



Research Article

An Analysis of Risk Factors for Fever with Thrombocytopenia in Children Under 12 Years of Age

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ABSTRACT

Background: Children with thrombocytopenia (TP) who are hospitalized for fever may experience a stormy course with significant morbidity and mortality. Certain prognostic criteria are required during admission to predict the prognosis and to alert the treating paediatrician.

Aim of the study: An investigation of risk factors for fever with thrombocytopenia within children under the age of 12

Methods: One hundred children who were admitted to GGH (Government General Hospital) SMC (Siddhartha Medical College), Vijayawada between March 2021 and February 2022 participated in this prospective observational study. Using a pre-structured proforma, many parameters were collected. To analyze the data, SPSS version 21.0 was utilized.

Results: One hundred cases in all were examined. 70% (70 cases) consisted only of fever, 7% (7 cases) consisted of fever with bleeding, 18% (18 cases) consisted of fever with shock and 5% (5 cases) had both bleeding and shock with fever. 17% of the 18% of children who experienced fever and shock were hospitalised for >4 days. Of the 5% of children who experienced shock and bleeding with fever, 4% were hospitalised for >4 days. Included admission, 22% of children had leukopenia, 64% had a normal WBC count and 14% had leukocytosis. There is no significant influence of the total WBC counts in predicting the outcome. Of the children admitted, 49% had positive dengue serology, 22% had positive malarial smear results, 13% had Widal test, 12% had positive scrub serology results and 4% had positive urine culture and sensitivity results.

Conclusion: One of the most difficult issues with the concealed presentation of common diseases in children as opposed to unusual disorders is fever with thrombocytopenia. Thrombocytopenia is frequently caused by infections such as enteric fever, septicemia, malaria, and dengue fever. High morbidity in the form of bleeding and shock, or both, was more likely to occur in children with platelet counts below 5000, increased hematocrit, abnormal renal function tests, elevated liver enzymes, and abnormal coagulation profile at the time of admission. According to the study, dengue fever and malaria were the main causes of thrombocytopenia.

Keywords: *Thrombocytopenia, leucopenia, leukocytosis, dengue, bleeding and shock*

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INTRODUCTION

Extremely low platelet counts in the blood might result in thrombocytopenia (TP). Platelets are tiny blood cells that are

formed from larger cells found in the bone marrow. Platelets aggregate together to seal wounds after injuries. The term "blood clot" refers to this blockage [1]. Infections such as

leptospirosis, dengue, malaria, viral fevers and septicemia are common causes of fever with TP [2, 3]. To determine the aetiology, every child with a fever has a thorough assessment. The NHANES (National Health and Nutrition Examination Survey) characterizes TP as a platelet count below the normal range for the population and supports the customary figure of 150,000 per cubic millimetre as the lesser bound of the usual variety [4]. Rarely, when the platelet count drops below 10000/mm³, there may be serious symptoms like GIT bleeds and CNS bleeds etc., TP with or without disseminated intravascular coagulation can be brought on by infections with bacteria, viruses, or protozoa [5]. Meningococci, leptospira, numerous viral infections, dengue, malaria, scrub typhus, and other rickettsial illnesses are among the common conditions that cause fever in patients with TP. In OPD settings, fever with TP is frequently observed, particularly in the monsoon and pre-monsoon seasons. Occasionally, these children may proceed to have a turbulent course with multi-organ dysfunction, which is connected with a elevated danger of mortality and morbidity requires admission and intensive care management [6]. While some infections resolve on their own, certain individuals need to be closely watched to avoid potentially fatal consequences. Disease-related mortality and morbidity can be reduced by early detection and timely intervention commencement. An investigation of the prognostic variables is deemed significant due to the rising number of instances that have been identified. To understand the prognostic variables associated with fever and TP in children receiving tertiary care, the current study was designed.

Materials and methods

We performed this Prospective observational study in the Department of Pediatrics, GGH, SMC, and Vijayawada, India. Study Group, all the fever cases with TP in children aged one month to twelve years who were admitted to our hospital from March 2021 to February 2022.

