

## Frequency of Benign Blood Disorders in Children: A Bone Marrow based analysis at a tertiary care hospital

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### ABSTRACT

**Aim:** To identify the spectrum of various benign blood disorders in children under fifteen years of age at a tertiary care hospital of Lahore, Pakistan.

**Settings:** Clinical pathology laboratory at department of pediatrics, Mayo hospital/KEMU, Lahore during January 2008 to December, 2013.

**Design:** Retrospective study.

**Methods:** Clinical charts of patients under fifteen years of age, who were admitted for the diagnosis of hematological disorders during the study period were reviewed retrospectively. All these children were referred for bone marrow aspiration. Trepine biopsy was done in cases suspected of hypoplasia, aplasia, lymphoma and secondary metastatic deposits.

**Results:** A total of 952 marrow aspirations/trepine biopsies were performed during the study period. Three hundred eighteen (33.4%) children were declared as suffering from malignant blood disorders while 634 (66.6%) cases had benign etiology. Among the benign group 375 (59.1%) had male and 259 (40.9%) had female gender. Three hundred and ninety (61.5%) children had micronutrient deficiency anemias: megaloblastic anemia 284 (44.8%), mixed deficiency anemia 76 (12%)

**Conclusion:** Megaloblastic anemia is the most common benign blood disorder in our study, followed by hypoplastic/aplastic morphology anemia and then idiopathic thrombocytopenic purpura. Most of these commonly occurring benign blood disorders are controllable, reversible and treatable.

**Keywords:** Benign blood disorders, Bone marrow aspiration, Megaloblastic anemia

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### INTRODUCTION

Non-cancerous or benign blood disorders range from mild to severe in intensity. They usually are not life threatening but their presence can cause symptoms of fatigue, shortness of breath, pain, bleeding manifestations and infections. Most of these benign blood disorders start in bone marrow where production of erythrocytes, leucocytes and thrombocytes may be affected hence they present with abnormal functions of these blood cells. Benign blood disorders may be classified as inherited or acquired. Sometimes they result from cancer itself or its treatment. Unlike malignant blood disorders, these may resolve with appropriate treatment, may not be causing any distressing symptoms and may not affect overall longevity of life. Although some disorders are chronic in nature, but still they do not affect the

overall life span. The common conditions included in this group are anemias, hemophilia, thalassemia, sickle cell anemia, idiopathic thrombocytopenia and chronic malaria.

Bone marrow aspiration is an essential diagnostic procedure to determine the cellularity of bone marrow, type of cellular maturation and metastatic secondary deposits<sup>1</sup>. Clinical findings, complete blood counts, peripheral blood cells morphology with bone marrow study collectively provide a definite clue to diagnosis. Bone marrow aspiration, although invasive, is still relatively safe and almost free of complications. It can be performed safely in outpatient, even in the presence of thrombocytopenia, and the only absolute contraindication is hemophilia<sup>2</sup>.

### RESULTS

The patient age in our study ranged from 02 months to 15 years. Amongst 634 children 374 (59%) were male and 260 (41%) females. The male to female ratio was 1.4:1. Their average age was 6.60 years and 7.40 years respectively. In our study 334 (52.7%) children were in age group of 02 months to 05 years, 185 (29.2%) children in age group 06 to 10 years and

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the lowest number 115(18.1%) in age group of 11 to 15years(Table 1).

Pallor and generalized weakness were most common presenting symptoms in our study, while fever, bruising, epistaxis and gum bleeding were less commonly described. Splenomegaly, lymphadenopathy and hepatomegaly were common signs on clinical examination(Table II).

Out of 634 children diagnosed as suffering from benign blood disorders (Fig. 1), micro-nutrient deficiencies were most common 390(61.5%) with megaloblastic bone marrow as a leading cause,i.e., 284(44.8%). Mixed deficiency anemia was seen in 76(12%). The iron deficiency anemia was least common in 30(4.7%). Hypoplastic/ aplastic anemia was the second commonest and lethal non-

cancerous etiology 70(11%). Its frequency is much more in developing countries than in developed western communities<sup>3</sup>.

