Original Article

A Study on the Clinical and Laboratory Profile of Patients Having Thrombocytopenia in Pediatrics

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Abstract

Introduction: Fever is a symptom which is caused by a variety of illnesses and it usually occurs in response to an infection or inflammation. Patients presenting with fever in tropical country like India usually have an infectious etiology, and many have associated thrombocytopenia.

Aim: This study aims to assess the clinical and laboratory profile of patients having thrombocytopenia (<1 lakh) in pediatrics.

Materials and Methods: The patients of both sexes aged 2 months–12 years. Patients with platelet count <1 lakh at during the course of hospital stay, irrespective of the cause for admission were included. Data regarding the patient were entered into preset pro forma as regard to the history, general and systemic examination, Hess test, and vital signs. The bleeding manifestation's patients presented with or developed during their course in hospital were recorded.

Results: The most common age group of presentation of thrombocytopenia among the study group is 6–10 years, constituting 47.3% of the cases. Mortality is highest among infants. The most common etiology for newly diagnosed thrombocytopenia among children admitted is dengue. The most common presenting symptom among the study group is fever (95.5%) with vomiting being the second most common symptom (65.2%). 76.1% of children with vomiting had bleeding manifestations. In children with thrombocytopenia, the presence of altered sensorium, tachycardia, tachypnea, shock at presentation, and seizures was all significantly associated with low platelet counts, bleeding, and mortality.

Conclusion: Febrile thrombocytopenia is a commonly observed hematological entity commonly caused by infections such as viral illnesses, dengue, malaria, and enteric fever. Dengue shock syndrome is the leading cause of mortality in the present study.

Key words: Dengue, Platelet, Thrombocytopenia

INTRODUCTION

Normal hemostasis is not only a complex but also an ingenious system which maintains blood in the vascular system free from clots, the vital element of the process being the platelet. Decreased platelet count is not as common as anemia, the hematological cousin. Literature quotes the incidence of thrombocytopenia to vary from 13% to 58% in various studies. However, it is far more dangerous and resource consuming to the emergency department and the intensive care unit (ICU) setting. It can be associated with bleeding ranging from minor bleeds to life-threatening intracranial hemorrhage.[1-3]

There is very often a poor correlation between the extent of thrombocytopenia and the severity of the bleed. Guidelines on platelet transfusions are also varied and confounding. Hence, the treatment of thrombocytopenia has to be guided by an understanding of the cause and clinical course. It is often said that the main treatment goal in all patients with decreased platelet count is to maintain a safe platelet level so as to prevent significant bleeding. However, what constitutes a safe count in a specific patient varies, depending on the etiology of the thrombocytopenia as regard to whether it is transient or chronic, as well as the patients expected level of disease activity.[4,5]

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There has been a plethora of studies on anemia and its impact on various disease processes. However, thrombocytopenia is still a grey waiting to be explored. Again, there are lot of studies in the adult population detailing the outcome of patients with thrombocytopenia in the intensive care setting. However, similar studies in the pediatric age group are lacking. No particular study has been addressed toward studying the relative frequency of different disease conditions presenting as newly diagnosed thrombocytopenia in pediatric patients presenting to an Indian tertiary care hospital. The need arises to look at thrombocytopenia as a whole and to gather knowledge regarding the common disease entities presenting as such and whether or not active treatment modalities such as platelet transfusions, steroids, and platelets are required in them. This knowledge will give the clinician an idea of approach to pediatric patients detected to have thrombocytopenia on admission to a tertiary care hospital in India.

Aim
This study aims to assess the clinical and laboratory profile of patients having thrombocytopenia (<1 lakh) in pediatrics.

MATERIALS AND METHODS

This descriptive, cross-sectional study was done on children who were admitted to the children medical ward of Tirunelveli Medical College Hospital during the period from December 2011 to April 2012. 112 consecutive patients who satisfied the following inclusion criteria were studied. Prior ethical committee approval was obtained for the study.

