Original Article

A Clinical Study of Fever with Thrombocytopenia with Infectious Etiology

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ABSTRACT

Background and Aim: Fever is a pervasive and ubiquitous theme in human myth, art and science. The aim of the study was to elucidate possible infective etiology for fever with thrombocytopenia and to correlate clinical features, laboratory studies and etiology.

Materials and Methods: This study was done on patients, who were admitted to Chalmeda Anand Rao Institute of Medical Sciences Hospital during a period of August 2018 to December 2019. We prospectively collected a series of 120 patients with fever and thrombocytopenia. All the adult patients aged 16-65 years with fever and thrombocytopenia of infective etiology.

Results: In the present study subjects were in the age group of 16-65 years. Youngest 16 years old and oldest 64 years. Out of 120 patients of fever with thrombocytopenia, had definitive diagnosis with Dengue 62 cases as the commonest cause, followed by, Malaria 22 cases, Mixed malaria and dengue 2 cases, Leptospirosis 3 cases, Septicemia 3 cases, varicella 2 cases, and unknown/viral 28 cases.

Conclusion: Among the diagnosed cases, Dengue fever (62) formed the largest group. Other cases diagnosed were of Malaria (22); Leptospirosis (3), Septicemia (3), varicella (2) and unknown infective cause. Bleeding manifestation of thrombocytopenia was present only in 35 cases and in 85 cases it was not present. 100% of patients of very severe thrombocytopenia and 25% patients with severe thrombocytopenia manifested with bleeding diathesis.

Keywords: Fever, thrombocytopenia, infectious etiology

INTRODUCTION

Fever is a pervasive and ubiquitous theme in human myth, art and science. 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.[1] Thrombocytopenia is defined as platelet count <100,000/µl. This is due to decreased production, increased destruction (immunogenic and non immunogenic), increased sequestration in spleen. Of these infections being the important cause of thrombocytopenia.[2,3,4] At times the fever course is prolonged and fever with thrombocytopenia narrows the differential diagnosis of the clinical entity.

Infections like malaria, dengue, leptospirosis, typhoid, septicemia, 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 and thus treatment.[5]

The purpose of study was to elucidate possible infective etiology for fever with thrombocytopenia and to correlate clinical features, laboratory studies and etiology.

MATERIALS AND METHODS

Study Design

A Prospective clinical study of 120 patients presenting with fever and thrombocytopenia was undertaken to study the possible infective etiology, and correlate clinical features, Lab values and Etiology.

Study Centre

This study was done on patients, who were admitted to Chalmeda Anand Rao Institute of Medical Sciences Hospital, Karimnagar during a period of August 2018 to December 2019.

Inclusion criteria

- All the adult patients aged 16-65 years with fever and thrombocytopenia of infective etiology

Exclusion criteria

- Patients with fever with thrombocytopenia other than infective etiology were excluded.

Procedure

Once the patients admitted with fever and those who had thrombocytopenia, a careful history was recorded, general physical examination was done. Detailed examination of various systems was done. Routine investigation was done; the specific and special investigations were done as and when indicated.[6]

In whom a final definite diagnosis was reached, were treated for the disease and in those platelet count was repeated at the time of discharge. Details of history, general physical examination and laboratory and technical investigation reports were noted down from time to time.

Once the specific diagnosis was reached, patients were treated for it specifically and symptomatically. For bleeding complications platelet transfusions was done if platelet count was <20,000/cumm or had bleeding manifestation.[7]

The causes of fever with thrombocytopenia are so numerous; a simple workable classification is presented in:

1. Viral causes: CMV, Dengue, Parvo-B19; HSV, HIV, Hantana, HBV etc.
2. Bacterial causes: Gram +ve and –ve septicemia, military tuberculosis, leptospirosis, typhoid etc.
3. Protozoal causes: Malaria

Ethics Approval

This study was reviewed and approved by the Institute Ethics Committee, CAIMS, Karimnagar.