The third commonest benign blood disorder proved on bone marrow study results was idiopathic thrombocytopenic purpura 60(9.5%), in which children presented with mucocutaneous hemorrhagic manifestations and showing significant thrombocytopenia on peripheral blood smear examination. Other relatively less common benign blood disorders diagnosed in descending order were thalassemia 49((7.7%), hemolytic anemias 27(4.3%), hypersplenism 14(2.2%), leishmaniasis 10(1.6%), chronic malaria 8(1.3%) and Gaucher disease 6(0.9%) (Fig-1).

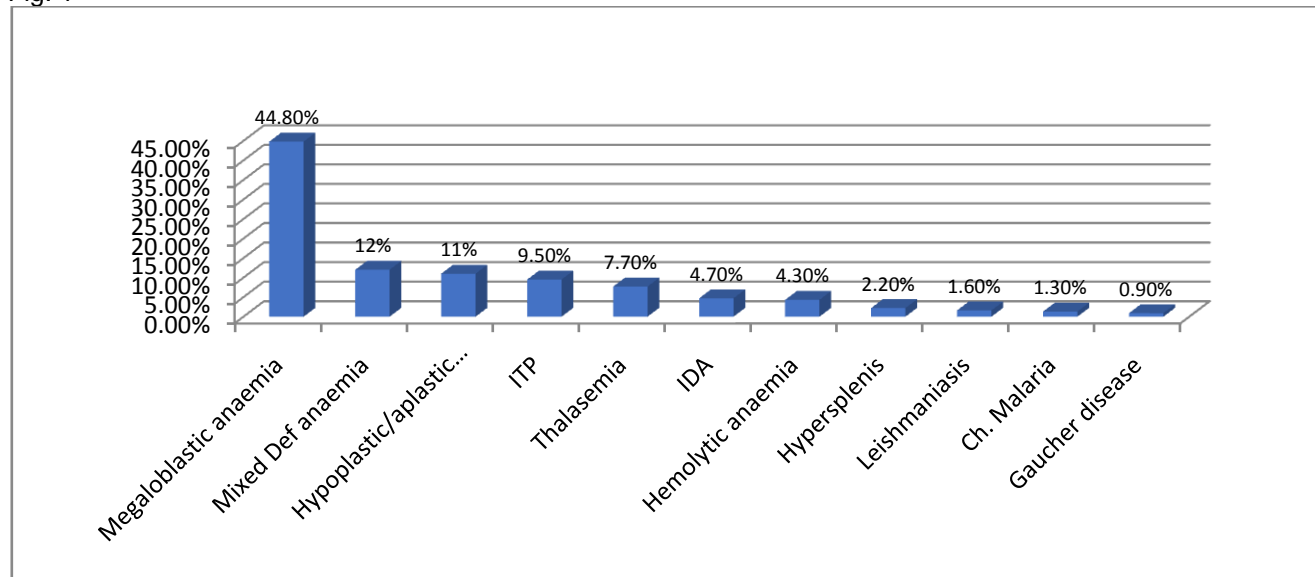
Table I: Sex and age distribution of children.

Age	Male child	Female child	Total (%)
2 months to 5 years	192 (30.3%)	142 (22.4%)	334 (52.7%)
6 years to 10 years	108 (17.0%)	77 (12.1%)	185 (29.2%)
11years to 15 years	74 (11.7%)	41 (6.5%)	115 (18.1%)

Table II: Symptoms and Signs of Benign Blood Disorders.

Clinical Features	Frequency	Percentage
Pallor	544	86.0
Generalized weakness	524	83.0
Fever	145	23.0
Bruises	120	19.0
Epistaxis	62	9.8
Bleeding gums	42	6.6
Splenomegaly	40	6.3
Lymphadenopathy	34	5.4
Hepatomegaly	24	3.8

Fig. 1



## DISCUSSION

Bone marrow aspiration/trephine biopsy is an essential tool to diagnose and to monitor the therapeutic response in hospitals having less resources. Final diagnosis in majority of patients suffering from benign blood disorders is declared after performing a bone marrow aspiration/ trephine biopsy, as safe and complications free procedure commonly employed in pediatric disorders diagnosis<sup>21</sup>.

Anemia is defined as a decrease in the concentration of hemoglobin or erythrocytes count below the lower limit of normal, for age and sex of the individual<sup>4</sup>. In our study micronutrient anemia was the most commonly diagnosed benign blood disorder 390(61.5%). In two other similar studies in Pakistan, its frequency was declared as 31.6% and 44.7%<sup>5,6</sup>. One study from India concluded the frequency of micronutrient deficiency anemia as (72.3%)<sup>7</sup>.