Inclusion criteria: Every patient, ranging in age from one month to twelve years, had fever and TP (platelets < 150,000/ μ L).

Exclusion criteria:

The patient was diagnosed with immune thrombocytopenic purpura despite presenting with TP without fever. Patients with cirrhosis and chronic liver disease, patients on antiplatelet medication and other liver management results in TP, patients whose parents did not grant consent to participate in the study, and patients with documented instances of platelet malfunction were excluded. Patients with TP who had previously been diagnosed with a haematological disorder, or cancer or were undergoing treatment with chemotherapy and other immunosuppressive agents were also excluded.

Methodology

The parents were surveyed using a proforma to gather information. The study group's results were analyzed by using the following admission parameters, platelet count, total WBC count, packed cell volume (PCV), liver enzymes, renal function test (RFT), serum proteins, C-reactive protein (CRP), coagulation profile, age, sex, location, day of fever, respiratory distress, abdominal distension and so on. Following consent,

medical history, clinical information and results of examinations were gathered and recorded in the proforma.

The patient's medical history is recorded at the time of admission, along with any warning indicators such nausea, vomiting, hematemesis, and decreased urine production.

When a patient is admitted, their overall health, respiratory distress (tachypnea, retractions), abdominal distension, hepatomegaly, and dehydration (dry mouth, increased thirst) are all recognized as clinical characteristics. The findings of blood investigations are documented at the time of admission. Total WBC counts (age-specific values considered normal), platelet counts, liver enzymes (normal AST <40, ALT <40, ALP <150), PCV, RFT (normal Urea <40, creatinine <1), serum proteins, coagulation profile, C-reactive protein (positive >6 mg/dl), serological studies, culture sensitivity, chest x-ray, and USG abdomen are among them. As a result, morbidity in the form of straightforward fever, fever with bleeding, and fever with shock or bleeding was assessed.

Statistical Analysis: Data gathered and documented throughout the study period were transferred into an Excel spreadsheet and subjected to the Kruskal-Wallis test to determine whether different risk factors for fever with TP and its related morbidity and mortality are statistically significant or not. Using by SPSS software version 21.0.

Results

Of the 100 cases collected, 70% (70 cases) consisted only of fever, 7% (7 cases) consisted of fever with bleeding, 18% (18 cases) consisted of fever with shock and 5% (5 cases) had both bleeding and shock with fever. Among admissions, 8% (8 cases) of children were younger than 1 year, 31% (31 cases) were between 1 and 5 years, and 61% (61 cases) were older than 5 years. Concerning the morbidity of these children the age factor has no significance. Table 1 shows the demographic factors and outcomes.

The sex of the child did not significantly affect the morbidity of these children who were hospitalized for fever with TP; of those admitted, 45% (45 cases) were male and 55% (55 cases) were female.

When a child is admitted for fever with TP, the location has no discernible impact on their morbidity. Of the children, 36% were from cities and 64% were from rural areas.

Of the children admitted, 25% had fevers lasting less than four days, 35% had fevers lasting four to six days, and 40% had fevers lasting more than six days. The outcome is significantly impacted by the day of fever at presentation. Six percent of the youngsters (seven percent) who experienced fever and bleeding were hospitalized for more than four days. Fever lasting longer than four days was a reason for admission for 17% of the 18% of children who experienced fever with shock. Of the five percent of children who experienced shock and bleeding from fever, four percent were hospitalized for more than four days.

Out of all the children hospitalised, 75% had a normal general condition, and 25% had an altered general condition. The outcome is significantly influenced by the general situation. Among the 75% of children who were admitted in alert condition, 60% had only a fever. Among the 25% of children

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who were admitted with an altered general condition, 15% had either shock or bleeding or both. 12% of the children hospitalised had respiratory distress. Respiratory distress had an impact of major significance on the

outcome. Among 12% of children with respiratory distress, 1% had only a fever, among the remaining 11% of 12% cases 1% had a fever with bleeding, 6% had a fever with shock and the remaining 4% had both bleeding and shock with fever.