Inclusion Criteria
The patients of both sexes aged 2 months–12 years. Patients with platelet counts <1 lakh anytime during the course of hospital stay, irrespective of the cause for admission.

Exclusion Criteria
Patients with spurious thrombocytopenia-laboratory induced errors where immediate repeat platelet counts or the peripheral smear did not grossly correlate with the first count were excluded from the study. Patients who were earlier diagnosed to have conditions that are known to cause thrombocytopenia (e.g., known cases of hematological malignancies, aplastic anemia, myelodysplastic syndromes, and immune thrombocytopenia). Patients who have already received platelet transfusion before admission. Patients who were very sick at admission or expired within few hours of admission who could not be subjected to the full set of investigations.

Data regarding the patient were entered into preset pro forma as regard to the history, general and systemic examination, Hess test, and vital signs. The bleeding manifestation's patients presented with or developed during their course in hospital were recorded. An awareness questionnaire on dengue with three simple questions was also included for the parents. Informed consent was obtained.

Once the specific diagnosis was reached, patients were treated for specifically and symptomatically (mechanical ventilation, shock correction, and steroids). Blood products were transfused as per the treating physician's discretion. The proportion of study patients requiring interventions to improve platelet count such as platelet transfusion, steroids, and the reason for such interventions were recorded.

RESULTS

The total number of admissions during the study period in children medical ward is 702. The number of patients who had thrombocytopenia or developed it subsequently during the course of hospital stay is 112 (after application of the exclusion criteria), which means one among every 6.25 children admitted developed thrombocytopenia (15.95% incidence). In 107 patients, a cause for the thrombocytopenia could be identified with the panel of investigations applied. Five patients were left undiagnosed despite full battery investigations. The most common age group of presentation of thrombocytopenia among the study group is 6–10 years, constituting 47.3% of the cases. Mortality is highest among infants. Of 11 infants studied, 5 expired (45.5%). However, this is not statistically significant ($P > 0.05$).

The most common etiology for newly diagnosed thrombocytopenia among children admitted is dengue. Total dengue cases were 66, comprising 58.8% of the study population. Among the dengue cases, dengue fever (DF) with or without hemorrhage DF was most common (32.1%) [Table 1]. Leading cause of mortality in the study population is dengue shock syndrome (DSS), causing four of the eight total deaths. DSS comprised only 8% of cases with thrombocytopenia but had the highest mortality rate of 44.4%. The next leading cause of mortality was septicemia. Infections caused most of the thrombocytopenia. 44.6% of the children presented with fever of 5–7 days duration. Mean duration of hospital stay in the study group is 6.15 days. Mean duration for which fever lasted is 7.69 days (Standard deviation = 3.498). 47.35% of children became afebrile after 5–7 days. Children who had prolonged fever >15 days had the worst outcome (25% mortality). However, this is not statistically significant ($P = 0.383$).

The most common presenting symptom among the study group is fever (95.5%) with vomiting being the second most common symptom (65.2%). 76.1% of children with vomiting had bleeding manifestations. This is statistically significant ($P = 0.003$) [Table 2]

In children with thrombocytopenia, the presence of altered sensorium, tachycardia, tachypnea, shock at presentation, and seizures was all significantly associated with low platelet counts, bleeding, and mortality ($P < 0.05$). Children requiring inotrope support, mechanical ventilation also had poor outcome ($P < 0.05$). The mortality was also significantly high ($P < 0.05$) in malnourished children with thrombocytopenia. Occurrence of seizures in cases with septicemia and thrombocytopenia had strong correlation with death (100%) [Table 3].

Among the platelet counts, the initial values were not significantly related to the mortality while the second repeat platelet value had a significant bearing on the outcome ($P < 0.05$). Bleeding manifestations were seen in a total of 67 patients (59.8%). GI bleed was the most common bleeding manifestation associated with thrombocytopenia, seen in total of 46 patients. 39.3% of patients had malena and 20.5% of children had hematemesis. 3.6% had more than one bleeding manifestation. Children with hematemesis had a significantly poor outcome ($P = 0.000$) compared to children with malena ($P = 0.52$).

