

Clinical Outcomes of Patients Presenting As Fever with Thrombocytopenia in Marathwada Region

Nikalje Anand¹, Talib S.H.², Pagar Bhushan³, Patil Sumit⁴, Patil Piyush⁵, Kurhade Aniket⁶

¹Associate Professor, Dept. of Medicine, MGM Medical College & Hospital, Aurangabad (Maharashtra)

²Prof. & H.O.D, Dept. of Medicine, MGM Medical College & Hospital, Aurangabad (Maharashtra)

^{3, 4, 5, 6}Chief Resident, Dept. of Medicine, MGM Medical College & Hospital, Aurangabad (Maharashtra)

Abstract: *This study was performed to evaluate the cause of fever with thrombocytopenia, its clinical profile and related complications with the same. In this study unspecified viral fever was the most common cause in Marathwada region of Maharashtra, followed by Dengue and malaria. ARDS is the most common complication in this study.*

Keywords: Fever, Thrombocytopenia, Platelet Count, viral fever, Dengue, Malaria

1. Introduction

There is an alarming increase in the incidence of fever with thrombocytopenia. Routinely we come across many cases, both as inpatients and outpatients presenting as fever with thrombocytopenia. Infections like malaria, dengue, leptospirosis, typhoid, viral fever are some of the common causes of fever with thrombocytopenia, and septicemia with or without a known focus of infection also often presents with thrombocytopenia. Therefore a well-organized systematic approach that is carried out with an awareness of causes of fever with thrombocytopenia can shorten the number of investigations and bring out diagnosis. Hence, we proceeded to know the various causes and complications of fever with thrombocytopenia. It also helps to know the various complications of thrombocytopenia and its management. Thrombocytopenia in fever being a prognostic factor can predict the cause and thus helps in early diagnosis and treatment of the same, preventing further fatal outcome associated with it such as intracerebral bleed, hemorrhage into vital organs, shock and finally leading to death. Though patients can initially present with simple fever in due course it can lead to unpredictable outcomes including death at times therefore the aim of the study is to analyze the clinical profile of fever with thrombocytopenia, as early diagnosis and timely intervention prevents adverse outcomes and saves life.

2. Objectives of the Study

- To evaluate clinical profile of fever with thrombocytopenia.
- To identify the cause of fever with thrombocytopenia
- To assess the complications associated with fever and thrombocytopenia.

3. Methodology

Method of Study:

The data for this study was collected by patient evaluation which will be done by detailed history taking, Clinical examination, and relevant investigations using a proforma

specifically designed for this study for patients admitted in MGM Hospital Aurangabad during the period of June 2013 to June 2015. We prospectively collected a series of 150 patient's age more than 18 years with fever and thrombocytopenia.

Inclusion criteria:

- Patients of both sexes aged > 18 years.
- Patients admitted with fever and found to have thrombocytopenia (platelets count < 1.5 lakh) are included in the study.

Exclusion criteria:

- Diagnosed cases of Thrombocytopenic purpura on treatment
- Patients with thrombocytopenia already diagnosed to have hematological disorder / malignancy, on treatment with chemotherapy and other immunosuppressant
- Diagnosed cases of platelet disorders and dysfunction
- Patients on treatment with antiplatelet drugs and other drugs causing thrombocytopenia
- Patients with cirrhosis and chronic liver disease

4. Observations

A total number of 150 cases admitted over a period from June 2013 to June 2015 in our institute were studied. The study subjects were more than 18 years. Out of 150 cases of fever with thrombocytopenia, 88 were males and 62 were females. The duration of hospitalization varied between 3 days to 21 days. The average duration of hospitalization was 7 days.

Out of 150 cases of fever with thrombocytopenia, 71 of them had diagnosis of undifferentiated fever (47%) as the commonest cause, followed by dengue fever 62 cases (42%); malaria (11%); septicemia (2.66%), mixed infection of dengue and malaria (8%). In our study 58 (39%) had platelet count more than 50,000/cu mm, 69 (46%) cases had count between 20,000 to 50,000/cu mm and 23 (15%) with count less than 20,000/cu mm.

In 8 mortality cases, 3 (38%) were due to dengue fever, 2 (25%) were due to mixed malaria, 2(25%) were of undifferentiated fever and 1(13%) of mixed infection of dengue and malaria. Out of 150 cases 88 i.e. 59% were males and 62 i.e. 41% cases were females. Highest number of cases were seen in the age group of 18-40 years namely 112 cases (75%) followed by 40-60 years were 26 cases (16%), then above 60 years were 12 cases (9%).

