Original Research Article

Study of acute febrile illness with thrombocytopenia in a tertiary care centre

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ABSTRACT

Background: In the recent period there is an upsurge in the incidence of fever with thrombocytopenia in the Northern Kerala. This may be due to the several emerging and re emerging infections which causes frequent epidemics in the region. Early diagnosis and meticulous management will prevent fatal out come. Studies on fever with thrombocytopenia are very few in the Northern part of Kerala.

Methods: This was a descriptive study conducted at Academy of Medical Sciences Pariyaram over a period of one year from November 2015 to October 2016. The study includes 251 cases attending outpatient and inpatients units in the department of medicine. All patients with a platelet count less than 150000 was included in this study and detailed clinical and laboratory evaluation was done and assessed for the etiology and outcome.

Results: Among the 251 cases, Dengue fever accounts 54.5 % of cases and 26.2% are other viral fever where the exact causative organism was not detected. Leptospirosis, malaria were also important causes of fever with thrombocytopenia. Major incidence of hemorrhagic manifestation occurred in the age group of 20 to 30 years whose platelet count was in the range of 10000 to 40000/mm^3.

Conclusions: In this study more than 50 % had dengue fever and in 26.2% cases an exact etiology cannot be determined. This finding highlights the fact that there may be many unidentified infection which cause fulminant thrombocytopenia and there is a need for wider screening of infection.

Keywords: Bleeding manifestation, Dengue fever, Infection, Prognosis, Thrombocytopenia

INTRODUCTION

In the recent period there is an upsurge in the number of patients with fever and thrombocytopenia.[1] This may be due to several emerging and re-emerging infections in the recent period. Patient with severe thrombocytopenia and bleeding manifestations have high mortality and early detection of etiological factor is important in reducing the mortality. Platelets play a central role in normal haemostasis and also in thrombosis.[1] Bleeding due to thrombocytopenia usually occurs in small vessels and this manifests as petechiae over the skin, hemorrhages from mucosa of gastrointestinal and genitourinary tract.[2,3] Intracranial haemorrhage is a critical event in thrombocytopenic patients.[4] Several studies have shown that arboviral infections like dengue fever, chickugunya, kyasanur forest diseases and scrub typhus and leptospirosis and malaria, military tuberculosis typhoid and Human immunodeficiency causes fever and thrombocytopenia.[5,6]

There is seasonal variation in the epidemic of fever. At times non-infective causes and drugs can also cause thrombocytopenia and fever. The mortality is very high when there is severe thrombocytopenia 2 and mortality increases due to hemorrhagic manifesations. So, it is imperative that there should be regional studies to assess the etiology of fever with thrombocytopenia. Though

there are frequent epidemics of several arboviral infections in our area, there are only few studies which focuses the thrombocytopenia in patients with fever. Therefore, a well-structured systematic approach that is conducted with an awareness of different causes of fever with thrombocytopenia streamlines the differential diagnosis and determines the etiology. This study was conducted to full fill this objective.

METHODS

This was a descriptive study conducted at Academy of Medical Sciences, Pariyaram which is a tertiary care centre situated in the northern part of Kerala. All the patients admitted with fever and thrombocytopenia attending the outpatient department and medical wards were included for the study. The study was for a period of one year from November 2015 to October 2016. All the patients with a history of fever less than two weeks with a temperature more than 37.20C (>98.90F) and those with a platelet count less than 150000 in the age group of more than 15 years to years 85 were included. All patients with inherited thrombocytopenia, and on antiplatelets, autoimmune disorders, HIV, chronic liver diseases and hematological malignancy were excluded.

Once the patient is admitted with fever and for those who had thrombocytopenia, a careful history, general physical examination, detailed examination of various systems will be done. Routine investigations including the specific and special investigations will be done as and when indicated. In whom a final definite diagnosis is reached and treated for the disease full assessment will be repeated at the time of discharge. Details of history, general physical examination and laboratory and technical investigation reports will be noted down from time to time. The clinical profile will be assessed with procured data. Sampling method is universal sampling. Investigations such as Complete blood count, Urine routine, Chest X- ray, Renal function test, Liver Function Tests, Blood culture, Malarial parasite smear, Widal test, IgM dengue, IgM leptospira, USG abdomen, viral markers if required. Peripheral smear study, Bone marrow study if required.

Statistical method

Descriptive statistical method like mean, standard deviation (SD), frequencies, proportions, was used. The data was entered and analyzed using appropriate software SPS 16.

