

# Hematological Malignant Diseases in Pediatrics - A study of 342 children based on Bone Marrow

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## ABSTRACT

**Aim:** To identify frequency of different malignant hematological diseases in pediatric patients who were admitted in a tertiary care hospital of Lahore, Pakistan.

**Settings:** Pathology Department of King Edward Medical University, Lahore from July 2009 to December 2014.

**Study Design:** Study was retrospective.

**Methods:** Files of children who were admitted with diagnosis of malignant hematological disease in oncology section of Pediatric Ward. Mayo Hospital, were studied retrospectively and important data regarding diagnosis was saved on a standard proforma. Bone marrow aspiration was performed in all children and trephine biopsy was done only in cases suspected of metastatic deposits in marrow or lymphomas.

**Results:** During this study period number of bone marrow studies performed were 936. Three hundred forty two (36.5%) children were diagnosed and labelled as malignant disorders. Two hundred twenty two (65.0%) were male and 120 (35.0%) were female children. One hundred ninety two (57.5%) children were diagnosed as cases of acute lymphoblastic leukemia ( ALL) and fifty children (15.0%) as acute myelogenous leukemia.

**Conclusion:** Our study concluded that acute lymphoblastic leukemia is the commonest malignant disorder and juvenile chronic myeloid leukemia (JCML) is the occasional and least one.

**Keywords:** Acute myelogenous leukemia, Juvenile chronic myeloid leukemia, Acute lymphoid leukemia.

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## INTRODUCTION

Hematology is defined as study of blood and blood forming organs and primarily it deals with cellular compartment of blood. Problems pertaining to blood cells, blood vasculature, bone marrow, spleen, lymph nodes and plasma clotting proteins are all dealt with under the heading of hematological disorders. Cancers of blood, bone marrow and lymphoid system are included in malignant hematological diseases group. Lymph vessels and all lymphoid tissue collections like lymph nodes, tonsils, peyer patches, spleen and thymus gland are included in lymphatic system. Hematological diseases are commonly seen in children and frequency of different malignant disorders varies in different countries<sup>1</sup>.

Malignant hematological diseases are commonly seen in pediatric patients. Acute lymphocytic leukemia (ALL), most common cancer of childhood and frequently diagnosed between three to seven years of age<sup>2</sup>. Acute myeloid leukemia (AML), although seen much less frequently than ALL, but still it contributes 10-14% of total pediatric leukemias. It is documented that when children are kept isolated from social surroundings in their early childhood and prevented from frequent exposure to microbial agents, are more liable to suffer from leukemia as their immune system remains less developed as a result of less stimulation by childhood microbiological agents<sup>3,4</sup>. At the same time neonatal aggressive infections may initiate

different immune response which may ultimately lead to leukemia<sup>5</sup>.

Bone marrow aspiration / trephine biopsy is an important diagnostic procedure, when a child present with signs and symptoms which are not conclusive and create uncertainty in arriving a final diagnosis. Bone marrow test is frequently advised procedure in many hematological disorders for final confirmatory diagnosis, therapeutic management and to check prognosis. It is no doubt an invasive technique but even in the presence of marked thrombocytopenia, can be carried out without bleeding risk after procedure. Other clinical uses of marrow aspiration / trephine biopsy are evaluation of different cytopenias, in diagnosing and clinical staging of malignant neoplasms and for confirmatory diagnosis of storage diseases<sup>6</sup>. Bone marrow aspiration / trephine biopsy has a vital role in assessing marrow cellularity, developmental status of marrow cells and presence of secondary deposits<sup>7</sup>. Marrow aspiration in hemophilia is strictly prohibited due to increased risk of profound bleeding during and after procedure<sup>8</sup>.

Marrow trephine biopsy is suggested in cases suspected of lymphomas, hypoplasia or aplasia of bone marrow. There is a long list of malignant pediatric diseases in which bone marrow study is utilized to confirm provisionally suspected pathology.

Our study aimed at identifying the frequency of different causative etiologies of malignant disorders in children by utilizing bone marrow procedures as our vital tool.

