

ORIGINAL ARTICLE

Fever with Thrombocytopenia in the Pediatric Age GroupDURFISHA DILSHAD¹, AMMARA JAMAL², MUNIBA FIROZ³, MEHAK GUL⁴, MAIRAH RAZA⁵, AYESHA YASIR⁶, SHARMEEN NASIR⁷, SANIA SAEED⁸¹Senior Registrar, Department of pediatrics, Liaquat National Hospital, Karachi²Professor of pediatrics, Department of pediatrics, Dow University of health sciences, Karachi³Consultant child specialist, CBM health center, Malir Cantt, Karachi⁴Medical Officer, Department of pediatrics, Sindh Institute of child health and Neonatology, Korangi 5, Karachi^{5,6}Medical Officer, Department of pediatrics, University Hospitals Birmingham, UK,⁷Senior Registrar, Department of pediatrics, Dow University of health sciences, Karachi⁸Department of pediatrics, Dow university of health sciences, KarachiCorresponding author: Muniba Firoz, Email: munibafiroz@gmail.com.**ABSTRACT**

Introduction: Fever with thrombocytopenia refers to a reduction in platelet count below 150,000/L in association with fever. Although febrile thrombocytopenia may occur due to aplastic anemia, malignancy or megaloblastic anemia, its commonest cause in the pediatric age group is infections like Dengue fever, Malaria and Enteric fever. Since infectious diseases are highly prevalent in our region we decided to determine the frequency of diseases associated with febrile thrombocytopenia in the pediatric age group.

Objective: To determine the frequency of diseases associated with febrile thrombocytopenia in the pediatrics age group

Study Design: Descriptive Cross-Sectional Study

Place and Duration: Department of Paediatric Medicine, Civil Hospital, Karachi, Pakistan from November 22, 2018, to May 21, 2019

Methodology: After obtaining informed consent data related to signs, symptoms, clinical and confirmed diagnosis, and relevant lab results were recorded for children who fulfilled the inclusion criteria. Data were analyzed in terms of frequencies and percentages for qualitative variables like age group, gender and outcome variables.

Results: Mean \pm SD of age was 4.74 ± 3.28 . Out of 89 patients, 45(50.56%) were male and 44(49.44%) were female. In distribution for common causes of thrombocytopenia, 19 (21.3%) had malaria, 8 (9%) had dengue, 25 (28.1%) had an enteric fever, 32 (36%) had sepsis, 2 (2.2%) had malignancy and 3 (3.4%) had megaloblastic anemia.

Conclusion: Sepsis, dengue, and malaria were the most frequent causes of thrombocytopenia. Therefore, anytime thrombocytopenia is found, more investigations can usually assist us in making the right diagnosis.

Keywords: Febrile Thrombocytopenia, Malaria, Sepsis, Dengue, Enteric.

INTRODUCTION

A clinical condition known as "fever with thrombocytopenia" describes a drop in platelet counts to less than 150,000/L in conjunction with a fever. [1]. Reduced generation, increased destruction (both immunogenic [2-4] and non-immunogenic [4-9]), or increased sequestration in the spleen of platelets are all possible causes of thrombocytopenia. The causes of thrombocytopenia are varied but in the pediatric age group, it is mostly because of infections or malignancy or idiopathic. Febrile thrombocytopenia is frequently the result of infections [1].

Infectious diseases are especially more prevalent among the pediatric population in tropical countries like Pakistan and India [10-15]. Many of these infections which may be associated with thrombocytopenia include malaria (35%) [1], dengue fever (34%) [1], enteric fever (18.39%) [16], sepsis (26%) [17], leptospirosis (34%) [18], influenza viral infection (28.32%) [19] and chikungunya (35%) [20]. However, it may also occur due to non-infectious diseases including aplastic anemia (23%) [21], malignancy (17.40%) [21] and megaloblastic anemia (13.04%) [21].

The most dreadful complication of thrombocytopenia is bleeding manifestation from various sites like mucocutaneous bleeding (e.g. petechiae, purpura, epistaxis, bleeding from gums, hematuria and Malena). Major hemorrhage may occur in the form of severe gastrointestinal hemorrhage, urinary tract hemorrhage and intracranial bleeding which may potentially lead to death [22]. The risk of bleeding depends upon the level of platelet count. There is a high risk of spontaneous bleeding when a patient has severe thrombocytopenia (platelets <20,000/L), the risk of spontaneous bleeding is low with moderate thrombocytopenia (platelets 20,000-50,000/L) but the risk increases in case of trauma or surgical procedure. The risk of bleeding is low in mild thrombocytopenia (platelets 50,000-150,000/L) unless there is a major operation or severe trauma [23].

The presence of Fever with thrombocytopenia is a frequent and most important sign that indicates infection.

