Original article

A Study of clinical and laboratory profile of patients having fever with thrombocytopenia and its outcome

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ABSTRACT

Background:- Fever with thrombocytopenia have diverse aetiology ranging from idiopathic, infectious to malignancies. In tropical country like India usually it has infectious aetiology and the most common infection is malaria. Outcome depends upon the underlying cause more than the severity of thrombocytopenia.

Aim and objectives:-

- To study clinical and laboratory profile in patients with fever with thrombocytopenia.
- To find correlation between degree of thrombocytopenia and bleeding manifestations.
- To study outcome of patients having fever with thrombocytopenia.

Material and Methods:- It is a study of 100 patients aged > 14 years, during March 2015 to December 2015. From the patient's records, the clinical details of patients having fever with thrombocytopenia along with relevant investigations as the case may be and outcome were noted down.

Results:- Among all the cases 78% were having infectious aetiology and malaria (28.2%) was the common cause. There was 8% mortality and septicemia (87.5%) was the common cause of mortality. There was no correlation found between degree of thrombocytopenia and bleeding manifestations and also between severity of thrombocytopenia and mortality.

Conclusion:- Infections were the commonest cause & Malaria was the major cause of fever with thrombocytopenia. There was 8% mortality and septicemia was the major cause. A well organized systemic approach for fever with thrombocytopenia can help to diagnose the cases early which will reduce morbidity, mortality & cost associated with it.

Key words– Fever, Thrombocytopenia, Malaria, Septicemia, Bleeding manifestations, Mortality

INTRODUCTION

Fever is a common symptom caused by various diseases. It usually occurs as a response to infection or inflammation. Many times fever is associated with thrombocytopenia. [1] Platelet is important element in the blood for blood coagulation. Thrombocytopenia is defined as a reduction in the peripheral blood platelet count below the lower limit of 1,50,000/cmm. Thrombocytopenia results from artifactual thrombocytopenia, deficient production, accelerated destruction and abnormal distribution or pooling of platelets within the body. There is no absolute relationship between the platelet count and the occurrence and severity of bleeding. When there is associated infection bleeding may occur with relatively mild thrombocytopenia, functional defects contributing to bleeding. [2], [3] The etiology of thrombocytopenia is diverse and range from

idiopathic, infectious to malignancies. In tropical country like India patients getting acute febrile illness usually have an infectious etiology and many of these are associated with thrombocytopenia. Infections like Malaria, Dengue, Leptospirosis, Typhoid, HIV, Milliary tuberculosis, Septicemia are some of the common causes of fever with Thrombocytopenia. [3] Early diagnosis can prevent fatal outcome such as intracerebral bleed, hemorrhage into vital organs, shock and death. [2-8]

Most of the time patients of fever with thrombocytopenia do not show clinical bleeding manifestations. So in every case of fever, platelet count should be carried out as a routine investigation to find out the associated thrombocytopenia which will help to short list the differential diagnosis of fever. Thus a well organized systemic approach needs to be carried out for fever with thrombocytopenia which can help to diagnose the cases early. This will reduce the cost, morbidity and mortality associated with it. [1, 5, 7-12] This prospective study was carried out with the aim to evaluate clinical and laboratory profile in patients having fever with thrombocytopenia, its various causes, to find correlation between degree of thrombocytopenia and bleeding manifestations which will help the clinicians to know the correct time for platelet infusion thus minimizing unnecessary platelet transfusion, to study outcome of patients having fever with thrombocytopenia. This type of study will guide the clinicians for approach of a patient with febrile illness to diagnose the case early which will help to reduce the morbidity and mortality associated with it.

MATERIALS AND METHODS

This prospective study was carried out on patients of fever with thrombocytopenia who were admitted in Medicine ward of KIMS, Karad, Maharashtra for a period from March 2015 to December 2015. A total of 100 patients of fever with thrombocytopenia were included in the study.

- **Inclusion criteria:-**

  The patient aged more than 14 years, admitted with fever i.e. A.M. temp of $>37.2^0$C ($>98.9^0$F) and P.M. temperature of $>37.7^0$C (99.9^0F) and found to have thrombocytopenia.

- **Exclusion criteria:-**

  1) Patient aged below 14 years,

  2) Patient with fever but not associated with thrombocytopenia,

  3) Patient with thrombocytopenia but having no fever.

- **Study procedure** :-

From the patient's clinical records, the details of patients with respect to age, sex, history, physical examination was noted down. Results of CBC- complete blood count (by five part hematology analyzer) and the other relevant routine & special investigations- as the case may be, like-Urine routine, Peripheral smear, Reticulocyte count, PT, INR, Rapid malarial test (RMT), Bone marrow study, Serological tests like Widal, Dengue, HIV, HBsAg and HCV; Biochemical tests like Renal function tests and Liver function tests; ECG, USG, X- ray chest etc. were noted down.

All the patients included in this study were followed up during their stay in the hospital.