Table 1: Demographic factors & outcome

	O.F (N=70)	F.B (N=7)	F.S (N=18)	F.B & F.S (N=5)	Total (N=100)	P-Value
Age groups						
<1 yr	5 (7.15%)	2 (28.57%)	1 (5.55%)	0	8 (8%)	0.264
1-5 yr	24 (34.28%)	1 (14.28%)	6 (33.33%)	0	31(31%)	
>5 yr	41 (58.57)	4 (57.15%)	11 (61.12%)	5 (100%)	61(61%)	
Sex						
Male	34 (48.57%)	1(14.28%)	9 (50%)	1 (20%)	45 (45%)	0.246
Female	36 (51.43%)	6 (85.72%)	9 (50%)	4 (80%)	55 (55%)	
Locality						
Rural	43 (61.42%)	4 (57.15%)	14 (77.77%)	3 (60%)	64 (64%)	0.452
Urban	27 (38.57%)	3 (42.85%)	4 (22.23%)	2 (40%)	36 (36%)	
Day of fever						
<4 days	22 (31.42%)	1(14.28%)	1 (5.55%)	1 (20%)	25 (25%)	0.014
4-6 days	19 (27.14%)	4 (57.15%)	11 (61.12%)	1 (20%)	35 (35%)	
>6 days	29 (41.42%)	2 (28.57%)	6 (33.33%)	3 (60%)	40 (40%)	
General Condition						
Alert	60 (88.71%)	4 (57.15%)	11 (61.12%)	0	75 (75%)	<0.001
Lethargy	10 (14.28%)	3 (42.85%)	7 (38.88%)	5 (100%)	25 (25%)	
Respiratory Distress						
Yes	1 (1.42%)	1 (14.28%)	6 (33.33%)	4 (80%)	12 (12%)	<0.001
No	69 (98.58%)	6 (85.72%)	12 (66.67%)	1 (20%)	88 (88%)	

O.F=only fever; F.B= Fever with bleeding; F.S= fever with shock; F.B & F.S=fever with bleeding and shock

The cause and result are given in Table 2. In terms of admissions, 28% of children had a platelet count of less than 50,000, 26% had a value between 50,000 to 1 lakh, and 46% had a count of more than 1 lakh. The results are significantly influenced by the platelet counts (<0.001). Among 7% of children who developed fever with bleeding, 6% of them were admitted with platelet count <50,000. Among 18% of children who developed fever with shock, 17% of them were admitted with platelet count <1 lakh. Among 5% of children who urbanized fever with bleeding and shock, all 5% of them were admit with platelet count <50,000. Platelet counts have a major significance in the outcome.

Of the children admitted, 14% have leukocytosis, 64% have normal numbers, and 22% have leukopenia. The total WBC counts do not significantly affect the result prediction.

6% of the children admitted had abnormal renal function tests. Abnormal renal function tests at presentation have a major impact on the result. Two percent of the six percent of children who were admitted due to abnormal kidney function testing experienced shock and fever. One percent of them experienced bleeding fever, and three percent experienced both bleeding and shock fever.

5% of the children admitted had elevated liver enzymes, and the prognosis is significantly affected by elevated liver enzymes upon presentation (p=0.007). Of the five percent of children who were admitted with increased liver enzymes, four percent experienced shock and fever, and one percent experienced fever and haemorrhage.

Not a single child with decreased serum proteins was admitted, and in the present study packed cell volume (PCV), had not shown any significance in accessing the morbidity.

There is a significant link between C-reactive protein and outcome, as evidenced by the positive C-reactive protein levels seen in 47% of the admitted youngsters. The result is significantly influenced by C-reactive protein. Fever and bleeding occurred in 7% of the youngsters; 5% of these patients had positive CRP results at admission. Of the 18% of children who experienced fever and shock, 14% required hospitalisation due to a positive CRP test. Five percent of the children who experienced shock, bleeding, and fever were admitted if their CRP was positive.