Table 1: Etiology of cases of fever with thrombocytopenia

Diagnosis		Percent	Count
MALARIA	Falciparum malaria(FM)	3%	5
	Vivax malaria(VM)	4%	6
DENGUE	IgG	2%	3
	IgM	13%	19
	NS1	26%	39
	IgG-IgM(both+ve)	1%	1
Undifferentiated Fever		47%	71
FM+DENGUE		5%	8
VM+DENGUE		3%	5
MIXED MALARIA (FM+VM)		4%	6

In our study we found 58 cases (38.66%) with mild thrombocytopenia, 69(46%) cases with moderate thrombocytopenia, 23(15.33%) with severe thrombocytopenia.

9 (39.13%) cases of undifferentiated fever, 8(34.78%) cases of dengue fever, 2(9%) cases of malaria, and 4 (17.39%) cases of mixed infection of both had severe thrombocytopenia. 53 (35%) cases were observed to have bleeding manifestations, 23 cases with platelet count less than 20,000/cu mm, 20 had count between 20,000-50,000/cu mm and 10 cases demonstrated bleeding manifestation with count between 50,000- 1lakh/cu mm and no bleeding was seen with count more than 1lakh/cu mm. i.e. bleeding tendencies increases as platelet count decreases.

Table 2: Clinical presentation of cases of fever with thrombocytopenia

Feature	Numbers	Percentage
Rigors	100	67%
Myalgia	81	54%
Headache	52	35%
Breathlessness	16	11%
Bleeding Manifestation	53	35%

Table 3: Systemic Complications in cases of fever with thrombocytopenia

Complications	Percent	Number of Patients
ARDS	10%	15
ARF	7%	10
NC(non complicated)	81%	121
SEPTICEMIA	3%	4
SPONT.BLEEDING	1.5%	2

Table 4: Outcome of Cases of fever with thrombocytopenia

Outcomes	Percent	Count
Expired	5%	8
Good	95%	142
Total	100%	150

Out of 150 cases 8(5.33%) cases died, of them 3 were of dengue, 2 were of mixed malaria, 2 were of undifferentiated fever, and 1 was of mixed infection of malaria and dengue. Deaths were due to multiorgan failure in all the 8 cases.

5. Discussion

For a study of fever with thrombocytopenia, cases must satisfy the above mentioned criteria, case collection is necessary and careful follow up is required. Once the case admitted with fever and those who had thrombocytopenia, a careful history was recorded, general physical examination and detailed examination of various systems was done. Routine investigations, the specific and special investigations were done as and when indicated. In the patients in whom a definite diagnosis was reached, were treated for the that specific disease and platelet count was repeated at the time of discharge. Patients discharged were not followed up. **Nair PS et al¹. (2003)** studied the profile of thrombocytopenia as associated with acute febrile illnesses and to determine the etiology of these febrile illnesses. They studied total of 109 patients, 76 males and 33 females with male as to female ratio of 2.3:1. **Gandhi A et al (2015)²** found that malaria(42%) was the most common cause followed by dengue (26%), undifferentiated fever(17%), enteric fever (4.46%) and septicemia (4.5%). **Raikar s (2013)³** found that dengue(52%) was the most common cause of thrombocytopenia then malaria (42%), enteric fever (3%). In our study out of 150 cases commonest cause was undifferentiated fever, with 71 (47%) cases followed by dengue fever with 62 (42%) cases followed by malaria with 17(11%) cases then by mixed infection with dengue and malaria both were 13(8%). In our study hematological conditions are excluded, and in those cases all the available investigations are negative they are labelled as probable diagnosis of viral fever, which was labelled as unknown etiology in **Nair et al.(2003)¹** study.

Serological diagnosis of viral infections is expensive, limited and cumbersome. Owing to limited resources and laboratory facilities, the diagnosis of fever could not be made in 71 (47%) cases. Hence labeled as undiagnosed fever.

Disease category	Percentage of diseases according to study		
	Gandhi A et al ²	Putta S et al ⁴	Present Study
Malaria	42	36	11
Dengue fever	26	26	42
Enteric fever	5	6	0
Unknown(viral etiology)	17	28	47

Abdul Haque Khan et al⁵ (2010) showed typical clinical features in dengue fever were chills and rigors in 80%, myalgia in 70%, vomiting in 60%, headache in 50%, rash in 25%. Unusual clinical features were pharyngitis in 7% and bleeding manifestations in 5% of patients.

We observed in our study clinical features of fever with thrombocytopenia cases were rigors in 67%, myalgia in 54% cases, headache in 35% cases, bleeding manifestations in 35% cases. We also found ascites in 10% cases and pleural effusion in 14% cases. **G. LalithaMurthy et al⁶, KocharDK⁷** demonstrated deranged renal parameters in

24.68%, 6.25% malarial cases respectively. In the present study levels of blood urea and serum creatinine were elevated in 24.66% cases of fever with thrombocytopenia. Acute renal failure as a complication of Falciparum malaria occurs due to hypovolemia, hyperviscosity, intravascular hemolysis and intravascular coagulation. **Bajpai et al⁸**, studied clinical profile, etiology, and postmortem findings of patients who died with short febrile illness, the data of 160 deceased patients showed 15% had renal failure, 6% had hepatitis, and 11% had both hepatorenal involvement. In our study we found 24.66% had deranged renal functions, 45.16% had elevated liver enzymes.