Baseline platelet counts were done on the day of presentation which were only included for analysis. Repeat platelet counts were done in cases with marked thrombocytopenia until normal or near normal values were reached. Patient's outcome was noted at the time of discharge, in terms of improvement in clinical condition, unchanged or

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death (mortality).Institutional Ethical Committee clearance was taken.

RESULTS

We obtained total of 100 cases of thrombocytopenia with fever, the results are as follows. Causes of fever with thrombocytopenia with its Gender distribution are shown in Table no.1. Fever with thrombocytopenia was more common in male and among its causes infections formed the largest group (78%). Malaria was the most common infection(28.2%). Among 22 cases of malaria, 16(72.73%) were of Plasmodium vivax, 02(9.09%) of Plasmodium falciparum and 04(18.18%) were of mixed infection (vivax + falciparum).

Table no.1.Causes of fever with thrombocytopenia with its Gender distribution

Disease	**Male**	**Female**	**Total**
Malaria	19	03	22
Dengue	08	04	12
Enteric fever	03	06	09
Viral fever other than dengue	06	09	15
Septicemia	10	10	20
Pyrexia of unknown origin(PUO)	05	04	09
Acute febrile illness	03	04	07
Alcoholic Liver Disease	05	00	05
Unknown bite	00	01	01
Total	**59**	**41**	**100**

Infections showed seasonal variation & majority (68%) were in late monsoon & early winter (August to November). Of the total, 57 cases were having platelet count of >50000/cmm, 23 were having 20,000-50,000/cmm and remaining 20 had < 20,000/cmm. Among all the cases, 53 were having bicytopenia (thrombocytopenia with anemia/leucopenia) followed by pancytopenia in 30 and only thrombocytopenia in 17 cases.

Different bleeding manifestations and mean platelet count are as shown in Table no.2. All the bleeding manifestations were seen with mean platelet count ≤ 50,000/cumm. Spontaneous bleeding occurred in 69.24% and petechiae/purpura in 30.76% .

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Table no. 2.Different bleeding manifestations and mean platelet count

Bleeding manifestation	Number of cases	Mean Platelet count/cumm
Epistaxis	02	15,000
Petechiae	02	22,000
Purpura	02	30,000
Gum bleeding	01	15,000
Hematemesis	06	50,000

Distribution of cases having bleeding manifestations are shown in Table no.3. There was only one case of unknown bite which showed bleeding manifestations (100%), whereas viral fever showed bleeding manifestations only in 13.33 % of cases.

Table no. 3.Distribution of cases having bleeding manifestations

Disease	No. of cases (%)
Septicemia	4 (20)
Dengue	3 (25)
Viral fever	2 (13.33)
PUO	2 (22.22)
Unknown bite	1 (100)
Alcoholic liver disease	1 (20)

Table no.4 is showing co-relation of bleeding manifestations with platelet count. Maximum bleeding manifestations were seen in cases with platelet count upto 30,000/cumm. Not all the cases with low platelet count showed bleeding manifestations.

Table no.4.Co-relation of bleeding manifestations with platelet count

Platelet count/ cumm (Range)	No. Of cases with Bleeding manifestations	Total no. of cases	Percentage (%)
≤15,000	06	21	28.57
16000-30000	04	14	28.57
31000-45000	00	11	00
46000-60000	01	10	10
61000-75000	01	11	9.09
76000-90000	01	16	6.25

Outcome of patients with various diseases is as shown in Table no.5. Cases of malaria, enteric fever, viral fever had 100% recovery, whereas unknown bite had 100% mortality. Septicemia accounted for 87.5% of total mortality cases.

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Table no. 5.Outcome of patients

Diagnosis	Improved	Unchanged	Death
Malaria	22	-	-
Dengue	11	01	-
Enteric fever	09	-	-
Viral Fever	15	-	-
Septicemia	11	02	07
PUO	06	03	-
Acute febrile illness	05	02	-
Alcoholic liver disease	03	02	-
Unknown bite	-	-	01
Total	**82**	**10**	**08**

Platelet range in mortality cases has been shown in Table no. 6. There was no relation of severity of thrombocytopenia with mortality.

Table no. 6.Platelet range in mortality cases

Platelet range	No. of cases
<15000-30000	03
31000-60000	01
61000-90000	02
>90000-<150000	02

DISCUSSION

Thrombocytopenia is associated with large number of cases of febrile illness. In our study infections formed the largest group with 78% cases & malaria was the commonest infection seen in 28.2% cases as cause of fever with thrombocytopenia. Our finding correlates with similar other studies. [1,5,6,7]As in our study, Dash et al [6] also found septicemia as the next common infectious cause of fever with thrombocytopenia. However in the studies done by Patil et al [1], Lakum et al [5] and Gandhi et al [7] ; dengue fever formed the second common cause.