Of the patients admitted, 49% had positive dengue serology, 22% had positive malaria smear results, 13% had high Widal titers, 12% had positive scrub serology results, and 4% of the children had positive urine culture and sensitivity results.

Table 2: Etiology and Outcome

	O.F (N=70)	F.B (N=7)	F.S (N=18)	F.B & F.S (N=5)	Total (N=100)	P-Value
Platelet count						
<50K	10 (14.28%)	6 (85.72%)	7 (38.88%)	5 (100%)	28 (28%)	<0.001
<1L	16 (22.86%)	0	10 (55.56%)	0	26 (8%)	
>1L	44 (62.86%)	1 (14.28%)	1 (5.56%)	0	46 (46%)	
Total WBC counts						
Normal	50 (71.43%)	2 (28.57%)	10 (55.56%)	2 (40%)	64 (64%)	0.069
Leukopenia	13 (18.57%)	3 (42.85%)	5 (27.78%)	1 (20%)	22 (22%)	
Leukocytosis	7 (10%)	2 (28.57%)	3 (16.66%)	2 (40%)	14 (14%)	
Packed cell volume						
<35	47 (67.15%)	6 (85.72%)	8 (44.44%)	3 (60%)	64 (64%)	0.010
35-40	20 (28.57%)	1 (14.28%)	3 (16.67%)	1 (20%)	25 (25%)	
>40	3 (4.28%)	0	7 (38.89%)	1 (20%)	11 (11%)	
RFT abnormality						
Normal	70 (100%)	6 (85.72%)	16 (88.89%)	2 (40%)	94 (94%)	0.001
Abnormal	0	1 (14.28%)	2 (11.11%)	3 (60%)	6 (6%)	
Liver enzyme elevation						
Normal	70 (100%)	6 (85.72%)	18 (100%)	1 (20%)	95 (95%)	0.007
Abnormal	0	1 (14.28%)	0	4 (80%)	5 (5%)	
CRP						
Positive	23 (32.85%)	5 (71.42%)	14 (77.78%)	5 (100%)	47 (47%)	0.001
Negative	47 (67.15%)	2 (28.58%)	4 (22.22%)	0	53 (53%)	
Microbiology						
Dengue	28 (40%)	5 (71.42%)	13 (72.22%)	3 (60%)	49 (49%)	0.005
Malaria	19 (27.14%)	1 (14.29%)	2 (11.11%)	0	22 (22%)	
Enteric fever	13 (18.57%)	0	0	0	13 (13%)	
Scrub	6 (8.57%)	1 (14.29%)	3 (16.67%)	2 (40%)	12 (12%)	
UTI	4 (5.72%)	0	0	0	4 (4%)	

O.F=only fever; F.B= Fever with bleeding; F.S= fever with shock; F.B & F.S=fever with bleeding and shock

Discussion

A platelet count of less than 150,000/ μ L is referred to as "thrombocytopenia" (TP). When there is a history of easy bruising or bleeding, it is clinically suspected. It can also happen by accident during normal evaluations or examinations carried out for unrelated purposes. It is common in infants and young children. In contrast to adult instances, the vast majority of cases of paediatric thrombocytosis are reactive, meaning they are benign and secondary. Children are more susceptible to bacterial, viral and other infections when they are recovering from an illness. The method used to assess a child exhibiting bleeding symptoms and/or unexplained TP, as well as the precise reasons for TP (such as immune TP, leukaemia, or aplastic anaemia), are crucial. In some children, it can cause fatal haemorrhage, shock or both and even death.

This study collected and examined one hundred cases in total. Of them, 70% consisted only of fever, 7% consisted of fever with bleeding, 18% consisted of fever with shock, and 5% had both bleeding and shock with fever.