The infectious diseases which are mentioned in the literature to be associated with thrombocytopenia are quite common in

Pakistan therefore we decided to determine the frequency of diseases associated with febrile thrombocytopenia in the pediatrics age group. With the help of frequency, we would like to see the burden of diseases in our pediatrics population. If the results of this study show a high frequency of patients who remain undiagnosed, we would like to recommend the establishment of labs to identify those diseases along with strategies for the prevention and treatment of those diseases.

METHODOLOGY

From November 22, 2018, to May 21, 2019, the Department of Paediatric Medicine at the Civil Hospital in Karachi carried out this descriptive cross-sectional study.

By using the WHO sample size calculator taking statistics for megaloblastic anemia=13% [21] with a margin of error of 7%. The calculated sample size was 89. Non-probability, Consecutive Sampling technique was applied for patient selection.

This study involved children between the ages of one month and twelve years, both male and female, admitted to the paediatric ward of Civil Hospital Karachi with a fever exceeding 37.7°C (99.9°F) and found to have thrombocytopenia (platelet count below 150,000/L).

Patients with thrombocytopenia without fever or vice versa, those already diagnosed as a case of idiopathic thrombocytopenia (ITP), chronic liver disease (CLD), connective tissue disorder, platelet function disorder and congenital thrombocytopenia were excluded. Patients taking clopidogrel, non-steroidal anti-inflammatory medicines (aspirin, ibuprofen, naproxen, etc.), valproate, quinine, carbamazepine, amiodarone, phenytoin, vancomycin, and ethambutol were also prohibited from participating in the trial.

A total of 89 patients who met the study's inclusion criteria were enrolled after the ethical review board gave its approval. Parental or guardian consent was acquired after proper disclosure.

These included patients were evaluated clinically by detailed history and physical examination for the probable cause of febrile thrombocytopenia. Lab tests were conducted according to the

suspected diagnosis. For diseases requiring invasive investigations like bone marrow biopsy, separate informed consent was obtained from the parents.

The platelets count was repeated from time to time and platelet transfusion was given if the platelet count was less than 10,000/L even without overt signs of bleeding in patients with dengue shock syndrome and in septicemia with DIC (Disseminated Intravascular Coagulation). In addition, patients were managed according to specific diagnoses. The identity of the patients was kept confidential. Data was recorded on predesigned Performa. The relevant operational definitions for the purpose of this study are as under:

Statistical analysis was done using SPSS version 22.0. Data were analyzed in terms of frequencies and percentages for qualitative variables (age group, gender and outcome variable). The mean and SD was calculated for age. Through stratification, effect modifiers like age and gender were taken into account. A chi-square post-stratification test was used. A P value less than 0.05 was regarded as significant.

RESULTS

Out of 89 patients 45 (50.56%) were male and 44 (49.44%) were female as shown in FIGURE 1.

The mean ± SD of age was 4.74±3.28 with C.I (4.05.....5.43) years as shown in TABLE 1.

In distribution for common causes of thrombocytopenia, 19 (21.3%) had malaria, 8 (9%) had dengue, 25 (28.1%) had enteric fever, 32 (36%) had sepsis, 2 (2.2%) had malignancy and 3 (3.4%) had megaloblastic anaemia as shown in TABLE 2.

In stratification of age group 0–6 and >6 years non-significant difference was found in relation to common causes of febrile thrombocytopenia i.e. (P>0.05) as mentioned in TABLE 3.

In the stratification of gender, a non-significant difference was found in relation to common causes of febrile thrombocytopenia i.e. (P>0.05) as mentioned in TABLE 4.

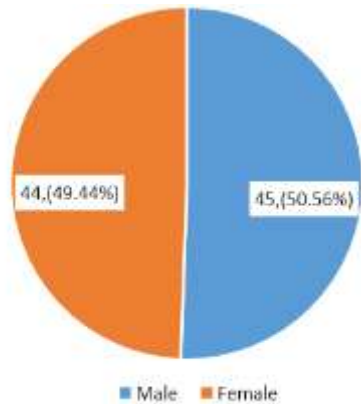


Figure 1: Frequency of Gender n= 89

Table 1: Descriptive Statistics of Age n=89

Descriptive	Statistic
Mean age in the years	4.7461
95% Confidence Interval for Mean	Lower Bound 4.0531
	Upper Bound 5.4390

Table 2: Distribution of Common Causes of Febrile Thrombocytopenia n=89

Common Causes	Frequency	Percent
Malaria	19	21.3
Dengue	8	9%
Enteric fever	25	28.1%
Sepsis	32	36%
Malignancy	2	2.2%
Megaloblastic Anaemia	3	3.4%

Table 3: Stratification of Age Group with Respect to Common Causes of Febrile Thrombocytopenia n=89

