

An aetiological profile of febrile thrombocytopenia in children

Sujatha Ramabhata¹, *Pushpalatha Kariyappa¹, Bharathi Kondappa¹, Udaya Kumar Rao¹, Hareesh Sanikam¹

Sri Lanka Journal of Child Health, 2018; 47(2): 146-148

Abstract

Objective: To establish the possible aetiology of febrile children presenting with thrombocytopenia.

Method: In this observational study, all children, aged 1 month to 18 years, admitted to paediatric wards of the ESIC Medical College & Postgraduate Institute of Medical Sciences and Research, Bengaluru, India, from October 2012 to September 2013, with fever and thrombocytopenia, were included. A thorough history was obtained and a general and systemic examination done. Routine investigations were done in all cases and specific investigations as and when required.

Results: Of 1551 children admitted with febrile illness during the study period, 306 with thrombocytopenia fulfilled the inclusion criteria. Thirty five percent of children had mild thrombocytopenia. The commonest cause of thrombocytopenia was dengue fever (83%). The mortality was low (0.7%) and was seen only in dengue fever in our study.

Conclusions: The commonest cause of febrile thrombocytopenia in this study was dengue fever, accounting for 83% of cases.

DOI: <http://dx.doi.org/10.4038/sljch.v47i2.8481>

(Key words: Febrile thrombocytopenia, platelets, dengue fever)

Introduction

Fever in children is one of the most common manifestations of an illness that make parents to seek medical attention early. Every child with fever has to be assessed carefully to find an aetiology¹. Common causes of fever with thrombocytopenia are infections like malaria, dengue, leptospirosis, viral fever and septicaemia.

¹ESIC Medical College and Post Graduate Institute of Medical Science and Research, Bengaluru, India

*Correspondence: dr.pushpalathaani@yahoo.in
(Received on 13 July 2017; Accepted after revision on 18 August 2017)

The authors declare that there are no conflicts of interest

Personal funding was used for the project.

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Thrombocytopenia is defined as a platelet count below the normal range for the population, and a traditional value of 150,000 per cubic millimetre is supported by the National Health and Nutrition Examination Survey as the lower limit of normal².

Objectives

To establish the possible aetiology of febrile children presenting with thrombocytopenia.

Method

This observational study was conducted on children admitted to paediatric wards in the ESIC Medical College & Postgraduate Institute of Medical Sciences and Research, Bengaluru, India, from October 2012 to September 2013. All children, aged one month to 18 years, presenting with fever and thrombocytopenia were included in the study. Children with haematological disorders, malignancies, collagen vascular disorders and those on drugs known to cause thrombocytopenia were excluded from the study. The study was approved by the hospital ethical committee and written consent was taken from all the parents before enrolment. A thorough history was obtained and a general and systemic examination done. Routine investigations were done in all cases and specific investigations when indicated. Investigations included complete haemogram, blood urea, serum creatinine, serum electrolytes, aspartate and alanine aminotransferases, prothrombin time and activated partial thromboplastin time, blood culture, smear and card test for malaria parasite, serological tests to detect dengue, leptospira, chikungunya, enteric fever, rickettsiae, urine analysis, chest radiograph and ultrasonogram of abdomen.

Results

A total of 2217 children was admitted to the paediatric wards during the study period, of which 1551 had febrile illnesses. Three hundred and eleven (20%) children developed thrombocytopenia. Five were excluded from the study, 2 due to leukaemia, 2 due to idiopathic thrombocytopenia and 1 due to systemic lupus erythematosus. The study group thus consisted of 306 children with febrile thrombocytopenia.

One hundred and fifty five (50.7%) children were more than 10 years of age, 101 (33%) in the 6-10 year age group, 43 (14.4 %) in the 1-5 year age group and 7 (2.3%) were infants. Of the children, 184 (60%) were males. A definitive diagnosis was

made in 280 (91.5%) children. Twenty six (8.5%) children were diagnosed as probable viral fever after excluding other causes. Table 1 shows the causes of febrile thrombocytopenia.

Table 1
Causes of fever with thrombocytopenia (n=306)

Cause	No. of patients (%)
Dengue fever	254 (83.0)
Viral fever	26 (08.5)
Enteric fever	22 (07.2)
Malaria	03 (01.0)
Hepatitis A	01 (0.3)

The platelet count was between 100,000-150,000/mm³ in 107 (35%) children, 50,000-100,000/mm³ in 85 (28%), 20,000-50,000/mm³ in 88 (29%) and less than 20,000/mm³ in 26 (8%) children. Eighty seven (28.4%) children had bleeding symptoms. Among them, 55 (63%) had subcutaneous bleeding. Mucosal bleeding, in the form of epistaxis, gum bleeding, haematuria, melaena, haematemesis and intracranial haemorrhage, was seen in 32 (37%) children.