In a study conducted by Chakradhar Venkata [13] on patients with sepsis & septic shock; he found thrombocytopenia as a common finding in these patients. Some studies conducted on Dengue fever found that majority of cases (>75%) were associated with thrombocytopenia. [9,14, 15]Comparison of causes of fever with thrombocytopenia is as shown in Table no.7. Our finding of occurrence of Fever with thrombocytopenia, more in male than female is similar to some other studies. [4, 5, 6, 8] In our study maximum (68%) cases were seen during late rainy season & early winter season. Similar observations were seen in study by Raikar et al. [8] Also in studies

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conducted on Dengue fever [9,14, 15] , authors found clustering of Dengue cases in rainy season and early winter.

Table no. 7.Comparison of causes of fever with thrombocytopenia

Disease	Patil et al [1] (%)	Lakum et al [5] (%)	Dash et al [6] (%)	Gandhi et al[7] (%)	Present study (%)
Malaria	54	46.8	45	41.07	22
Dengue	15	35.4	20	26.79	12
Enteric fever	06	4.6	10	4.46	09
Septicemia	04	7.8	21	4.46	20
Others	21	5.4	04	23.22	37

Our finding of occurrence of more cases of P.vivax infection than P.falciparum correlates with that in studies done by Lakum et al [5] , Dash et al [6] , & two other studies on malaria. [9, 10] Whereas, Bhalara et al [4] & one study on malaria by Khan et al [11] found P.falciparum infection as common cause of malaria. Table no. 8 is showing comparison of occurrence of various species of malaria.

Table no. 8.Comparison of occurrence of species of malaria

Species of malaria	Bhalara et al [4] study(%)	Dash et al [6] study(%)	Present study (%)
P.Vivax	37.3	47	72.73
P.Falciparum	59.5	31	9.09
Mixed	3.2	22	18.18

Platelet count ranges in our study are similar to that in studies by Bhalara et al [4] & Gandhi et al. [7] In our study 17% cases had only thrombocytopenia, 53% had bicytopenia & 30% had pancytopenia whereas in the study carried out by Bhalara et al. [4] only thrombocytopenia seen in 31%, bicytopenia in 59.4% & pancytopenia in 9.4% of cases.

In our study out of total 13 patients showing bleeding manifestations, petechiae/purpura was seen in 30.76% & spontaneous bleeding in 69.23%, this finding differs from finding in the study by Patil et al [1] & by Dash et al [6] in which petechiae accounted for 73.9%, 66% & spontaneous bleeding in 26.9% & 34% respectively.

In present study bleeding was seen in cases having platelet count upto 90,000/cumm which is different from finding of bleeding only in cases with platelet count < 50,000/cumm in study by Patil et al [1] but the finding that not all the cases with low platelet count had bleeding is similar.

According to study by Raikar et al [8] there is no correlation between platelet count & bleeding manifestations & the condition in which thrombocytopenia develops has an influence on

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bleeding . When associated with infection or uraemia, bleeding can occur with mildly reduced platelet counts as additional functional defects contribute. In our study also we found that degree of thrombocytopenia does not have correlation with bleeding. Comparison of presence of bleeding manifestations is shown in Table no. 9.

Table no. 9.Comparison of bleeding manifestations

Bleeding manifestations	Patil et al [1] (%)	Dash et al [6] (%)	Present study (%)
Present	23	53	13
Absent	77	47	87

In our study good recovery was seen in 82% of cases with rise in platelet count with treatment of underlying cause & platelet transfusion in few cases with very low platelet count. Similar observation of good recovery in 95% & 78% cases was seen in studies by Patil et al [1] and Dash et al [6] respectively. Mortality was 8% & Septicemia (87.5%) was the major cause in our study. Similarly septicemia was major cause of mortality in Patil et al [1] & Dash et al [6] study with mortality of 5% & 22% respectively. Table no.10 is showing comparison of cause mortality of patients.

Table no.10.Comparison of causes of mortality of patients

Cause of mortality	Patil et al (%) [1]	Dash et al (%) [6]	Present study(%)
Septicemia	60	77	87.5
Malaria	20	18	-
Dengue	-	5	-
Others	20	-	12.5

In the study by Dash et al [6] common range of platelet count in mortality cases was in range of 10-20 thousands in 15 cases, 21-30 thousands in 5 cases, 31-40 thousand in 2 cases & so this study inferred that outcome depends on severity of underlying condition & platelet count. A similar study by Raikar et al [8] found no correlation of severity of thrombocytopenia with mortality. In our study mortality was seen even with mild thrombocytopenia i. e. with platelet count range of > 90 thousands – < 1.50 lakhs, so outcome depends mostly on severity of underlying condition.

CONCLUSION

Infections formed the largest group and & Malaria was the common cause of fever with thrombocytopenia. As thrombocytopenia is not always associated with clinical bleeding manifestations, a routine CBC investigation in all febrile cases helps to find its association with thrombocytopenia which will narrow the differential diagnosis of fever. Further investigations of these cases will reveal the specific cause for fever with thrombocytopenia.

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Thus a well organized systemic approach needs to be carried out with an awareness of different causes of fever with thrombocytopenia which can help to diagnose the case early. This will reduce the cost, morbidity, and mortality associated with it. Outcome depends on the underlying cause of fever and not on the severity of thrombocytopenia.

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