Original Article

Frequency of Disorders Causing Childhood Thrombocytopenia

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Objective: To study the relative frequency of the disorders causing childhood thrombocytopenia.

Patients & Methods: This descriptive study was conducted in the Department of Hematology and Transfusion Medicine Division, the Children Hospital and the Institute of Child Health, Lahore and the Department of Pediatrics, Services Hospital Lahore. The duration of the study was 1 year from March 2005 to April 2006. Two hundred cases having platelet count less than 1, 50,000/mm^3 were included in this study. Causes of thrombocytopenia were determined on the basis of history, physical examination and various investigations. The data were collected on a proforma and analyzed using SPSS for Windows version 8. The results were compared with other studies. Chi-Square test was applied to determine P-values.

Results: Acute lymphoblastic leukemia was found to be the commonest cause of childhood thrombocytopenia observed in 60 (30.0%) cases, followed by hypoplastic / aplastic anemia 40 (20%) cases, AML in 30 (15%), ITP in 28 (14%) cases and megaloblastic anemia in 20 (10%) cases. Drugs and infections together caused thrombocytopenia in a considerable number of patients. 96 children (48.0%) had platelet count in the range of 11-40 x 10^9/L. Hemorrhagic manifestations were seen in 123 (61.5%) children. Epistaxis and purpura / bruises were the main presenting bleeding manifestations.

Conclusion: Thrombocytopenia is associated with different disorders and acute lymphoblastic leukemia was found be the most common of childhood thrombocytopenia.

Key Words: Thrombocytopenia, ALL, ITP, low platelets, purpura

Introduction

Thrombocytopenia is a common cause of abnormal bleeding.[1] It may be defined as a reduction in the platelet count below the lower normal limit of 150,000/ul.[2] The normal range in health is approximately 150-400 x 10^9/L, average values being about 250 x 10^9/L. Platelet life span has been estimated to be 8-12 days in humans.

The breakdown in the haemostatic integrity is a life threatening experience that requires an urgent diagnosis and immediate management because spontaneous bleeding is one of the most distressing events in children.[3] Blood vessels, platelets and coagulation factors are three major components for normal haemostatic mechanism and they act in a coordinated fashion to arrest bleeding. Platelets have a critical role in hemostasis and the presence of adequate number of viable platelets is necessary for this function.[4]

Hemorrhage is the most important clinical manifestation of thrombocytopenia and skin is the most common site of bleeding (petechiae, purpura and ecchymoses). There may be mucosal bleed like epistaxis and gum bleed.[5] Rarely cerebral hemorrhage may occur in severe thrombocytopenia and it may invariably prove fatal. Serious spontaneous bleeding is usually a risk only in patients with platelet levels under 20 x10^9 /L.[6]

Thrombocytopenia occurs when the platelets are destroyed, sequestered in the body or not produced.[7.] Determining the true cause of thrombocytopenia is a difficult and challenging clinical problem. Thrombocytopenia may be benign, incidental finding in an asymptomatic patient or the sign of a potentially life threatening disorder.[8] Therefore, a careful medical history, physical examination, complete blood count and peripheral smear can assist the physician to arrive at the diagnosis of thrombocytopenia.[9]

A lot of work has been done regarding the etiological factors of thrombocytopenia in the West. Different etiological factors have been implicated in the causation of thrombocytopenia in various populations of the world. Since the treatment of thrombocytopenia is determined by the underlying mechanism, it is imperative to have a clear understanding of the etiology and pathophysiology

of thrombocytopenia.[10] Therefore, the aim of this study was to find out the common causes of thrombocytopenia in our community.

Material and Methods

It was a descriptive study which was conducted in the Department of Hematology and Transfusion Medicine Division, Children Hospital and the Institute of Child Health, Lahore and Department of Pediatrics, Services Hospital, Lahore. 200 consecutive patients who had thrombocytopenia and who presented with different diseases in these departments were selected for this study. Inclusion criteria included children between 1 and 12 years of age and patients having platelet count below $150x10^9$/L. Exclusion criteria included children below 1 year, greater than 12 years and patients who were taking immunosuppressive drugs and ionizing radiations. Detailed clinical history, including drug history, history of cytotoxic therapy, risk factors such as infections and family history of bleeding disorders and complete physical examination especially skin and mucous membranes for the evidence of purpura, bruises, nose bleeding and gum bleeding, lymph nodes, spleen and liver were carried out and recorded on a proforma. Later on investigations were carried out and results of all the investigations were also noted on the proforma. Investigations were based upon the clinical and hematological indications. These included bone marrow aspiration stained by Leishman's stain and special stains, where indicated bone marrow biopsy processed by paraffin embedding technique and stained by hematoxylin and eosin, reticulin stain, coagulation tests (PT, APTT), reticulocyte count, direct antiglobulin test, fibrinogen level, fibrin degradation products, liver function tests, renal function tests, blood cultures and other serological procedures, viral serology, x-rays and/or abdominal ultrasound.

Results were reported as frequencies and percentages for the various etiologies of thrombocytopenia. The results of the study were compared with other local and international studies by calculating P-values through Chi Square test.

