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Original Research Article

A Study to Assess Clinico-Etiological Profile of Febrile Thrombocytopenia in Children Aged between 1 Month to 12 Years

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Abstract

Aim: The aim of the present study was to assess the etiological profile of febrile thrombocytopenia in children aged between 1 month to 12 years admitted to the pediatric department.

Methods: The present study was a hospital based observational study done in the department of Pediatrics at JLNMCH Bhagalpur, Bihar, India for the period of one year. Patients between 1 month to 12 years of age who presented with fever in whom complete blood picture showed thrombocytopenia (platelet count <1,50,000 /mm3) at the time of hospitalization were taken up for the study. Patients less than 1 month and greater than 12 years of age and patients on drugs known to cause thrombocytopenia were excluded from the study.

Results: Majority of the cases (52%) belonged to the age group 1-6 years, and (45.5%) belong to the age group of 7-12 years. Among these cases females (55%) are more common than males (45%). The most common etiology of fever with thrombocytopenia was dengue fever (61%), followed by malaria (12%), enteric fever (10%), other undifferentiated viral fevers (10%) and MIS-C (multisystem inflammatory syndrome in children) (5%), immune thrombocytopenic purpura (2%), leukaemia (0.5%) and hepatitis A (0.5%). The common symptoms associated with patients having febrile thrombocytopenia were headache in 70%, followed by body ache in 51%, retro-orbital pain 42%, pain abdomen 30% and bleeding manifestations 22% cases. 104 patients had mild thrombocytopenia, 36 patients had moderate thrombocytopenia and 60 patients had severe thrombocytopenia. Among the total dengue cases (n=122), severe thrombocytopenia was seen in 71 children. Duration of hospital stay in majority of cases (65%) was prolonged to due to bleeding manifestations and associated complications.

Conclusion: Febrile thrombocytopenia is a common clinical presentation in children. Majority of the dengue cases responded well to treatment given as per WHO guidelines. In most of the other infections, thrombocytopenia was transient and asymptomatic with lesser severity and resolved with the treatment of underlying condition.

Keywords: Febrile, Thrombocytopenia, Dengue, Etiology.

Introduction

A decrease in the peripheral blood platelet counts below the lower normal limit of 150,000/µL is referred to as thrombocytopenia. [1] It may result in poor clot formation and is associated with a higher risk of bleeding. [2] It is frequently used as a reason for bone marrow biopsy and bone marrow aspiration. Hypo-proliferation in the bone marrow or platelet breakdown in the periphery can both cause thrombocytopenia. The testing of the bone marrow is frequently used to distinguish between these two groups. The range of the normal platelet value is 150,000 to 450,000/µL. Thrombocytopenia is defined by platelet counts less than 150,000/µL; however, these numbers do not show the underlying pathophysiology.[3] Thrombocytopenia can be classified into three stages which include a mild category having platelet count between 100,000 - 150,000/µL, moderate thrombocytopenia having platelet count between 50,000 - 100,000/µL and severe thrombocytopenia having platelet count < 50,000/µL. [3]

Thrombocytopenia is a significant finding in any hospital setting that is seen in numerous conditions with variable spectrums. Its severity ranges from an incidental finding otherwise undetected to severe life-threatening bleeding. So the early detection of the cause of thrombocytopenia followed by proper treatment may prove lifesaving. A bone marrow examination is a helpful and affordable diagnostic method in haematological practice. Both neoplastic and non-neoplastic haematological conditions are identified using the aid of a bone marrow aspiration. Thrombocytopenia is characterized by bleeding

most often from small vessels. This can manifest as petechiae over the skin, hemorrhage from mucosal of gastrointestinal and genitourinary tract and sometimes even dangerous consequences like intra cerebral hemorrhage. Though thrombocytopenia is encountered in various diseases, it is fortunate that potentially fatal bleeding due to thrombocytopenia is rare. [4] The risk of complications like bleeding is inversely proportional to the platelet count. Thus, thrombocytopenia correlates inversely with the mortality and morbidity in various febrile illness and serial monitoring of platelet count has prognostic value. This highlights the importance of thrombocytopenia in various febrile disorders. [5] The association of fever with thrombocytopenia narrows the differential diagnosis of the clinical entity. Septicemia and other infections like dengue, leptospirosis, malaria, typhoid, HIV are the common causes of fever with thrombocytopenia. [6]

The aim of the present study was to assess the etiological profile of febrile thrombocytopenia in children aged between 1 month to 12 years admitted to the pediatric department.

