Khan study in Aligarh.[51] Malaria patients presented with chief complaints of fever with chills and rigors, and also had complaints of cough (26%) and headache (28%). This observation was similar to studies by Umm-e-Asma, FarhaTaufiq, Wajihullah Khan,[51] Hasan Abu Zaid et al.[52]

In contrast patients with Dengue fever were admitted with chief complaints of chills and rigors, but a significant number of patients had complaints of rash (59.3%) and itching (31.5%) similar to a study carried out in Chennai by Emmanuel Bhaskar et al (46%).[45] The most common sign on examination was petechiae (39.9%) followed by Icterus was present in 18 patients (16.8%). Splenomegaly was present in 3 patients of 107 cases (2.8%) all of which

had Malaria. Most common sign was petechiae comparable to many other studies like Emmanuel Bhaskar45, Christopher C G et al,[46] Lee M S et al,[53] Karoli R et al,[47] Khan et al,[48] Nair P S etal,[49] Dash H S et al.[43] Of all the total malaria cases splenomegaly was present in 9 out of 42 cases (21.4%) This similarity was also depicted in various studies conducted in Doha (Qatar) conducted by Hassan Abu Zaid et al,[52] Aligarh by Umm-e Asma, FarhaTaufiq, Wajihullah Khan and New Delhi by Sharma S et al which indicates splenomegaly is the most common presentation in cases of malaria.[51,54] These variations can be attributed to variation in the immune status of patients in different endemic areas of malaria.

Among the bleeding manifestations which were present in 52 patients (49%), Petechiae was the most common bleeding manifestation (95%) which was consistent with other studies such as Dash H S et al (66%),[43] Gregory C J et al (21%),[46] Karoli R et al (26%),[47] Khan et al,[48] Nair P S et al,[49] Lee M S et al.[53] Bleeding gums was the second most common manifestation present in 25 patients (23.58%). In contrast, gingival bleeding was the commonest bleeding manifestation in the study conducted in Chennai by Emmanuel Bhaskar et al,[45] accounting for 68% of bleeding manifestations.

Dengue fever with 54 cases was the leading cause of febrile thrombocytopenia in our study, similar to a study conducted in Bhavnagar, Gujarat by Raikar S R et al in 2013.[50] However the study by Nair P S et al,[49] revealed that Septicemia was leading cause of febrile thrombocytopenia. On the contrary, in a study by Dash H S et al, Malaria was the leading cause of fever associated with thrombocytopenia.[43]

Table 6: Diffrences with respect to etiologies.[43,49]

Mostcommon Causes (%)	Our study	Raikar S R et al	Nair P S et al	Dash H S et al
First	Dengue fever (50.5%)	Denguefever (52%)	Septicemia (26.6%)	Malaria (45%)
Second	Malaria (37.4%)	Malaria (45%)	Typhoid Fever (14.7%)	Septicemia (21%)

Table 7: Comparison of bleeding manifestations between present study and other studies.[43,49]

Bleeding manifestations	Present study		Nair et al		Dash et al	
	No. of Cases	Percentage	No. of cases	Percentage	No. of cases	Percentage
Present	52	49.05%	45	41.28%	53	53%
Absent	55	50.95%	64	58.72%	47	47%

Table 8: Diffrences of incidence of bleeding manifestations

Bleeding manifestations	Our study	Nair P S et al
Most common	Petechiae (40.2%)	Petechiae (9.2%)
Second most common	Bleeding gums (23.4%)	G I Bleed (9.2%)
Third most common	G I bleed (11%)	Epistaxis (6.4%)
Fourth most common	Epistaxis (3.77%)	Bleeding gums (5.5%)

Table 9: Complications in cases of malaria in comparison with other studies

Complications in malaria	Our study	Saya R P et al	Sharma S et al	Bhattacharjee P et al	Kochar DK et al
Hepatopathy	30 %	38%	25.6%	16%	58%
AKI	29.16%	-	-	12%	6%
ARDS	18.75%	-	5.6%	13%	2%

The difference in incidence of etiologies is probably due to epidemic of Dengue fever in the year 2015. Another important factor to be considered is that diagnostic modalities for Dengue fever were limited in year 2003 when Nair P S et al conducted his study in New Delhi.[49]

Out of 107 patients, 19 patients (17.8%) had platelet count in range of 41,000 – 60,000 cells/cumm as compared to study by Dash H S et al which had 26 patients (26%) in the range of 61,000 – 80,000 cells/cumm43. This difference can be attributed to difference in prevalence of disease, associated drug resistance and varying serotypes of the causative organisms.

Petechiae/pupurawas commonest bleeding manifestations in all three studies.

The present study indicated that 55.50% of patients had platelet count less than 50,000 cells/cumm whereas 39.62% had between 50,000 to 1,00,000 cells/cumm and 3 patients had more than 1,00,000 cells /cumm correlating with results of study by Ruhi Khan et al, who conducted a study in Aligarh on patients with Dengue fever, had 69.7% patients in the range of 0 – 50,000 cells/cumm, 4.7% patients between 50,000 – 1,00,000 cells /cumm, and 25.6% patients above 1,00,000 cells /cumm55.