In the present study, 25% had fevers lasting less than four days, 35% had fevers lasting four to six days and 40% had fevers lasting more than six days. The day of fever at presentation has a major impact on the outcome. Six per cent of the seven per cent of children who developed a fever with bleeding were hospitalized for more than four days. This was

equivalent to the findings of the Aroor et al. investigation [7], which produced similar findings.

The location of children hospitalized for fever with TP does not appear to be correlated with the morbidity; 36% of the children were from urban areas and 64% were from rural regions. Eleven per cent of the twelve per cent of children who were hospitalized due to respiratory distress experienced either shock, haemorrhage, or both. Sixty-nine per cent of the eighty-eight children who were hospitalized, without respiratory distress had only fever. This conclusion was similar to that of another study conducted by Aroor AR et al. [7], which likewise demonstrated the negative effects on outcomes that children arriving with respiratory distress had.

Out of all the children hospitalized, 75% had normal general condition, and 25% had altered general condition. Among the 75% of children who were admitted in alert condition, 60% had only simple fever. Among the 25% of children who were admitted with an altered general condition, 15% had either shock or bleeding or both. These findings were comparable with the study done by Shewale et al. [8], which also showed there was more morbidity if the child presented with an altered general condition at admission.

With a p-value of 0.001, the initial platelet count at presentation had a significant impact on the outcome of the current study. Of the children hospitalized, 28% had platelet

counts of less than 50,000, 26% had values between 50,000 and 1 lakh, and 46% had counts of more than 1 lakh. This outcome was similar to that of the Gomber et al. research [9], which likewise found that children who presented with low platelet counts had high rates of morbidity.

With a p-value of 0.001, the current study's findings were significantly impacted by hepatomegaly at presentation. Hepatomegaly was present in 60% of the children who were hospitalized. Of these children, 13% experienced fever with bleeding and 20% experienced fever with shock. This outcome was similar to that of Sawant et al. [10], which likewise showed high rates of morbidity in children who presented with hepatomegaly.

Not a single child with decreased serum proteins was admitted. There is a significant link between C-reactive protein and outcome, as evidenced by the positive C-reactive protein levels seen in 47% of the admitted youngsters. This outcome was similar to research by Rodrigo et al. [13], Haas et al. [12], and Balasubramanian et al. [11], which likewise revealed children with elevated CRP at presentation had higher morbidity.

A p-value of 0.007 indicates that higher liver enzymes upon presentation had a significant impact on the study's outcome. Five per cent of the children admitted had elevated liver enzymes, of the five per cent of children who were hospitalized due to elevated liver enzymes, four per cent experienced fever with shock, and one per cent experienced fever with haemorrhage. This outcome was similar to research conducted by Martina et al. [15] and Chen et al. [14].

49% of patients in the current study exhibited positive dengue serology, 22% had positive malaria smear studies, 13% had high Widal test, 12% had positive scrub serology and the remaining 4% had positive urine culture and sensitivity results.

Conclusion

Fever with TP is one of the most demanding harms with the occult presentation of common diseases rather than rare diseases in children. Infections like dengue fever, malaria, septicemia, and enteric fever are frequent causes of TP. High morbidity in the form of bleeding and shock, or both, was more likely to occur in children with platelet counts below 5000, increased hematocrit, abnormal renal function tests, elevated liver enzymes, and abnormal coagulation profile at the time of admission.

According to the study, dengue fever and malaria were the main causes of thrombocytopenia. Immunization is recommended for vaccine-preventable diseases and preventive measures for vector-borne diseases.

Limitations of the study:

The current study is subject to a major limitation only a Prospective observational study was made on 100 patients. Very few parameters were evaluated viz total WBC count, PCV, liver enzymes, RFT, serum proteins, CRP etc. This needs to be addressed by the study of a large sample size and the evaluation of more parameters in the future.

Human Ethics:

Consent was obtained or waived by all participants in this study. The Ethics Committee of SMC issued approval ECR/633/INST/AP/2014/RR-19.

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