Megaloblastic anemia was the commonest diagnosis amongst micronutrient deficiency disorder in our study 284(72.8%), whereas another study in Pakistan also declared almost the same result as 74.6%<sup>6</sup>. Among the benign blood disorders, megaloblastic anemia dominated with 284(44.8%), whereas it was declared as 33.3% in a similar study<sup>6</sup>. In other studies both international and national, the frequency of megaloblastic anemia varies between 24%<sup>8</sup> to 68%<sup>9</sup>. In children having megaloblastic anemia, the most consistent finding on complete blood counts was cytopenias of variable degree in our as well as in other national studies<sup>10-13</sup>. Sometime thrombocytopenia is the only finding on CBC report in megaloblastic anemia<sup>14</sup>. Final diagnosis of megaloblastic anemia depends on the presence of megaloblastic maturation in bone marrow<sup>15</sup>. Diagnosis of iron deficiency anemia 30(7.7%), was much less common than megaloblastic anemia. The mixed deficiency anemia 76(19.5%), had a bit higher percentage. In another study done in Pakistan it was documented as 10.9%<sup>6</sup>.

Hypoplastic/aplastic anemia was the second most common but life threatening blood disorder in our children 70(11.0%). Etiology was unknown in majority of the cases as history of drug intake and / or radiotherapy was available in few cases only. Autoimmune mechanism has also been suspected as etiology in some of the cases<sup>16</sup>. Studies done in China<sup>16</sup> and Thailand<sup>17</sup> reported almost same etiological factors and results. In aplastic anemia, neutropenic children are more prone to serious recurrent infections, so these repeated infections along with hemorrhagic complications and congestive

cardiac failure are the common causes of death in these children.

Third most common benign blood disorder in our study was idiopathic thrombocytopenic purpura, 60(9.5%) cases. Our study results were almost consistent with the results of other similar studies done in Pakistan (12.9%) and India (12.8%)<sup>6,7</sup>. Bone marrow aspiration is not required for diagnosis in majority of cases of idiopathic thrombocytopenic purpura, but it is done frequently to rule out acute leukemia and before start of steroid as treatment especially when the child presents with pallor, fever and petechiae.

Other benign blood disorders in our study in descending order were, 49(7.7%) confirmed cases of thalassemia on hemoglobin electrophoresis, followed by 27(4.4%) children of other hemolytic anemias, 14(2.2%) cases of hypersplenism, 10(1.6%) of leishmaniasis, 8(1.3%) of chronic malaria and 6(0.9%) cases of Gaucher disease. Other three studies in Pakistan declared frequency of hypersplenism as 2.0%<sup>5</sup>, 2.6%<sup>6</sup> and 3.0%<sup>19</sup>. Frequency of leishmaniasis in similar studies was 3.2%<sup>5</sup>, 6%<sup>6</sup> and 6.6%<sup>19</sup>. In three similar national studies percentage of Gaucher disease was 0.8%<sup>5</sup>, 0.5%<sup>19</sup> and 1.8%<sup>20</sup>.

## CONCLUSION

Bone marrow aspiration/trephine biopsy is a valuable diagnostic laboratory technique for the confirmation of clinical diagnosis of benign, malignant and metastatic hematological diseases as well as storage disorders. Post marrow aspiration complications like bleeding, air embolism and introduction of infection are rarely reported. Sometimes this invasive procedure give us a tremendous support by diagnosing an unexpected disorder which was suspected on clinical grounds. Micronutrient anemias were the most common diagnosis followed in descending order by hypoplastic/aplastic anemia, idiopathic thrombocytopenic purpura, thalassemia, hemolytic anemias, hypersplenism, leishmaniasis, chronic malaria and Gaucher disease. Megaloblastic anemia was most common amongst the micronutrient anemias while iron deficiency was rather uncommon. If megaloblastic anemia is diagnosed at an early stage and treated promptly it will surely reduce its morbidity and mortality consequences.

Our study was designed with the aim to find out spectrum of benign hematological disorders in children. The study will guide the pediatricians to think rationally and treat promptly specially when working at sub-tertiary care level. It is concluded that

early recognition of benign blood disorder through bone marrow aspiration will certainly help to reduce the morbidity and mortality. Early diagnosis and prompt start of specific therapy will reduce the misery of sick children.

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