Children with anemia had a significantly poor outcome ($P = 0.008$). The mean Hb in the discharged patients was 11.32 g% compared to 8.69 g% in children who expired ($P = 0.007$). The other laboratory parameters did not significantly alter the outcome [Table 4].

Patients with enteric fever and thrombocytopenia had higher incidence of bleeding compared to even dengue cases. In fact, coinfection with both diseases had the highest incidence of bleed (75%). In children with dengue, counts <20,000 had high association with bleeding, while in enteric fever, there was no such correlation with the counts for the predisposition to bleed.

DSS children had a higher incidence of bleeding manifestations (77.8%), and the bleeding risk in DSS was high when the counts were <10,000. Comparatively, only 11.1% of DF cases had bleeding. In dengue hemorrhagic fever (DHF) too, the incidence of bleeding manifestations was high (71.4%), but there was no correlation with lower counts to occurrence of bleeding manifestations [Table 5].

The mean hemoglobin value in the study group is 11.13 g%. The mean hematocrit value is 35.99%, and the outcome is significantly poor among children with hematocrit below the mean ($P < 0.05$) probably indicative of the mortality risk associated with bleeding. Anemia with thrombocytopenia was common in leukemia and septicemia (4.27 g% and 9.96 g%, respectively) [Table 6].

Abnormal X-ray findings had a significant association with mortality ($P < 0.05$). Ultrasound abdomen was a very useful radiological tool among the study population. It was able to pick up features of polyserositis with high sensitivity in both DHF and DSS. However, the findings were not specific for dengue alone [Table 7]. Anemic patients with thrombocytopenia had significantly increased need for transfusions ($P < 0.05$). The mean Hb of transfused patients was 9.65 g% compared to 11.46 g% in non-transfused patients ($P = 0.006$).

There was also statistically significant association between need for transfusion and mortality ($P < 0.05$). All the poor predictors of mortality also had a significant association with the need for transfusions. Hence, it can be implied that transfusions have not significantly altered the outcome.

Table 1: Etiology and disease-wise mortality of thrombocytopenia

Diagnosis	Frequency *n*=112 (%)	Death *n*=8 (%)
DF	36 (32.1)	0 (0)
DHF	21 (18.7)	0 (0)
DSS	9 (8)	4 (44.4)
Enteric	13 (11.6)	0 (0)
Dengue/enteric coinfection	4 (3.6)	0 (0)
Malaria	3 (2.7)	0 (0)
All	5 (4.5)	0 (0)
Septicemia	5 (4.5)	0 (0)
Undiagnosed	5 (4.5)	0 (0)
Miscellaneous	11 (9.8)	2 (18.2)

DHF: Dengue hemorrhagic fever, DSS: Dengue shock syndrome, DF: Dengue fever

Table 2: Symptom analysis of cases based on etiology

Features	Total *n*=112 (%)	Dengue *n*=66 (%)	Enteric *n*=13(%)	D/E *n*=4(%)	All *n*=5(%)	Sepsis *n*=5 (%)
Fever	107 (95.5)	66 (100)	13 (100)	4 (100)	5 (100)	5 (100)
Abdomen pain	59 (52.7)	35 (53)	9 (69.2)	3 (75)	1 (20)	0
Vomiting	73 (65.2)	42 (63.6)	11 (84.6)	3 (75)	2 (40)	4 (80)
Cough	42 (37.5)	23 (34.9)	3 (23)	3 (75)	1 (20)	5 (100)
Myalgia	60 (53.6)	35 (53)	6 (46.2)	2 (50)	3 (60)	0 (0)

