Original Research Article

A Descriptive Study of Clinical Profile of Fever with Thrombocytopenia at Tertiary Care Centre of Maharashtra

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ABSTRACT

Introduction: Fever is a pervasive and ubiquitous theme in human myth, art and science. Fever is such a common manifestation of illness that it is not surprising to find accurate descriptions of the febrile patients in early-recorded history. A fever rarely comes without other symptoms and sign. It is   often accompanied by specific complaints or pattern. Many times, it is associated with low platelet count. The normal platelet count is 150000-450000/ μL. Thrombocytopenia is defined as platelet count less than 150000/ μL.

Material and Methods: The present study was prospective observational study conducted on patients, who were admitted at tertiary care hospital in urban setting during Feb 2013 to July 2014. This study conducted at Government medical college and Hospital, Latur. Sample size was 200.

Results: The present study, conducted on 200 patients with fever and thrombocytopenia, revealed that the majority of cases occurred in young adults, with 57% belonging to the 15–30 years' age group and a male predominance (M: F = 2.12:1). Dengue fever (40%) emerged as the leading cause, followed by malaria (33%), while septicemia (8%) was the most common contributor to mortality. Most patients presented with platelet counts less than 50,000/cumm showed bleeding manifestations 34% of cases, predominantly petechiae and purpura (70%). The overall recovery rate was good (96%), with mortality observed in 4% of cases, largely due to septicemia and severe thrombocytopenia (< 20,000/cumm).

Conclusion: These findings emphasize that fever with thrombocytopenia is a significant clinical presentation in hospitals, requiring careful evaluation to differentiate between infectious etiologies.

Keywords: Fever, Thrombocytopenia, Petechiae, Purpura

INTRODUCTION

Fever is a pervasive and ubiquitous theme in human myth, art and science. Fever is such a common manifestation of illness that it is not surprising to find accurate descriptions of the febrile patients in early-recorded history.[1] Fever is known as pyrexia from Greek "pyrites" meaning fire;

Febrile is come from the Latin word Ferris, meaning fever.[2] Fever is defined as an elevation of the body temperature above the normal circadian range as the result of a change in the thermoregulatory center located in the anterior hypothalamus. An AM temperature of $> 37.2°C$ (98.9°F) or a PM temperature of $> 37.7°C$ (99.9°F) would define fever.[1]

Fever usually occurs in response to an infection or inflammation. However, many other causes are possible, including drugs, poisons, cancer, heat exposure, injuries or abnormalities in the brain, or disease of the endocrine system. A fever rarely comes without other symptoms and sign. It is often accompanied by specific complaints or pattern. Many times, it is associated with low platelet count. The normal platelet count is 150000-450000/ µL. Thrombocytopenia is defined as platelet count less than 150000/ µL. It results from either decreased production, increased destruction, increased sequestration in spleen. Of these, infections being the commonest cause of thrombocytopenia.[3]

Patients with an acute febrile illness in a tropical country like India usually have an infectious etiology and may have associated thrombocytopenia. Infections like malaria, dengue, leptospirosis, typhoid, HIV and military TB 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. If we can analyze the low platelet count as one of the diagnostic markers of some common infections, we can narrow the differential diagnosis. Hence, a need for study to know the causes and complications of fever with thrombocytopenia.

MATERIAL AND METHODS

The present study was prospective observational study conducted on patients, who were admitted at tertiary care hospital in urban setting during Feb 2013 to July 2014. This study conducted at Government medical college and Hospital, Latur.

Sample size: Assuming that 40% of the subjects admitted in hospital for fever having thrombocytopenia,[4] and an expected response rate of 95%, for estimating the expected proportion with 7% absolute precision and 95% confidence then the study would require a sample size of: 199. So, our final sample was 200.

Sampling method: By using convenient sampling method, all patients with fever having thrombocytopenia admitted at tertiary care hospital in urban setting during Feb 2013 to July 2014 were enrolled in our study. We prospectively collected a series of 200 patients with fever having thrombocytopenia.

Inclusion criteria: The patients of both sexes aged > 14 years. Patients admitted with fever, i.e. A.M temperature of > 37.2°C (> 98.9°F) and P.M temperature of > 37.7. C (>99.9°F), and thrombocytopenia i.e. platelet count of < 1.5 lakhs /µL.