RESULTS

In the present study subjects were in the age group of 16-65 years. Youngest 16 years old and oldest 64 years. In the present study out of 120 cases of fever with thrombocytopenia, 83 were males and 37 were females (Table 1).

Out of 120 patients of fever with thrombo-cytopenia, had definitive diagnosis with Dengue 62 cases as the commonest cause, followed by, Malaria 22 cases, Mixed malaria and dengue 2 cases, Leptospirosis 3 cases, Septicemia 3 cases, varicella 2 cases, and unknown/viral 28 cases.

Out of 22 cases of malaria, falciparum malaria 5 cases, vivax malaria 6 cases and mixed malaria 11 cases. Mixed infection with both falciparum and vivax was the commonest. In our study 56.7% of the patients had platelet count less than 50,000 cells/cumm, followed by 35% and 8% of the patients had platelet count in the range of 50,000 –1,00,000 and >1,00,000 respectively.

Out of 35 patients with bleeding manifestation 35 patients (100%) had petechiae, 25 patient (71.4%) had purpura and Subconjunctival bleed is seen in 8 patients (22.9%) and bleeding gums in 5 patients (14.3%), malena in 3 cases(8.5%), epistaxis in 2 cases(5.7%).

In this study, 113 of them had good recovery and 7 of them expired. In 7 mortality cases, 2 cases were due to ARDS, 5 cases were due to multiorgan failure were of unknown cause. In 7 mortality cases, 2 patients had platelet count in the range of <10000 cells/cumm and 3 patients had platelet count 10000-20000 cells/cumm, 2 patients had platelet count 20000-25000 cells/cumm.

Table 1: Age distribution of patients studied

Age in years	No. of Patients	Frequency
<20	15	12.5
21-30	32	26.7
31-40	30	25.0
41-50	18	15.0
51-60	15	12.5
61-65	10	8.3
Total	120	100.0

Table 2: Gender distribution of patients studied

Age in years	No. of Patients	Frequency
Male	83	69.0
Female	37	31.0
Total	120	100.0

Table 3: Bleeding manifestations

Bleeding Manifestations	No. of Patients	%
Present	35	29.17
Petechiae	35	29.17
Purpura	25	20.83
Subconjunctival		
Hemorrhage	8	6.67
Bleeding Gums	5	4.17
Malena	3	2.5
Epistaxis	2	1.67

Skin bleeding was the commonest type of bleeding manifestation in our study. Petechiae (35) is the commonest type of skin bleeding noticed followed by pupura (25). 8 cases of subconjunctival hemorrhage, 5 cases of bleeding gums, 3 cases of malena, 2 cases of epistaxis were also seen in our study.

Cases of hematuria were not found in our study. Though hematuria/hematemesis / CNS bleed described in the literature but of lower incidence (Table 3).

Table 4: Platelet count at the time of admission

Platelet count	No. of Patients	%
=20000	24	20.0%
20000-50000	44	36.7%
50000-75000	25	20.8%
75000-100000	17	14.2%
100000-150000	10	8.3
Total	120	100.0

Thrombocytopenia has been arbitrary classified as:

- Very severe < 20000/cumm
- Severe 25000 – 50000/cumm
- Moderate 50000 – 100000/cumm
- Mild 1.0 – 1.5 lakhs /cumm

In the present study there were 24 patients with very severe thrombocytopenia followed by 44 with severe thrombocytopenia, 42 with moderate thrombocytopenia and 10 patients with mild thrombocytopenia (Table 4).