Bleeding Manifestations	Nair et al.(2003)		Present study	
	No. of cases	Percentage	No. of cases	Percentage
Present	45	41.3	53	35.33
Absent	65	58.7	97	64.66

Distribution of platelet count in thousands	Nair et al (2003)		Present study	
	No. of cases	Percentage	No. of cases	Percentage
0 – 20	19	17.5	23	15.33
20 – 50	28	25.7	69	46
>50	62	56.8	58	38.66

In **Nair et al.(2003)¹** study group during the course of follow up platelet count showed increasing trends accounting for 63.3% and continuously falling counts in 7.3%. But in this present study it showed increasing trends in platelet count at the time of discharge in all cases who recovered.

Gomber et al(2001)⁹ and **Narayanan et al(2002)¹⁰** have documented that bleeding manifestations increases as platelet count decreases and we also found bleeding manifestations increase as the platelet count decreases as in our study we found that 53 (35%) cases were observed to have bleeding manifestations, 23 cases with platelet count less than 20,000/cu mm, 20 had count between 20, 000-50,000/cu mm and 10 cases demonstrated bleeding manifestation with count between 50,000- 1lakh/cu mm. and no bleeding was seen with count more than 1lakh/cu mm. i.e. bleeding manifestations increases as platelet count decreases.

G. LalithaMurthy et al⁶, KocharDK⁷ demonstrated acute renal failure in 24.68% and 6.25% cases respectively. They also found Acute Respiratory Distress syndrome in 11.39% and 2.08% cases respectively in malarial cases. We found deranged renal functions in 41% cases and Acute Respiratory Distress syndrome in 14% cases of malaria. Our findings are consistent with above mentioned studies in malarial cases.

Kochare et al⁷ noted mortality in complicated malaria was 10.93%, in our study we found mortality in 11.76% cases. The presentation with multiple organ dysfunction was very high and was the important cause of death in our study. This indicated that multi-organ dysfunction carried poor prognosis as concluded by the other similar studies.

Studies on dengue fever cases by **Anuradha et al.(1998)¹¹, Kabra et al¹².(1999) Gomber et al.(2001)⁹, Narayanan et al (2002)¹⁰** demonstrated mortality in 6.6%, 7.5%, 4.8%, 3.4% respectively.

Our study shows mortality of 4.8% in dengue fever cases, which correlates with above mentioned studies. All the cases that died had deranged renal functions and acute respiratory distress syndrome same as in above mentioned studies. Out of 150 cases 8(5.33%) cases died, of them 3 were of dengue, 2 were of mixed malaria, 2 were of undifferentiated fever, and 1 was of mixed infection of malaria and dengue. Deaths were due to multiorgan failure in all the 8 cases.

6. Conclusions

- The range of cases was >18 years and male to female ratio was 1.4 : 1
- A definitive diagnosis was not made in 71(47%) cases and labelled as undifferentiated fever.
- Among 62 (42%) cases of dengue, 39 (62.90%) cases were of NS1 positive, 19(30%) were of IgM positive, and 4 (7%) cases of mixed infection (positive for Dengue and Malaria).
- Among 17 cases of malaria, 5 cases were of falciparum malaria, 6 were of vivax malaria and 6 cases with mixed malarial infection.
- Renal dysfunction was seen in 37 (24.66%) cases and 16 of these cases were of undifferentiated fever, 14 cases of dengue, 7 cases of malaria.
- Elevated liver enzymes were seen in 62 cases, (28/71) of undifferentiated fever, (20/62) of dengue and (14/17) of these cases were of malaria.
- Out of 150 cases 58 cases (38.66%) with mild thrombocytopenia, 69(46%) cases with moderate thrombocytopenia, 23(15.33%) with severe thrombocytopenia.
- Bleeding manifestations were noted with platelet count of 10,000/cu mm as well as 95,000/cu mm.
- Mortality noted in 8(5.33%) cases, out of them 3 were of dengue, 2 were of mixed malaria, 2 were of undifferentiated fever, and 1 was of mixed infection of malaria and dengue. Deaths were due to multiorgan failure in all the 8 cases.
- Vigilance and awareness is needed in the management of cases of fever with thrombocytopenia, since multiorgan dysfunction and death can occur in some cases.
- In future various pathological and microbiological imaging modalities should be needed for research and diagnosis of many viral hemorrhagic fevers. Serological diagnosis of viral infections is expensive, limited and cumbersome. Owing to limited resources and laboratory facilities, hence the diagnosis of fever could not be made in majority of cases. Extensive analysis of particular febrile illness has not been attempted due to multiple etiologies of febrile thrombocytopenia.

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