Exclusion criteria: Patients < 14 years, Patients with fever and no thrombocytopenia, as well as patients with thrombocytopenia and no fever are excluded. Patients with Inherited causes for thrombocytopenia, patients on drugs causing thrombocytopenia, patients with Autoimmune causes for thrombocytopenia, patients with Cirrhosis of liver, patients with Leukemia and myelodysplastic syndrome were excluded.

The study was approved by institutional ethical committee. Once the patients admitted with fever with thrombocytopenia, a data was collected by using standardized assessment form. Purpose of the study was carefully explained to the patient and /his/her relatives and written informed consent was taken. A careful history was recorded; history of acute and chronic illness, significant past and family history were recorded. General physical examination was done. Detailed examination of various systems was done.

Routine investigations like complete blood count, peripheral blood smear, random blood sugar, liver and renal function, CXR PA and other specific and special investigations were done as and when indicated. Repeat platelet count was done on day 0, 3, 5 and then on discharge in patients with platelet count between 40000/cumm – 150000/cumm. In patients with platelet count less than 40000/cumm - or having bleeding manifestation platelet count was repeated daily for at least 3 days or till rising trend of platelet is seen. Special investigations were done in order to achieve the diagnosis. Once the specific diagnosis was reached the patients were treated for it specifically and symptomatically. Platelet transfusion was considered in patients with platelet count of 10000/cumm as absolute indication. Bleeding manifestation with any platelet count was another absolute indication for platelet transfusion. The temperature was measured orally by clinical thermometer. The thermometer was kept for 2 min and patient was asked to breath from nose. The platelet counting was done by 2 methods, 3-part cell counter is an automated cell counter with features of counting RBC"s, WBC"s, platelets, blood indices and Hb concentration all together. Direct visualization: 0.02 ml EDTA blood was diluted with 2 ml of diluting fluid followed by charging the Neubaur`s chamber with the fluid and number of platelets was counted.
Thrombocytopenia: Platelet count less than 150,000/cumm considered as thrombocytopenia. Thrombocytopenia further classified into mild thrombocytopenia (150,000/cumm to 50,000/cumm), moderate thrombocytopenia (50,000/cumm to 20,000/cumm) and severe thrombocytopenia (< 20,000/cumm).

Data collection tool: A standardized structural questionnaire was used which was prepared in English language and translated into the regional language. After participant information sheet, written informed consent was taken and then personal interview was conducted.

Procedure for data management: Data collection was done by google forms and was generated in MS office Excel. For Data Analysis we used Epi Info™ software Version 7.2 (CDC) & IBM SPSS 30.0. All the information related to study is kept confidential and used for medical research only.

RESULTS

The present study was prospective observational study conducted on patients, who were admitted at tertiary care hospital in urban setting during Feb 2013 to July 2014. This study conducted at Government medical college and Hospital, Latur, Maharashtra.

In this study, out of 200 patients 136 (68%) were males and 64 (32%) were females and male to female ratio was 2.12:1 (Table-1). Significantly more no. of cases of fever with thrombocytopenia were below age of 45 years of age. Majority (57%) of patients were from age group 15-30 years. Duration of hospitalization was ranged from 3 to 21 days, with average of 6 days (Table-1). Among 200 patients Dengue fever was the leading cause present in 80 cases (40%) followed by malarial fever 66 cases (33%) (Table-1). Among 200 patients, 59 % patients showed mild thrombocytopenia (150,000/cumm to 50,000/cumm), 28 % patients showed moderate thrombocytopenia (50,000/cumm to 20,000/cumm) and 13 % patients showed severe thrombocytopenia (< 20,000/cumm) (Table-1). Clinical manifestation of thrombocytopenia was present in 68 patients (34%). Among 68 cases having bleeding manifestation, petechiae/purpura was the commonest form of bleeding manifestation present in 48 cases (70%) followed by hematuria were present in 12 cases (18%) (Table-1). Among 200 patients, good clinical outcome was present in 192 cases (96%), while 8 cases were died (4%) (Table-1).