RESULTS

The present study includes 251 patients, who were admitted for fever with thrombocytopenia in Academy of Medical Sciences, Pariyaram. It was observed that those in the age group of 20 to 30 are affected age group people. Leptospirosis affected more among in the above 50 years. The duration of fever in the present study

ranged from 1-14 days with mean duration of 4.98±2.35 (SD) days. 90% of the total cases had duration of < 10 days and majority recovered from fever with a period of 5 days. Considering the etiology, Dengue fever was found to be the commonest and most important cause for fever with thrombocytopenia contributing for more than 50% of cases. The other causes for fever with thrombocytopenia are Non-specific viral fever (26.2%), Malaria (8%), Leptospirosis (5.6%) in decreasing order (Table 1).

Table 1: Distribution of different etiology.

Diagnosis	Cases	Percent
Dengue fever	137	54.5
Viral fever	66	26.2
Malaria	20	8.0
Leptospirosis	14	5.6
Viral hepatitis	8	3.2
Lower respiratory tract infection	4	1.6
Pyelonephritis	2	0.8

Headache (52%) contributed to most common symptom next to fever in the present study. Other prominent symptoms in the descending order include joint pain (42%), myalgia (35%), abdominal pain (22%) and vomiting (17%). Fever was present in 100% of cases. Jaundice contributed to major sign in the present study (11%). Hepatosplenomegaly contributed to 8% followed by pallore in the present study. In the present study platelet count varied from 10000-150000/mm³ with mean platelet count of 68868±32268/mm³ (SD). Thrombocytopenia was found in 35% of cases and 5% of patients had platelet count <20000/mm³ and they are at a high risk of bleeding complications. Majority of patients had platelet count >50000/mm³ (Table 2).

Table 2: Distribution of platelet count.

Platelet count/mm³	No	%
10001-20000	12	5
20001-30000	24	10
30001-40000	20	8
40001-50000	28	11
50001-100000	134	53
100000-150000	33	13

Table 3: Thrombocytopenia in different infections.

Platelet Count	Dengue	Viral Fever	Malaria	Leptospirosis
<50000	63(46)	7(10.6)	3(15)	8(57.1)
50000-100000	65(47.4)	49(74.2)	13(65)	3(21.4)
>100000	9(6.6)	10(15.2)	4(20)	3(21.4)

Total platelet count varied according to the etiology. In dengue fever, 46% of cases had severe thrombocytopenia (count <50000/mm³). Of 56 cases of viral fever, 10% had counts <50000/mm³, 90% had platelet count of

>50000/mm³. In leptospirosis, 57% of patients had Thrombocytopenia which is even higher than the dengue and 14% of patients had platelet count <20000/mm³. In Malaria, 3 patients (15%) had a platelet count <50000/mm³ but none less than 40000/mm³ (Table 3).

Bleeding manifestation was found in 43 patients, 8(out of 9) patients had platelet count 10000-19999/mm³, 3(out of 6) patients had platelet count between 20000-29999/mm³. 21(out of 33) had between 30000-39999/mm³, 7(out of 34) had platelet > 50000/mm³ and 4(out of 134) had platelet count >50000/mm³. This suggests that bleeding episodes were more common in patients with low platelet count. Bleeding manifestations in the form of petechiae is a common manifestation of thrombocytopenia. Petechiae with and without gum bleeding/ epistaxis / conjunctival haemorrhage occurred in 12% of patients in the present study. There was 43 patients with bleeding manifestations out of which both mucosal and superficial bleeding was equally manifested in patients with platelet count between 10000-29999/mm³ and superficial bleeding was more seen in the category of patients with platelet count >30000/mm³.

DISCUSSION

This study was conducted in Academy of medical sciences, Pariyaram which is a tertiary care centre in Northern Kerala over a period of one year from November 2015 to October 2016. We studied 251 patients of which 127 were males and 124 were females. Though male to female ratio was almost equal, it was observed that males were more affected in the second and third decades which might be due to their increased travel. The age of patients varied from 15 to 85 yrs which includes all sections of the society. There was maximum incidence of fever among the age group of 21-30 years which constituted 22.3% of the study population. Only few cases were reported in the older age group.

In our study the most common presenting symptom was fever. In spite of being a major concern among general public and medical fraternity most of the cases of fever with thrombocytopenia recovered within 5 days of onset of fever.

Headache was the second most common symptom which was reported in 52% of patients. Other common symptoms were joint pain (42%), myalgia (35%), abdominal pain (22%) and vomiting (17%). If a patient present with these symptoms, we should actively search for diseases like Dengue fever, Leptospirosis, Malaria etc.

Most common clinical sign in the present study was jaundice and it was observed in 11% of the patients. The other common clinical findings were hepatomegaly (8%), splenomegaly (8%) followed by pallor and conjunctival hemorrhage. There were rash and petechial spots in many of our patients with Dengue fever. Jaundice was found to be frequently associated with Leptospirosis and Viral hepatitis due to hepatic involvement. Splenomegaly and Hepatomegaly was more seen in Malaria patients.