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## METHODS

Children were selected from pediatric oncology ward of Mayo hospital, Lahore. This study was approved by institutional Ethical Committee. Files of 342 children with confirmed diagnosis of malignant hematological disease were reviewed retrospectively in detail regarding patient age, sex, detailed history, physical examination findings and all relevant diagnostic investigations including bone marrow study results. These children were less than fourteen years and six months of age and were shifted to pediatric oncology ward from out-patient department and pediatric emergency during this period. During their stay in ward, all basic routine investigations like complete blood counts (CBC), urine complete examination, X-ray chest and ultrasonography were carried out along with a vital confirmatory procedure of bone marrow aspiration / trephine biopsy. All relevant information was recorded on a proforma.

## RESULTS

In our study age of these children ranged from 06 months to 14 years and 06 months. Out of 342 children, 196 (57.3%) children were having male and 146 (42.7%) female gender. Male to female ratio was 1.3 :1.0. Mean age was 5.8 years in male children and 6.6 years in female. One hundred forty five (42.4%) children were in age group of 06 months to 05 years, 120 (35.1%) children were between more than five years to ten years and remaining 77 (22.5%) showed age range of more than ten years to fourteen years and six months (Table I).

Majority of our children presented with easy fatigability, pallor, fever and anorexia and less frequent clinical presentation was hemorrhagic manifestations, joint pain and history of repeated infections. Enlargement of spleen and lymph nodes were observed frequently on clinical examination and after ultrasonography (Table II).

Table I: Gender and age data of patients

Age ranges of children	Male	Female	n
6 months-5 yrs	76 (38.8%)	69 (47.2%)	145(42.4%)
5-10 years	72 (36.7%)	48 (32.9%)	120(35.1%)
10-14 years and six months	48 (24.5%)	29 (19.9%)	77 (22.5%)
Total	196(57.3%)	146(42.7%)	342 (100%)

In our study group of 342, children who were diagnosed as confirmed cases of malignant hematological diseases, 198 (57.9%) children suffered from acute lymphoid leukemia. Majority of our ALL children fell in age range of three to seven years. Fifty-six (16.4%) cases of acute myeloid leukemia constituted the second commonest malignancy and less frequently diagnosed were twenty eight (8.2%) cases of lymphomas. Cases of myelodysplasia and secondary bone marrow deposits were diagnosed with much less frequency. Only 16 (4.7%) cases of juvenile chronic myelogenous leukemia (JCML) were admitted during study period (Table III). Children with secondary metastatic deposits in bone marrow after complete investigations were labelled as suffering from Wilms tumor, neuroblastoma, lymphoma and retinoblastoma.

Table II: Presenting manifestations of malignant hematological diseases in pediatrics. (Total number of children= n= 342)

Presenting features	n	%age
Easy fatigability	305	89.2
Low Hemoglobin (Pale appearance)	292	85.4
H/O Fever	266	77.8
Anorexia	236	69.0
Enlarged spleen	198	57.9
Enlarged lymph nodes	172	50.3
Repeated infections	170	49.7
Hemorrhagic manifestations	166	48.5
Bone/ Joint pain	160	46.8
Enlarged Liver	138	40.3
Pain Abdomen	126	36.8
Hepatosplenomegaly	118	34.5

Table III: Malignant hematological diseases and their Frequency

Malignant Disease	n	%age
Acute Lymphoid leukemia	198	57.9
Acute Myeloid leukemia	56	16.4
Lymphoma	28	8.2
Myelodysplastic syndrome	24	7.0
Secondary deposits in Bone Marrow	20	5.8
Juvenile Chronic myeloid leukemia	16	4.7