Table 5: Etiology of infection in the study population

Infections	Number of Patients	%
Dengue rapid test		
Positive	62	51.7
QBC for MP		
PF	5	4.2
PV	6	5.0
PF&PV	11	9.2
Leptospira – IgM		
Positive	3	2.5
Blood culture		
Positive	3	2.5
Varicella		
Positive	2	1.7
Unknown	28	23.3

51.7 % of the study population positive for Dengue, 50% cases with only dengue and 1.7% cases with mixed dengue with malaria co-infection. QBC total positive 22 out of which plasmodium falciparum 5 cases, plasmodium vivax 6 cases and mixed 11 cases. 3 cases of Leptospira, 2 cases of varicella infected were also noted. Blood culture was positive in 3 cases with septicemia and organism isolated was E.coli. There were 28 cases where the exact cause of infection could not be elucidated. All these 28 cases were negative to all the infective causes listed in the above mentioned investigation chart (Table 5).

DISCUSSION

During the course of follow up platelets showed increasing trends in 69 patients (63.3%) and continuously decreasing trends in 8 patients (7.3%). Totally infections represented the most important cause of fever with thrombocytopenia with a relative frequency ranging from 68%-100%.

The study conducted by Nair PS et al (2003) for period of one and half years. A total of 109 cases (76 male, 33 female patients) were studied with the same criteria as in our study. In our study 83 were males and 37 were female. [8]

In the present study Infections (76.7%) are the established diagnosis as compared to other study. In the present study Dengue fever 62 cases (51.7%) was the commonest cause as compared to Nair study in which septicemia (27%) was the commonest cause. This might be due to seasonal, regional variations and other multifactorial. In the present study dengue fever 62 cases (51.7%) was the commonest cause as compared to Srinivas study in which malaria (41%) was the commonest cause.

In the present study out of 62 cases of Dengue fever, only dengue positive are 60 cases, dengue with malaria are 2 cases. Hence Dengue alone or Dengue with other co-infection is the commonest infection causing fever with thrombocytopenia in the present study.

In the present study, dengue fever 62 cases (51.7%) was the commonest cause as compared to Srinivas study in which malaria (41%) was the commonest cause. In the present study bleeding manifestations were present in 29.2% of cases as compared to Srinivas study in which bleeding manifestations were present in 49% of cases. [9]

In the present study there were 22 cases of malarial, out of which plasmodium falciparum are 5 cases, plasmodium vivax are 6 cases and mixed infections are 11 cases. In this study there were 3 cases of Leptospira positive, 2 cases of varicella positive, and 3 cases of septicemia.

There were 28 cases of clinically suggestive of infection but negative for all the test in this study. All cases are negative to all the infective causes listed in the investigation chart.

In the present study, Petichae (100%) was the commonest bleeding manifestations followed by spontaneous bleeding like bleeding gums (4.2%) subconjunctival hemorrhage (6.7%), malena (2.5%), epistaxis (1.5%). In other study spontaneous bleeding was the commonest bleeding manifestation (68%) followed by petichae/ purpura accounting for (22.22%), others (9.88%).[10]

All cases were investigated for common infective etiology listed in the investigation chart but 28 cases remained undiagnosed might be because of the early introduction of empirical treatment and also limitation of the diagnostic modalities. Dengue, Malaria, Leptospirosis, Septicemia and other viral infections formed the major etiological factors of this group.

CONCLUSION

A definitive diagnosis could be made in 92 cases and 28 cases remained undiagnosed. Among the diagnosed cases, Dengue fever (62) formed the largest group. Other cases diagnosed were of Malaria (22); Leptospirosis (3), Septicemia (3), varicella (2) and unknown infective cause (28). Our study showed 113 cases had recovered totally and there was mortality in 7 cases.

In 113 cases who recovered, were followed up till discharge and platelet count were near normal at the time of discharge. In mortality group of 7 cases, 2 cases of ARDS were due to Dengue accounting for 28.5% and 5 were due to Multiorgan failure of unknown infective cause accounting for 71.5% of the total 7 cases. Common range of platelet count in mortality group was <10,000 in 2 cases, 10000-20000 in 3 cases, 20000-25000 in 2 cases.

CONFLICT OF INTEREST:

The authors declared no conflict of interest.

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