Results

Two hundred cases were included in this study. Out of these 137 (68.5%) were males giving a male to female ratio of 2.1:1. Age of the patients ranged between 1-17 years. Maximum number of patients (37.5%) was seen between the age group of 2-5 years (**Fig-1).**

Among 60 cases of acute lymphoblastic leukemia (ALL), 48 (80%) were males (male to female ratio of 4:1). Their mean age was 6.03 SD +3.58 and median was 5.25 years. Maximum number of patients (50%) was in the age group of 2-5 years. Among 40 cases of hypoplastic / aplastic anaemia, there were 28 (70%) males with a male to female ratio of 2.3:1**(Fig-2).** Their mean age was 9.63 SD+2.86 and median was 10.0 years. The children in the age group of 6-10 years were 62.5% **(Table-2).** Out of 30 cases of acute myeloid leukemia (AML), 22 (73.3%) were boys with a male to female ratio of 2.75:1 **(Fig-2).** Their mean age was 6.41 SD +3.9 and median was 5.0 years. However, only 4% of children were found to be in the age group of 11-17 years **(Table-2)**. Among 28 cases of ITP, there were 12 (42.8%) males with a male to female ratio of 0.75:1. Their mean age was 5.22 SD+3.83 years. Maximum numbers of patients (50%)

Table -1: Socio-demographic characteristics of the sample

Sr. No.	Disease	No. of Patients	Percentage
1.	Acute Lymphoblastic Leukemia	60	30
2.	Acquired Hypoplastic / Aplastic Anaemia	40	20
3.	Acute Myeloid Leukemia	30	15
4.	Immune Thrombocytopenic Purpura	28	14
5.	Megaloblastic Anaemia	20	10
6.	Septicaemia	04	02
7.	Fanconi Anaemia	03	1.5
8.	Hypersplenism	03	1.5
9.	Megakaryocytic Hypoplasia	02	1.0

10	Amegakaryocytic Thrombocytopenia Purpura	02	1.0
11.	Bernard Soulier Syndrome	02	1.0
12.	Hemophagocytic Syndrome	02	1.0
13.	Chronic Myeloid Leukaemia	02	1.0
14.	Gaucher's Disease	01	0.5
15.	Malaria	01	0.5
	Total	200	100

Table -2: Distribution of thrombocytopenic children by cause and age groups

Sr. No	Cause of Disease	Age Distribution (years) 1	2-5	6-10	11-17	Total
1.	ALL	1(2.0)	25(50)	19(38)	5(10)	50 (100)
2.	Hypoplastic / Aplastic Anaemia	0(0)	3(7.5)	25(62.5)	12(30)	40(100)
3.	AML	1(3.3)	15(50)	10(33.3)	4(4)	30 (100)
4.	ITP	4(14.2)	14(50)	6(21.4)	4(14.2)	28(100)
5.	Megaloblastic Anaemia	6(30)	6(30)	4(20)	4(20)	20(100)
6.	Infections / Drugs	4(40)	3(30)	2(20)	1(10)	10(100)

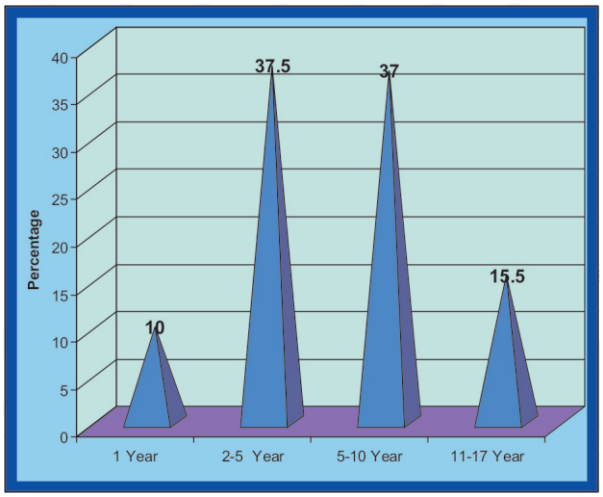

Fig-1: Distribution of patients by age group

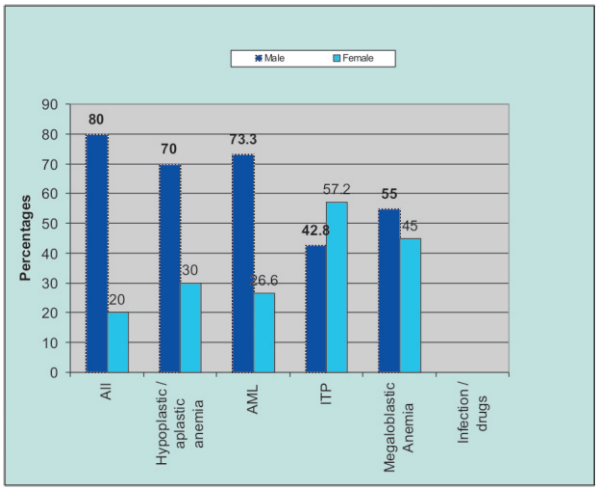

Fig-2: Distribution in children suffering from thrompocytopenia by diseases and sex