Common Causes	Age Group [Years]	Yes	No	P-value
Malaria	0 – 6	11 (12.4%)	48 (53.9%)	0.383
	> 6	8 (9.0%)	22 (24.7%)	
Dengue	0 – 6	4 (4.5%)	55 (61.8%)	0.258
	> 6	4 (4.5%)	26 (29.2%)	
Enteric fever	0 – 6	12 (13.5%)	47 (52.8%)	0.043
	> 6	13 (14.6%)	17 (19.1%)	
Sepsis	0 – 6	29 (32.6%)	30 (33.7%)	0.001
	> 6	3 (3.4%)	27 (30.3%)	
Malignancy	0 – 6	1 (1.1%)	58 (65.2%)	0.563
	> 6	1 (1.1%)	29 (32.6%)	
Megaloblastic Anaemia	0 – 6	2 (2.2%)	57 (64.0%)	0.738
	> 6	1 (1.1%)	29 (32.6%)	

Table 4: Stratification of Gender with Respect to Common Causes of Febrile Thrombocytopenia n=89

Common causes	Gender	Yes	No	P-value
Malaria	Male	12 (13.5%)	33 (37.1%)	0.216
	Female	7 (7.9%)	37 (41.6%)	
Dengue	Male	4 (4.5%)	41 (46.1%)	0.630
	Female	4 (4.5%)	40 (44.9%)	
Enteric fever	Male	14 (15.7%)	31 (34.8%)	0.544
	Female	11 (12.4%)	33 (37.1%)	
Sepsis	Male	14 (15.7%)	31 (34.8%)	0.336
	Female	18 (20.2%)	26 (29.2%)	
Malignancy	Male	1 (1.1%)	44 (49.4%)	0.747
	Female	1 (1.1%)	43 (48.3%)	
Megaloblastic Anaemia	Male	0 (0.0%)	45 (50.6%)	0.117
	Female	3 (3.4%)	41 (46.1%)	

DISCUSSION

In the present study, a total sample of 89 pediatric patients with febrile thrombocytopenia was studied, sepsis was the common cause and its prevalence was 36% among all the cases of febrile thrombocytopenia followed by enteric fever 28.1%, malaria 21.3%, dengue 9%, megaloblastic anaemia 3.4% and malignancy 2.2%.

The frequency of sepsis in our study is quite high compared to other studies discussed below.

Yadav V et al.'s study [24] on a sample of 500 cases included 298 males and 202 females. Viral fever was the most frequent cause of febrile thrombocytopenia in our study (35.6%). Dengue fever (26.8%), malaria (24.4%), septicemia (4.4%), leptospirosis (2.4%), and chikungunya fever (2%), on the other hand, were the other etiologies.

In another study conducted by Kumar P et al. [25] malaria was the commonest etiology, with the prevalence of malaria reported in 32.63% of patients, followed by septicemia (31.57%), dengue (15.78%), viral infection (6.31%) and enteric fever (3.6%).

Viral fever, which was found to be the most frequent cause of thrombocytopenia in Nair et al.'s study [26] (aside from dengue and chikungunya), accounted for 27.78% of cases, while dengue, enteric fever, chikungunya, malaria, septicaemia, ITP, hematologic malignancy, 1.67%, and megaloblastic anaemia accounted for the remaining 11.1%.

A study conducted in the neighbouring country of India by Kumaran et al. [27] reported viral fever as the commonest cause i.e. 50.3% of cases. In this study, the most common aetiology of thrombocytopenia was viral infection i.e. 50.3% followed by dengue fever 21.81%.

According to Patel U. et al. [28], malaria was identified as the primary cause in 41.07% of cases. Similar to this, Lakum discovered that malaria was the primary factor in 46.8% of instances of febrile thrombocytopenia [29].

Another study conducted by Bhalara et al [30], showed dengue (28.6%) as the most common etiology followed by malaria 22.8%, septicemia 6.3%, and megaloblastic anemia 1.9%.

In our study, there was an equal ratio of male and female children. The commonest age group affected was 1 to 8 years accounting for nearly 79.8% of all cases. This could possibly be explained by the prolonged outdoor activities by grown-up children compared to infants and increased exposure to mosquito bites. These were similar to the results from other studies.

Because our inclusion and exclusion criteria were strict, our study's strength was its use of sequential sampling, which was best suited for our study design and sample selection. The source of bias in our study is also reduced by the adoption of objective definitions for predictor and outcome variables.

The main shortcomings of our investigation were the use of a poor cross-sectional study design, weak analysis, and weak evidence. As a result, the study design did not call for any prior determination of sample size. Additionally, the small number of outcomes we chose for our study has an impact on its value. There were other variables and elements that were related to our outcome and predictor variables that may have been studied.

Non-probability sampling restricts generalizability, however, we had a small patient population and the follow-up period was brief. Because this study was hospital-based, the frequency and severity of the condition are not accurately represented by the figure. Additionally, the study was limited in its ability to generalize because it was only carried out in one department of a single hospital

CONCLUSION

It is to be concluded that sepsis was the most common cause of thrombocytopenia followed by dengue and malaria. As a result, whenever thrombocytopenia is found, additional studies can usually assist us in making a correct diagnosis to take the proper course of action. To verify the results of the current study, randomized trials utilizing high sample sizes and several study centres are required throughout Pakistan.

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