Table 3: Predictors of mortality in various diseases

Features	Total *n*=112 (% of *n*)	Death *n*=8 (%)	*P* value outcome	Dengue deaths *n*=4 (%)	Septicemia deaths *n*=2(%)
Altered sensorium	49 (43.8)	8 (100)	0.001	4 (100)	2 (100)
Tachycardia	48 (42.9)	8 (100)	0.001	4 (100)	2 (100)
Tachypnea	20 (17.9)	8 (100)	0.000	4 (100)	2 (100)
Shock	18 (16.1)	8 (100)	0.000	4 (100)	2 (100)
Seizure	13 (11.6)	3 (37.5)	0.018	1 (25)	2 (100)
Mechanical ventilation	7 (6.3)	6 (75)	0.000	2 (50)	2 (100)
Inotrope	8 (7.1)	7 (87.5)	0.000	3 (75)	2 (100)
Narrow pulse pressure <20	19 (17)	2 (25)	0.484	1 (25)	1 (50)
Malnutrition	63 (56.3)	1 (12.5)	0.041	1 (25)	0

Table 4: Comparison of the laboratory parameters

Investigation	Total *n*=112 (% of *n*)	Dengue *n*=66 (% of *n*)	Enteric *n*=13(% of *n*)	Leukemia *n*=5	Septicemia *n*=5 (% of *n*)
Leucopenia	32 (28.6)	17 (25.8)	5 (38.5)	2 (40)	1 (20)
Leukocytosis	29 (25.9)	13 (19.7)	4 (30.7)	3 (60)	0
Pancytopenia	4 (3.6)	1 (1.5)	0	2 (40)	0
Anemia (p<0.05)	40 (35.7)	15 (22.7)	3 (23)	5 (100)	4 (80)
Incesr.	41 (36.6)	14 (21.2)	7 (53.9)	4 (80)	4 (80)
Inc. urea/creatinine	27 (24.1)	17 (25.8)	1 (7.7)	1 (20)	2 (40)
Inc. liver enz.	33 (29.5)	15 (22.7)	5 (38.5)	0	0
Inc. bilirubin	12 (10.7)	2 (3.03%)	1 (7.7%)	0	0

Table 5: Comparison of platelet counts based on etiology

Counts	Dengue *n*=66 (% of *n*)	Enteric *n*=13 (% of *n*)	D/E mixed *n*–4 (%)	Malaria *n*=3 (% of *n*)	All *n*=5 (% of *n*)	Sepsis *n*=5 (% of *n*)
<10,000	2 (3)	0	0	0	1 (20)	1 (20)
11,000–20,000	10 (15.2)	0	0	0	1 (20)	0
21,000–50,000	22 (33.3)	4 (30.8)	3 (75)	2 (66.7)	2 (40)	2 (40)
51,000–100,000	32 (48.5)	9 (69.2)	1 (25)	1 (33.3)	1 (20)	2 (40)

Table 6: Comparison of mean hematological values based on etiology

Diagnosis	Mean Hb (g %)	Mean PCV (%)	Mean platelet count
DF	11.93	3.74	60666
DHF	11.98	39.77	46714
DSS	11.21	38.04	18000
Enteric	12.15	35.58	62076
Ent/den coinf	11.38	35.55	41500
Malaria	11.03	34.47	46333
Leukemia	4.27	13.36	35600
Septicemia	9.96	30.56	50800
Total (*n*=112)	11.13	35.99 (*P*=0.016)	48250

DHF: Dengue hemorrhagic fever, DSS: Dengue shock syndrome, DF: Dengue fever, PCV: Packed cell volume