## DISCUSSION

In pediatrics practice bone marrow aspiration / trephine biopsy is a vital tool in confirmation of provisionally suspected hematological malignancies as well as in follow up after completion of chemotherapy or radiotherapy courses. In this study out of 342 children, 57.3% were belonging to male and 42.7% to female gender, a 1.3 : 1.0 male to female ratio. Acute lymphoid leukemia with 198 (57.9%) cases was the commonest malignant disease. Among children having acute leukemia, ALL constituted 74.3 % of total cases. Other studies carried out in Pakistan, frequency of acute lymphoblastic leukemia was 69.2%<sup>9</sup>, 79.9%<sup>10</sup> and 73.7%<sup>6</sup>. Frequency of acute lymphoid leukemia was only 41.6%<sup>11</sup> in one study designed in India, much lower than our study. Another study carried out in India reported a much higher frequency of 98%<sup>12</sup> for ALL cases. One international study declared ALL as the commonest pediatric malignancy<sup>13</sup>. In our research easy fatigability (89.2%), pallor (85.4%), rise in temperature (77.8%), anorexia (69%) and enlargement of spleen (57.9%) were commonly described and appreciated clinical features.

Physical examination revealed enlargement of spleen (57.9%), lymph node enlargement (50.3%), bleeding manifestations (48.5%), joint tenderness (46.8%) and hepatomegaly in (40.3 %) of cases. One national study by Yasmeen N and Ashraf S declared in their study that pallor and fever are major clinical feature (86.0%) followed by enlargement of liver and spleen as 67% and 58%<sup>14</sup> respectively. Another national study reported anemia (88.0%), as the commonest feature followed by enlargement of spleen (55.0 %) and liver (44 %)<sup>15</sup>.

Acute myeloid leukemia (AML), was second common pediatric hematological malignancy in this study. Fifty six (16.4%) children were declared as suffering from AML. Presenting clinical features were decreased hemoglobin level (79.5%), fever (72.8%), enlargement of spleen (65%) and bleeding manifestation (45.0%). Study carried out by

Biswas S et al declared the commonest presenting features in AML as : fever (93%), enlargement of liver (78.8%), enlargement of spleen (67.0%) and bleeding gums(43.0%)<sup>16</sup>. An Indian study reported anemia in 100% of cases, followed by fever (50%), bleeding manifestations (33.4%), splenomegaly (33.4%) and lymphadenopathy (33.4%)<sup>15</sup>.

Juvenile chronic myelogenous leukemia (JCML), rarely seen in pediatric practice and constitutes only 02-03% of childhood leukemia. In our study JCML was the least diagnosed (n=16; 4.7%) malignant disorder and rarely seen leukemia (5.9%) in children. Male: female ratio in JCML was 1.6:1.0 and children age ranged between 04 years to 14 years. Other three different studies reported male dominance as 1.5, 1.4, 1.5 times respectively<sup>17,18,19</sup>. The age ranges in above mentioned studies were 3-15 years, 4-16 years and 1-18 years respectively. In present study generalized weakness (80%) and enlargement of spleen (68%) were presenting clinical findings followed by abnormal bleeding manifestations. An international study designed on fourty JCML cases declared anemia, splenomegaly and hemorrhagic manifestations as clinically characteristic features of this malignancy<sup>19</sup>.

## CONCLUSION

Bone marrow aspiration and trephine biopsy remains a vital procedure for confirmatory diagnosis of malignant pediatric disorders. Although invasive procedure with rare complications. It helps in differentiating benign or malignant nature of disorder. It also guides pediatric oncologist about marrow architecture, marrow cellularity, status of mature and maturing cells, secondary deposits and staging of malignant disorder<sup>20,21</sup>. It is a very useful procedure to be employed in institutions having poor resources. After marrow aspiration serious complications like profuse bleeding, air or marrow fragment embolism and infection are rarely noticed<sup>6</sup>. Bone marrow study is most frequently advised investigation for confirmatory diagnosis and management of all leukemias<sup>22,23</sup>.

This study was aimed primarily to know the frequency and pattern of malignant hematological diseases at a tertiary care hospital. Secondly it was designed to promote rational thinking in pediatricians working at sub-tertiary care centers. More over this study also emphasizes the vital role of bone marrow aspiration / trephine biopsy in confirming suspected malignancy, to know the extent of disorder and its staging, in planning disorder management and finally to judge the prognosis after chemotherapy / radiotherapy. Message for pediatrician from this study is that bone marrow aspiration / biopsy should be suggested on priority, as timely diagnosis of disease has favorable effect on children morbidity and mortality.

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