Complications of cases with febrile thrombocytopenia were analyzed in our study which indicated that 32 patients out of 107 had one or more organ involvement.

Among complications, hepatopathy consisted of 6 cases, AKI 7 cases, ARDS 6 cases and MODS consisted of 9 cases.Majority of cases of MODS consisted of triad of AKI, ARDS and Hepatopathy.

All the 3 deaths in our study revealed MODS (Multiorgan Dysfunction Syndrome).MODS

contributed to 67% of mortality consistent with a study in Rajasthan by Kochar D K et al wherein MODS contributed to 71% of mortality causes 57. 20 out of 40 cases of Malaria developed complications. Of these 15 were Vivax Malaria cases, 4 Falciparum Malaria and 1 Mixed Malaria.

Hepatopathy contributed to 12 cases out of 40 (30%) similar to studies in Mangalore by Saya R P et al (38%) 58, New Delhi by Sharma S et al (25.6%) 54, Kolkata by Bhattacharje P et al (16%) 59 and Bikaner by Kochar D K et al (58%)57

This study noticed complications in Vivax malaria at alarming rate which was usuallyconsidered as benign infections in the past. This warrants immediate attention and change in treat-ment strategy.

CONCLUSION

The present study was conducted among admitted patients of Shri B M PatilMedicalCollege,Hospital from December 2016 to June 2018 over a period of two years. 107 patients participated in the study.

1. Maximum prevalence was observed in younger age group.
2. Male preponderance was observed, with male to female ratio of 2.8:1
3. Fever with chills was the main presenting complaint which was also associated with rigors. Patients with Malaria presented with chief complaints of fever with chills whereas patients with Dengue fever presented with rash over the limbs associated with itching.
4. On clinical examination, Petechiae was the most common sign followed by Hepatomegaly and then Splenomegaly.
5. In all cases of Febrile thrombocytopenia, thrombocytopenia led to various bleeding manifestations and influenced the clinical profile of these illnesses.
6. Petechiae were the most common bleeding manifestation followed by bleeding gums and then malena.
7. Among the 107 cases, Dengue was the most common cause in 54 patients. Malaria comprised of 40 cases out of which 31 were Vivax Malaria, 5 were Falciparum Malaria, and 4 were mixed malaria.
8. The spectrum varied from mild self limiting disease to severe fatal disease.
9. In the present study there were no bleeding manifestations in many cases, hence signifying that there may not be bleeding manifestations in all cases of febrile thrombocytopenia. In majority of the patients platelet count improved to almost normal level with treatment, hence thrombocytopenia can be transient and asymptomatic.
10. Among the propensity to cause serious complications, Vivax Malaria had maximum tendency to cause complications.
11. However, of 5 undiagnosed cases, 4 patients had serious complications and 3 patients had MODS (Multiorgan Dysfunction Syndrome). This sadly points towards the conclusion that with the available diagnostic modalities there still exists a darker environment with respect to undiagnosed conditions. So much more awareness, vigilance and research is needed.
12. This highlights the need for rapid diagnosis and appropriate management of patients to prevent complications.

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Abbreviations

AGE - ACUTE GASTROENTERITIS
BBB - BLOOD BRAIN BARRIER
CMV - CYTOMEGALOVIRUS
CNS - CENTRAL NERVOUS SYSTEM
CR - COMPLEMENT RECEPTORS
CRP – C - REACTIVE PROTEIN
DEN - DENGUE FEVER
ENT - ENTERIC FEVER
EBV - EPSTEIN BARR VIRUS
EP - ENDOGENOUS PYROGENS
FM - FALCIPARUM MALARIA
HAV - HEPATITIS A VIRUS
HCV - HEPATITIS C VIRUS
HBV – HEPATITIS B VIRUS
HHV – HUMAN HERPES VIRUS
HIV -HUMAN IMMUNODEFICIENCY VIRUS
IE – INFECTIVE ENDOCARDITIS
IFN – INTERFERONS
IL – INTERLEUKINS
ITP –IMMUNE THROMBOCYTOPENIC PURPURA
LBP – LIPOPOLYSACCHARIDE BINDING PROTEIN
LPS – LIPOPOLYSACCHARIDES
LEPTO – LEPTOSPIROSIS
MM – MIXED MALARIA
MODS – MULTIORGAN DYSFUNCTION SYNDROME
OVLT - ORGANUM VASCULOSUM OF LAMINA TERMINALIS
PAF – PLATELET AGGREGATING FACTORS
PF – PLASMODIUM FACTORS
PMP - PLATELET MICROBICIDAL PROTEIN
PG – PROSTAGLANDINS

ROS – REACTIVE OXYGEN SPECIES
SLE – SYSTEMIC LUPUS ERYTHEMATOSUS
TLR – TOLL LIKE RECEPTORS
TF – THROMBIN FACTORS
TNF – TUMOUR NECROSIS FACTOR
UTI – URINARY TRACT INFECTION
VM – VIVAX MALARIA
VWF – VON WILLEBRAND FACTOR

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