Materials and Methods

The present study was a hospital based observational study done in the department of Pediatrics at JLNMCH Bhagalpur , Bihar, India for the period of one year. Patients between 1 month to 12 years of age who presented with fever in whom complete blood picture showed thrombocytopenia (platelet count <1,50,000 /mm3) at the time of hospitalization were taken up for the study. Patients less than 1 month and greater than 12 years of age and patients on drugs known to cause thrombocytopenia were excluded from the study. A total of 685 cases were admitted during the study period, of which 450 cases had febrile illness. Among 450 cases with fever, 180 cases had fever with thrombocytopenia. 200 children satisfying the inclusion criteria for febrile thrombocytopenia were taken up for the study. Ethical clearance from the institutional ethics committee was obtained.

All the details regarding cases having fever and thrombocytopenia were taken from the medical records. History, clinical examination and details of the investigations pertaining to the clinical condition were noted on a predesigned proforma. The data from the fully filled questionnaire were analysed using Microsoft excel as statistical tool and represented below as proportions. Investigations such as hemogram with peripheral smear, C-reactive protein, renal function test, liver function test, complete urine examination, malarial parasite smear, coagulation profile, blood culture sensitivity, serological tests to detect dengue, leptospira, rickettsia, enteric fever, ultrasonography of chest and abdomen, chest X-ray, COVID antibodies were done based on the clinical condition of the patient. At admission, a blood sample of 1 ml for hemogram was collected in sterile EDTA (ethylenediaminetetraacetic acid) bulbs by venipuncture after taking all aseptic precautions and immediately transferred to laboratory and results were obtained by an automated haematology analyser. Platelet counts were obtained by machine count and whenever there was low platelet count it was rechecked by manual method. For cases with bleeding manifestations, 1.8 ml of venous blood was collected in a bottle containing 0.2 ml of 3.8% sodium citrate. PT, APTT, INR were obtained by automated coagulation analyser. A platelet count of <1,50,000 /mm3 is defined as thrombocytopenia irrespective of age and gender. Thrombocytopenia has been arbitrarily classified as below. The patients are classified into these grades based on the lowest level of platelet count during the hospital stay.

- Mild thrombocytopenia is when the platelet count is 1,00,000 to <1,50,000 /mm^3.
- Moderate thrombocytopenia is when the platelet count is 50,000 to <1,00,000 /mm^3.
- Severe thrombocytopenia is when the platelet count is <50,000 /mm^3.

Results

Table 1: Age and gender wise distribution of febrile thrombocytopenia

Age in years	Male	Female	Total (%)
<1 years	0	5	5 (2.5)
1-6 years	54	50	104 (52)
7-12 years	56	35	91 (45.5)
Total	110	90	200 (100)

Majority of the cases (52%) belonged to the age group 1-6 years, and (45.5%) belong to the age group of 7-12 years. Among these cases females (55%) are more common than males (45%).

Table 2: Etiological distribution of febrile thrombocytopenia

Etiology	N (%)
Dengue	122 (61)
MISC	10 (5)
Malaria	24 (12)
Viral fever	20 (10)

Enteric fever	20 (10)
Hepatitis	1 (0.5)
Leukemia	1 (0.5)
ITP	2 (1)

The most common etiology of fever with thrombocytopenia was dengue fever (61%), followed by malaria (12%), enteric fever (10%), other undifferentiated viral fevers (10%) and MIS-C (multisystem inflammatory syndrome in children) (5%), immune thrombocytopenic purpura (2%), leukaemia (0.5%) and hepatitis A (0.5%).

Table 3: Clinical features of the cases with febrile thrombocytopenia

Clinical features	No. of cases (N= 200)	Percentage (%)
Fever	200	100%
Chills and rigor	48	24%
Headache	140	70%
Body ache/myalgia	102	51%
Retro-orbital pain	84	42%
Pain abdomen	60	30%
Loose motion	48	24%
Jaundice	50	25%
Cough and breathlessness	40	20%
Bleeding manifestations	44	22%
Weight loss	10	5%
Altered sensorium	12	6%

The common symptoms associated with patients having febrile thrombocytopenia were headache in 70%, followed by body ache in 51%, retro-orbital pain 42%, pain abdomen 30% and bleeding manifestations 22% cases.

Table 4: Distribution of cases based on severity of thrombocytopenia

Severity of thrombocytopenia	N (%)
<50,000 /mm^3	104 (52)
50,000-99999/mm^3	36 (18)
100000 - 150000/mm^3	60 (30)

104 patients had mild thrombocytopenia, 36 patients had moderate thrombocytopenia and 60 patients had severe thrombocytopenia.

Table 5: Distribution of dengue cases based on severity of thrombocytopenia (n=122)

Severity of thrombocytopenia	N (%)
<50,000 /mm^3	25 (20.50)
50,000-99999/mm^3	26 (21.30)
100000 - 150000/mm^3	71 (58.20)

Among the total dengue cases (n=122), severe thrombocytopenia was seen in 71 children.