DISCUSSION

As discussed in the literature, thrombocytopenia being associated with bleeding manifestations is now considered an independent parameter predicting outcome in the pediatric ICU. Here, critical analysis of the observations of our study is performed, comparing it with other Indian and foreign studies. Analysis of our study shows the highest incidence of thrombocytopenia in the 6–10 years age group, with a mean age of 6.56 years. The incidence of thrombocytopenia has been quoted to vary from 13% to 58% in various studies. The present study has shown 15.95% incidence, which is comparable to other studies, Agrawal *et al.* showing 23.2–22% in a neonatal ICU.[6] The present study had significantly less number of children with counts <10,000 compared to Agrawal *et al.* (20%).[6] Children with counts <10,000 had the worst outcome (57.1% mortality). Mortality in the present study was 7.1% with DSS contributing to 50% of the deaths. Krishnan *et al.* reported 17.1% mortality, while Agrawal *et al.* reported a mortality of 10.9%. Mortality was highest among infants (45.5%) and younger children (<3 years).[6] Gomber *et al.* defined 36.3% as the cutoff hematocrit for DHF.[7] In the present study, the mean hematocrit among dengue patients was well above this cutoff, indicating high predisposition for the development of severe dengue in the study group. Furthermore, the hematocrit values are significantly associated with mortality. Unlike previous studies, the incidence of coinfections in the present study was low (5.7%). However, the children with dengue/enteric coinfection had abdominal tenderness in a higher proportion. The mortality rate among dengue patients as

Table 7: Comparison of radiological abnormalities

Features	Total *n*=12 (%)	*P* value	DF *n*=36	DHF *n*=21	DSS *n*=9	Enteric *n*=13
X-ray eff/pneumonia	15 (13.4)	0.002	1 (6.6)	4 (26.6)	1 (6.6)	2 (13.3)
Gallbladder edema	31 (27.7)	0.001	0	11 (52.4)	4 (44.4)	8 (61.5)
Pleural effusion	29 (25.9)	0.008	0	15 (71.4)	5 (55.5)	4 (30.7)
Ascites	18 (16.1)	0.062	0	8 (38.1)	3 (33.3)	3 (23.1)
Hepatomegaly	45 (40.2)	0.338	10 (27.8)	9 (42.9)	3 (33.3)	10 (76.9)
Splenomegaly	27 (24.1)	0.397	6 (16.7)	5 (23.8)	0	4 (30.7)

DHF: Dengue hemorrhagic fever, DSS: Dengue shock syndrome, DF: Dengue fever

a whole was low (4/66 = 6.06%). Erythematous rash with flushing was very commonly observed in children with dengue in the present study (70.4%). This is in spite of the dark complexion in our children. Altered sensorium, tachycardia, tachypnea, shock (all having 100% association with death), requirement of inotrope support (87.5%), mechanical ventilation (70%), seizures, and malnutrition were all significantly associated with increased mortality. Requirement of mechanical ventilation in Agrawal *et al.* was 23.9%, whereas in the present study, it was 6.3%. The incidence of shock was 17.3% in Agrawal *et al.*, while in the present study, it was 16.1%.[6] Bleeding manifestations were seen in a total of 67 patients (59.8%) in the present study compared to 19.5% in Agrawal *et al.* GI bleed was the most common bleeding manifestation associated with thrombocytopenia, seen in total of 46 patients.[6] 17.9% of children in the present study required transfusions. They received 43.75 mL/kg/patient. In comparison, 21.9% of patients were transfused in the study by Agrawal *et al.*, and transfusions were reported to be significantly associated with mortality. Most of the patients transfused in our study were DSS patients (77.8%). The mean platelet count of transfused patients was 24,000. Yet, 80% mortality was seen in the transfused patients, which was also statistically significant. Patients with low platelet counts and bleeding manifestations also did not show statistically significant improvement in comparison to non-transfused patients. Hence, the role of prophylactic platelet transfusions is to be questioned until uniform guidelines are established. The WHO advises that platelet transfusion is to be avoided in dengue. The only clinical situation where platelet transfusion is needed in dengue is when the counts are <10,000.

CONCLUSION

Febrile thrombocytopenia is a commonly observed hematological entity commonly caused by infections such as viral illnesses, dengue, malaria, and enteric fever. DSS is the leading cause of mortality in the present study. It commonly manifests with clinical features of underlying disease condition and sometimes with bleeding manifestation also. Mortality in febrile thrombocytopenia is not directly associated with the degree of thrombocytopenia.

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