All children were given supportive and specific therapy based on the diagnosis. Three hundred and four children improved with increase in platelet counts within 4 days to 2 weeks. Two (0.7%) children with severe dengue succumbed.

Discussion

The present study was undertaken to find out the aetiology of febrile thrombocytopenia in the paediatric age group. A systematic analysis showed that infectious diseases constitute nearly two thirds of total childhood mortality globally³. Around 65-70% of inpatient admissions in our hospital were due to infectious diseases. Majority (51.3%) of the children in the study group were in the age group above 10 years followed by 5-10 year age group implying increased outdoor activity and thereby increased risk of exposure to mosquito vectors as compared to pre-schoolers. Morales AJR *et al* observed peak incidence of febrile thrombocytopenia in the age group of 3.94±3.54 years⁴. Males were more affected in our study similar to many studies done in adults showing increased exposure to mosquitoes⁵.

The aetiology was found to be dengue fever in 83% of the children in our study with 62.3% non-structural protein 1 antigen (NS1Ag) positivity similar to the study by Shankar RR, *et al* who observed dengue as the cause of viraemia in 52 out of 100 adult patients⁶. Masamatti SS, *et al* have observed dengue illness in 48.3% in their study⁷. Bhatnagar MK, *et al* in their study of fever with thrombocytopenia have observed that 45% of cases

were dengue⁸. Kumar P, *et al* have observed malaria as the aetiological factor in 32.6%⁵. Morales AJR, *et al*⁴ found thrombocytopenia in 59% of children with plasmodium vivax infection, while Shetty G, *et al*⁹ have observed thrombocytopenia in 71% of cases diagnosed as malaria. Malaria was seen in 1% of our study similar to the study by Masamatti SS, *et al* who observed malaria in 2.3%⁷. Our low incidence of malaria is probably due to low endemicity in Bengaluru, India.

Typhoid is the fifth commonest cause of infection induced thrombocytopenia (14%) with malaria, human immunodeficiency virus (HIV), dengue, Epstein Barr virus (EBV) infections superseding typhoid according to a study by Herlinger KH *et al*¹⁰. Malik AS *et al* have observed that thrombocytopenia is relatively common in typhoid fever with a reported incidence of up to 26% in children¹¹. Further, it has been considered as a marker of severity of the disease with an increased risk of complications¹¹. In contrast, enteric fever was diagnosed as a cause of thrombocytopenia in 7.2% in our study which is similar to the study by Chandrashekhara *et al* (13.4%)¹² and the study by Ahmed Y *et al* (10%)¹³. Hepatitis A was seen in 0.3% of our study as compared to the 5.1% in the study by Jagadishkumar K *et al*¹⁴. This could be because of outpatient management of the majority of our children with Hepatitis A where no serial measurements of platelet counts were done. Viral illnesses accounted for 8.5% in our study similar to the study by Kumar P *et al* where undiagnosed viral fevers accounted for 6.3%⁵. Viruses cause thrombocytopenia either by decreased platelet production or by enhanced platelet destruction/sequestration¹⁵. Thirty five percent of our children had mild thrombocytopenia with platelet count between 100,000-150,000 /mm³ similar to the study by Kumar P *et al* who found mild thrombocytopenia in 50% of the study group⁵. Bleeding was seen in 28.4% of 306 children with subcutaneous bleed and petechiae in 17.6% (63% of 87 children) in our study. Kumar P *et al* also noted bleeding in 11.1% in their study⁵.

Children diagnosed as dengue fever were given symptomatic treatment and platelet counts were followed up serially. Platelets were transfused to children who had significant mucosal bleed leading to haemodynamic instability or whose counts were less than 10,000 per cubic millimetre¹⁶. The remaining children in the study group were treated depending on their diagnosis. Most of them recovered and platelets started improving within 4 days to 2 weeks after admission. There were 2 (0.7%) deaths in our study and both were in children with severe dengue infection. The main limitation of our study is that it is a single centre,

hospital based observational study in Bengaluru, India which might not reflect the entire community.

Conclusions

Common causes of febrile thrombocytopenia in this study were dengue fever (83%), undiagnosed viral fever (8.5%) and enteric fever (7.2%).

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