Significantly a greater number of cases died due to septicemia. Among 8 deaths, septicemia was the leading cause of mortality present in 5 cases (62.5%) (Table-2). Among the 8 mortality cases, low platelet count < 20,000/cumm were present in 4 cases (50%) followed by 3 cases (37.5%) having platelet count between 20,000-50,000/cumm (Table-3). Significantly worst outcome was observed in patient with low platelet count < 20,000/cumm (Table-3). Statistically more no. of cases showing bleeding manifestation were 92.3% having low platelet count (Table-4).

Table-1: Socio-demographic details and clinical details of patients

Category	Sub-Category	Number of cases (n)	Percentage (%)
Age	15-30	114	57
	31 to 45	40	20
	46 to 60	32	16
	Above 60	14	07
Gender	Male	136	68
	Female	64	32
Duration of hospitalization (days)	Range 3-21 days	Average 6 days	
Diagnosis	Dengue fever	80	40
	malaria	66	33
	Enteric fever	22	11
	Septicemia	16	08
	Leptospirosis	06	03
	Undiagnosed cases	10	05
Platelet count (cumm)	0-20000	26	13
	20000-50000	56	28
	50000-150000	118	59
Bleeding Manifestations	Absent	132	66
	Petechiae /purpura	48	24
	Hematuria	12	6
	Epistaxis	05	2.5
	Per rectal bleeding	03	1.5
Clinical Outcome	Survived	192	96
	Died	8	04

Table-2: Incidence of diseases contributing to mortality

Disease	Survived	Died	Total	χ^2	P value
Dengue fever	79	01	80		
Malaria	64	02	66		
Enteric fever	22	00	22	34.26	0.000002 < 0.01
Septicemia	11	05	16		
Leptospirosis	06	00	06		
Undiagnosed	10	00	10		
Total	**192**	**08**	**200**		

Table-3: Distribution of platelet counts in mortality cases

Thrombocytopenia		Survived	Died	Total	χ^2	P value
Severe	0-20000	22	04	26		
Moderate	20000-50000	53	03	56	12.09	< 0.01
Mild	50000-150000	117	01	118		
	Total	**192**	**08**	**200**		

Table-4: Correlation of bleeding manifestations with platelet count

Thrombocytopenia		Bleeding	No Bleeding	Total	χ^2	P value
Severe	0-20000	24	02	26		
Moderate	20000-50000	23	33	56	110.13	<0.01
Mild	50000-150000	01	117	118		
	Total	**48**	**152**	**200**		

DISCUSSION

Patients with acute febrile illness in tropical countries like India usually have an infectious etiology and these conditions are more or less commonly associated with thrombocytopenia. Early diagnosis and treatment in such cases can reduce the severity and complexity associated with thrombocytopenia. This study was undertaken to evaluate the clinical profile of fever associated with thrombocytopenia in tertiary care setting. In this study we have attempted to study the age and sex distribution clinical presentation and percentage of bleeding tendencies as well as outcome of patients admitted as fever with thrombocytopenia. We also attempted to study the common diseases associated with fever with thrombocytopenia. Our study was conducted on 200 patients, who were above age 14 years, admitted as fever (>100° F) at least once a day during hospital stay and thrombocytopenia (platelet count <1,50,000/µl). Those patients who had underlying hematological malignancies, immunocompromised conditions, liver cirrhosis, chronic renal failure as well as those who are on antiplatelet medications, chemotherapy and immunosuppressant were excluded from study.

Sex wise distribution of cases: Out of 200 patients admitted as fever with thrombocytopenia 136 (68%) were males and 64 (32%) were females. In our study male patients outnumbered female patients. Male to female ratio was 2.12:1.Our study results was similar to study conducted by Nair PS et al[5] conducted at St. Stephen's Hospital, New Delhi in March 2002 in which out of 105 patients (males 76 and females 33) with male to female ratio 2.3:1. Similarly study conducted by Shankar R Raikar et al[6] in Sir T. Hospital and Government Medical College, Bhavnagar, Gujarat where male outnumbered female patient with male to female ratio was 2.69:1. Our study results were also similar to study conducted by Dr. HS Dash et al[7] in Oct 2010 at Alluri Sitha Rama Raju Academy of Medical Sciences, ELURU ,Andhra Pradesh where male patient (61%) and female patient (39%) ratio was 1.56:1.