This study has shown that commonest cause of fever with thrombocytopenia was Dengue (54.5%). This may be due to the fact that most of the patients admitted during the period have dengue and frequent epidemics were reported from the area. During this study detailed evaluation and diagnostic work up was done in all cases but interestingly in 26.2% a definite etiology or infectious agent was not detected. As shown in studies from several part of world different arboviral infection can cause thrombocytopenia. But these non-specific causes most of them have symptomatology of viral fever like head ache myalgia, fever.

Malaria is the third most common cause of fever with thrombocytopenia which constitutes around 8% of the patients and still continues to be a major health problem in the society. It was more commonly seen in the immigrant population. Early identification and prompt treatment should be administered before complications occur, especially in Leptospirosis and Malaria where specific drugs are available.[7]

In a similar study conducted by Nair et al, Septicemia was the leading cause of fever with thrombocytopenia (26.61%) followed by Typhoid fever (14.68%), Dengue (13.8%), Megaloblastic anemia (11.9%), Malaria (9.2%), Hematological malignancies (3.7%).[8] This might be due to the seasonal and regional variability where the study was conducted. In our study more than 54.6% cases had dengue but in the study by Nair et al[8] showed only 13.8% had dengue fever. This may be due to the regional variation in the epidemics or due to seasonal variations. Similarly, 15.6% cases were non-infective causes in study by Nair et al whereas non-specific causes constitute 26.2% cases in our study.

Study conducted by Gandhi et al leading cause of fever with thrombocytopenia was Malaria (42%) followed by Dengue (26%), and other viral fever (17%), septicemia (4.5%), enteric fever (4.45%).[9] Where as in our study dengue fever is the common cause followed by other viral fever causes 26.2% which is higher in our study. In Raikar et al study dengue (52%), malaria (42%), enteric fever (3%), non-specific viral fever (4.5%) in our study both dengue and non-specific viral fever was high.[10]

A detailed study of distribution of thrombocytopenia was done in our study and it was found that the distribution of platelet varied from 10000 to 150000 in our cases. Interestingly 35% of cases in this study had thrombocytopenia <50000 whereas platelet count less than 20000 occurred in 4.7%. Whereas Nair et al[8] 25.7% of patients had platelet count in the range of 20000-50000/mm³. In patients with leptospirosis out of 14 cases 14% had platelet count <20000/mm³. This clearly shows that severe thrombocytopenia also occurred in

Leptospirosis and is an important differential diagnosis of fever with thrombocytopenia. This finding shows that either dengue or leptospirosis should be considered early if severe thrombocytopenia noticed in febrile patients.

In patients with thrombocytopenia, Bleeding manifestations like petechiae, conjunctival haemorrhage, gum bleeding and malena were seen in 17% of patients. Petechia was the commonest bleeding manifestation observed in 31 patients, followed by spontaneous mucosal bleeding like gum bleeding, haematuria and malena. In Nair et al study spontaneous mucosal bleeding was the commonest bleeding manifestation followed by petechiae/purpura.[8]

CONCLUSION

This study was conducted at Academy of medical Sciences, Pariyaram, which is a tertiary care centre in the Northern part of Kerala and had shown that fever with thrombocytopenia is a common condition which required inpatient care in most of the patients. Dengue fever was the most common cause of fever with thrombocytopenia in this region which affected more than half of the study population. In 26% of cases with fever and thrombocytopenia we could not find a definite cause, it may be due to the limited screening facility available for other infections which lead to thrombocytopenia. Severe thrombocytopenia was noticed in 32% of patients and 3.5% had platelet count less than 20000/mm^3 and the majority of severe thrombocytopenia was caused by Dengue fever. In our study Headache was the second most common presenting symptom after fever, the other common symptoms being joint pain and myalgia. When a patient presents with these complaints possibility of fever with thrombocytopenia has to be considered. The bleeding manifestations were commonly associated with severe thrombocytopenia and especially when platelet count is less than 20000/mm^3.

This study showed that in the recent periods, dengue fever was the most common cause of thrombocytopenia in fever patients, and interestingly in more than 26.2% cases a definite cause of thrombocytopenia could not be ascertained. This shows that more commonly diagnosed condition like dengue, leptospirosis, malaria, typhoid or scrub still there are several infectious agents which cause fever and thrombocytopenia which cannot be easily diagnosed with routine laboratory tests. So, it is imperative that there should be more screening and diagnostic techniques for detecting other viral infections especially in cases with severe thrombocytopenia with hemorrhagic manifestations.

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