Table 6: Distribution of children with febrile thrombocytopenia based on duration of hospital stay

Duration of hospital stay	N (%)
1-5 days	50 (25)
6-10 days	130 (65)
11-16 days	20 (10)

Duration of hospital stay in majority of cases (65%) was prolonged to due to bleeding manifestations and associated complications.

Discussion

Febrile thrombocytopenia is the thrombocytopenia associated with fever irrespective of age and gender. [7] Thrombocytopenia is defined as platelet count less than 1,50,000 /mm3. [8] Fever is an acute phase response which is one of the most common manifestations of an infection/inflammation. [9] Fever is produced due to production of substance called pyrogen. Thrombocytopenia is due to decreased production, increased destruction

(immunological and non- immunological) or increased sequestration in spleen. [10] There is an increasing trend in the incidence of fever with thrombocytopenia especially in the pediatric age group.4 The presence of thrombocytopenia in a child with fever acts as an etiological clue which can aid in early diagnosis and treatment. Although thrombocytopenia has a varied etiology, infectious conditions are more common in tropical countries like India. [9]

Fever has been recognized as the cardinal feature of disease since ancient times as stated by the ancient scholars like Hippocrates. [11] Fever was initially seen as a disease but later recognized as variety of disease entities and a reliable marker of illness. [12] Fever is a very common symptom with which the patients presented in hospitals outdoors. Fever is defined as an elevation of body temperature above the normal circadian range; i.e. an A.M. temperature of >37.2ºC (>98.9ºF) or an P.M temperature of >37.7ºC (>99.9ºF). [13] Thrombocytopenia is defined as platelet count less than 1,50,000/µL. This is due to decreased production, increased destruction (immunogenic and non-immunogenic), and increased sequestrations in spleen. Of these, Infection being the commonest cause of thrombocytopenia. [14]

Majority of the cases (52%) belonged to the age group 1-6 years, and (45.5%) belong to the age group of 7-12 years. Among these cases females (55%) are more common than males (45%). This finding was not similar with other Gondhali et al who included more males than females in the study. [6] The most common etiology of fever with thrombocytopenia was dengue fever (61%), followed by malaria (12%), enteric fever (10%), other undifferentiated viral fevers (10%) and MIS-C (multisystem inflammatory syndrome in children) (5%), immune thrombocytopenic purpura (2%), leukaemia (0.5%) and hepatitis A (0.5%). The common symptoms associated with patients having febrile thrombocytopenia were headache in 70%, followed by body ache in 51%, retro-orbital pain 42%, pain abdomen 30% and bleeding manifestations 22% cases. Gondhali et al[6] observed body ache (92%) and headache (90%) as the most common symptoms and Mohammad F N et al [15] also found headache (52%) was the most common symptoms next to fever. 104 patients had mild thrombocytopenia, 36 patients had moderate thrombocytopenia and 60 patients had severe thrombocytopenia. This was similar to the findings by Nair et al where he noticed a predominance of bleeding manifestation in children with platelet count less than 10,000 /mm3. [ ]

Among the total dengue cases (n=122), severe thrombocytopenia was seen in 71 children. The pathogenesis of thrombocytopenia in dengue fever was not clearly understood. Increased peripheral destruction of antibody coated platelets was strongly suspected as the possible mechanism.[10] The second most common cause of febrile thrombocytopenia in our study was malaria. This was in contrary to the findings of the study done by Guthi et al [10] and Morales et al [16] in which malaria was the most common etiology of febrile thrombocytopenia. Duration of hospital stay in majority of cases (65%) was prolonged to due to bleeding manifestations and associated complications. Lohitashwa et al, also showed that purpura (63%) was the commonest bleeding manifestations followed by spontaneous bleeding (37%) in his study. [17]

Conclusion

Febrile thrombocytopenia is a common clinical presentation in children. Majority of the dengue cases responded well to treatment given as per WHO guidelines. In most of the other infections, thrombocytopenia was transient and asymptomatic with lesser severity and resolved with the treatment of underlying condition. The fever associated with thrombocytopenia is a common clinical presentation of disease where infection being the commonest cause. Dengue is the most common cause. Most of the patients with febrile thrombocytopenia don't show bleeding manifestations. But a significant number of cases showed bleeding manifestations consists of simple skin bleed to major life threatening bleeding like gastrointestinal bleed and intra cerebral bleed etc. Early diagnosis and treatment results in good clinical recovery and reduces mortality. Septicemia is the most common cause of mortality and it must be treated promptly and adequately. Hence, early evaluation of cause of febrile thrombocytopenia is very important in respect to prompt management and good outcome.

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