Age wise distribution of cases: In our study common age group affected by fever with thrombocytopenia was 15-30-year age group patients. Out of 200 patients 114 cases (57%) patients were in this age group followed by 31-45 age group where 40 cases (20%) were affected. Our results were similar to study by Shankar R Raikar et al[6] on 100 patients also shows younger age group age between 12-30 years were commonly affected, accounting for 52% cases followed by 18% cases which were from age group 30-45 years. In our study patients above age of 60 years were only 7% (14 cases). Similar results were found in study by Shankar R Raikar et al[6] where old age (> 60 years) accounts for 7% cases.

Incidence of various causes of fever with thrombocytopenia: In our study it was observed that out of total 200 cases 190 cases (95%) were having infection as common cause of febrile illness with thrombocytopenia, while 10 cases (5%) remain undiagnosed. Our results were similar to study conducted by Dr. HS Dash et al.[7] In their study infection accounts for 98% cases as fever with thrombocytopenia. Nair PS et al[5] study in 2003 also shown that 68% cases of fever associated with thrombocytopenia were due to infection. In our study we had observed that amongst infection Dengue fever was commonest cause of fever with thrombocytopenia followed by malaria. Dengue fever accounts for 40% (80 cases) and 33% (66 cases) had malaria as a source of fever with thrombocytopenia. Enteric fever was 3rd most common cause accounts for 11% cases (22 patients). Septicemia was 4th common cause of febrile illness, were present in 8% cases (16 patients). Leptospirosis accounts for 3% cases (6 patients). Similar results were found in study by Shankar R Raikar et al.[6] In their study Dengue fever was the leading cause of fever with thrombocytopenia, followed by malarial fever. Dengue was present in 52% cases and malaria accounts for 45% cases.

Study conducted by David EJ et al[8] at Wanless Hospital, Miraj in June 2002 also shown that Dengue fever was leading cause accounting for 94% cases. Study conducted by Prithviraj Patil et al[9] in D.Y. Patil hospital Kolhapur on 100 patients shown malaria (54%) as a commonest cause followed by Dengue fever (15%) as cause of fever with thrombocytopenia. Study by Shrinivas et al10 which was conducted in 2009 shown that malaria (41%) was common cause of fever with thrombocytopenia, followed by enteric fever (24%). In their study Dengue fever was 4th most common cause accounting for 14% cases. Study conducted by Dr. HS Dash et al[7] shown that malaria (45%) was leading cause followed by sepsis (21%) and Dengue fever was 3rd most common cause of fever with thrombocytopenia. But this variation may be due to seasonal and regional variation in the epidemiology of infectious diseases. Infection was commonest cause of febrile illness with thrombocytopenia in most of the studies.

Distribution of platelet count: In our study the common range of platelet distribution was in between 50000-80000/ µl. 37% patients had platelet count ranging in between 50000-80000/ µl followed by 20000-50000/ µl where 28% cases were found. Similar study results were found in study by Dr. HS Dash et al[7] in which common range of platelet distribution were in between 61000-80000/µl., accounting for 26% cases followed by 25% cases were having platelet count in between 21000-40000/µl. In our study all the patients were monitored for platelet count on daily basis and except the mortality cases (8%) all other patients showed increasing trend during the hospital stay. Later 34% patients were followed up after 7 days and their platelet counts were within normal range. There were no decreasing trends of platelet count observed in our study. In study conducted by Nair PS et al[5] during the course of follow up platelet counts showed increasing trends accounting for 69 patients (63.3 %), initial fall in counts followed by rising trends in 17 patients (15.6 %) and continuously falling counts in 8 patients (7.3 %).

Incidence of clinical manifestation of thrombocytopenia: In our study clinical manifestation of thrombocytopenia were present in 34% (68 cases) as compare to other study Nair PS et al[5] where 41.3% cases had clinical manifestation of thrombocytopenia. Similar results were found in Prithviraj Patil et al[9] study. In their study 23% cases had clinical manifestation of thrombocytopenia. Study conducted by Dr. HS Dash et al[7] also shows 53% cases have clinical manifestation of thrombocytopenia.