Out of two hundred thrombocytopenic children, 48% were having platelet count in the range of 10-40 x 10^9/L, whereas platelet count in the range of 101-150 x 10^9/L was seen only in 2% patients. Out of sixty cases of ALL, thirty two patients were having platelet count less than 50 x 10^9/L. Mean platelet count in ALL was 36.72 x 10^9/L, while two were having platelet count less than 10 x 10^9/L. Forty patients of hypoplastic / aplastic anaemia presented with thrombocytopenia and the mean platelet count was 30.35 x 10^9/L. Ten patients were having platelet count less than count 10 x 10^9/L. Thrombocytopenia was detected in 30 cases of AML and 40% of patients had platelet count between 11- 40 x 10^9/L (mean platelet count of 34.97 x 10^9/L). Platelet count between 11- 40 x 10^9/L were observed in fifteen cases of immune thrombocytopenic purpura and mean platelet count was 39.93 x 10^9/L. Twenty patients of megaloblastic anaemia presented with thrombocytopenia. Fourteen patients (70%) were having platelet count between 71-140 x 10^9/L (mean

platelet count was 68.85 x 10^9/L). The remaining 32 patients of various disorders had variable platelet counts.

Discussion

Thrombocytopenia may be the result of decreased platelet production, increase destruction of platelets, increase sequestration or combination of two or more of these mechanisms. All these three mechanisms are the result of different etiological factors that may be non-immune or immune mediated. The differential diagnosis of thrombocytopenia is extensive and complex and there is a significant overlap among disorders. However, a detailed history, comprehensive physical examination and laboratory criteria probably represent the most useful diagnostic method at present.

The present study was conducted in the Department of Hematology and Transfusion Medicine Division, Children Hospital and the Institute of Child Health, Lahore and Department of Pediatrics, Services Hospital Lahore, on a sample of 200 patients documented to have thrombocytopenia.

Out of these 200 children, 92 cases were diagnosed to have various types of leukemia; 90 cases were found to have acute leukemia, whereas 2 had chronic leukemia. The frequency of childhood leukemia in different studies is shown in **Table-1**. Acute lymphoblastic leukemia was diagnosed in 60 cases (30%) which was the most common disorder causing childhood thrombocytopenia. Among childhood leukemia, acute lymphoblastic leukemia was the most common (65.2%) as compared to acute myeloid leukemia (32.6%) with ALL to AML ratio of 2:1.

Among 60 cases of ALL, there were 48 males (80%). So male patients dominated females with an overall male to female ratio of 4:1. Male excess has been reported in most of the studies on childhood ALL. In a study held in Pakistan with a large sample conducted by Iftikhar and Kazi,[11] reported male excess with male to female ratio of 4:1 which is comparable to this study.

Hypoplastic/aplastic anaemia is the second most common disorder causing childhood thrombocytopenia and 40 cases (20%) were diagnosed with male to female ratio of 2.3:1. Similar results were also reported by Adil[12] at Agha Khan Hospital Karachi; however, in England Muir[13] reported male to female ratio of 1.04:1. So our results are comparable with local and international studies. The mean age of children with hypoplastic/aplastic anaemia was 9.63±2.86 (SD) which is comparable with 10.3 years as reported by Chuansumrit[14] in Thailand.

Acute myeloid leukemia was the second commonest childhood leukemia after ALL and third most common disorder causing childhood thrombocytopenia and 30 (15%) cases were diagnosed in the study. In AML, male to female ratio was 2.75:1. Male excess in AML has been reported by various Pakistani studies such as by Zaki who reported a ratio of 3.6:1.[15] Male excess of 1.25:1 has also been reported by international studies such as by Lavu.[16] The mean age of children with AML in our study was 6.41±3.9 which is comparable with 6.9±3.5 as reported by Lavu.[16] However, mean age in our study is lower than reported by Zaki[15] who reported 8±5(SD), but total number of cases was also less in his study.

Immune thrombocytopenic purpura was the next common disorder causing childhood thrombocytopenia. Twenty eight (14%) cases of ITP were diagnosed, with a male to female ratio of 0.75:1. In contrary to ALL, AML and hypoplastic / aplastic anaemia, female preponderance in ITP was observed. However in some international[17] and local[18] studies male excess has been reported. The likely reason for this female preponderance may be socio-cultural[17, 18]. The age of onset in ITP is quite variable. The mean age in our study was 5.22±3.83 with almost similar results in other local and international studies.[18,19]

Conclusion

Although the sample size was small, considering the fact that Children Hospital and Services Hospital are the pediatric referral centers and children admitted here represent a cross section of our society. Therefore, the conclusion drawn may be representative of the various aspects of the problems in this country and will have a fair degree of reliability.

The conclusion drawn from our study is that thrombocytopenia appears to affect all age groups and both sexes of children and acute lymphoblastic leukemia was found to be the most common cause of childhood thrombocytopenia.

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