Various clinical manifestation of thrombocytopenia: In our study petechiae/purpura was the commonest form of bleeding manifestation 70% (48 cases) followed by hematuria 18% (12 cases). Epistaxis was documented in 7% (5 cases), while per rectal bleeding was present in 5% (3 cases). Our study results were similar to study by Prithviraj Patil et al[9] where petechiae was the commonest

manifestation accounting for 74% cases. Hematuria (13%) was second most common bleeding manifestation. Bleeding per rectum were found in (8.6%) while epistaxis (4.34%) cases. Study conducted by Dr. HS Dash et al[7] also showed similar results. In their study 65% cases have petechiae /purpura as common bleeding manifestation. In our study petechiae was seen in 70% cases as common bleeding manifestation of thrombocytopenia.

Clinical outcome of fever with thrombocytopenia: In our study clinically good outcome was present i.e. 96% (192 cases) in the form of increasing platelet count at the time of discharge and survival. While mortality was 4% (8 cases). Study by Prithviraj Patil et al[9] also shows similar results. In their study good clinical outcome were present in 95% cases, while 5% cases accounts for mortality. In our study septicemia 62.5% (5 cases) was the leading cause of mortality followed by malaria (25%) 2 cases. Dengue fever remains 3rd major cause of mortality was seen with 12.5% cases. Our results were similar to study conducted by Dr. HS Dash et al.[7] In their study septicemia was the leading cause of mortality in fever associated with thrombocytopenia accounts for 77% cases, followed by malaria (18%). Dengue fever (5%) remain 3rd leading cause of mortality. Prithviraj Patil et al[9] study also shown sepsis was the major cause of mortality accounting for 60% cases. Malaria was second most (20%) followed by viral fever (20% cases) as a cause of mortality.

Platelet count distribution in mortality cases: In our study common rage of platelet count in which mortality was highest was in between 0-20000/µl. 50% cases (4 patients) were died when platelet count were <20000/ µ l. 37.5% (3 cases) died cases was having platelet count in-between 20000-50000/µl. 12.5% died cases (1 patient) had platelet count 50000-80000/µl. Mortality was higher in patients who had severe thrombocytopenia (< 20000/µl).Similar study results was seen in study by Dr. HS Dash et al,[7] where 68% mortality was seen with platelet count (< 20000/µl).Thus our study results were comparable with all these studies suggesting correlation of low platelet count mortality in cases with fever with thrombocytopenia.

CONCLUSION

The present study, conducted on 200 patients with fever and thrombocytopenia, revealed that the majority of cases occurred in young adults, with 57% belonging to the 15–30 years' age group and a male predominance (M: F = 2.12:1). Dengue fever (40%) emerged as the leading cause, followed by malaria (33%), while septicemia (8%) was the most common contributor to mortality. Most patients presented with platelet counts less than 50,000/cumm showed bleeding manifestations 34% of cases, predominantly petechiae and purpura (70%). The overall recovery rate was good (96%), with mortality observed in 4% of cases, largely due to septicemia and severe thrombocytopenia

(<20,000/cumm). These findings emphasize that fever with thrombocytopenia is a significant clinical presentation in hospitals, requiring careful evaluation to differentiate between infectious etiologies.

Recommendations

1. Early Screening and Diagnosis: All patients presenting with fever and thrombocytopenia should undergo rapid diagnostic tests for common infections such as dengue, malaria, and enteric fever to enable timely management.
2. Monitoring Platelet Count and Bleeding Risk: Patients with platelet counts <50,000/cumm should be closely monitored, with special attention to those with <20,000/cumm, as they are at high risk for bleeding complications and mortality.
3. Prompt Management of Septicemia: Since septicemia contributed to the majority of deaths, early recognition and aggressive management with appropriate antibiotics and supportive care are crucial to improve survival.
4. Public Health Measures: Vector control programs for dengue and malaria, improved sanitation, and safe water practices are essential to reduce the burden of these infections in the community.
5. Awareness and Education: Healthcare professionals should be trained to recognize early warning signs of severe thrombocytopenia and institute prompt interventions. Community-level awareness regarding prevention of vector-borne diseases should also be strengthened.
6. Further Research: Larger multicentric studies are recommended to validate these findings and to explore other less common causes of fever with thrombocytopenia, including viral and autoimmune etiologies.

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