Etiological Spectrum of Pancytopenia / Bicytopenia in Children 2 Months to 12 Years of Age

Muddassar Sharif*, Najaf Masood*, Muhammad Zahoor ul Haq*, Mobina Ahsan Dodhy**, Rai Muhammad Asghar*
*Department of Paediatrics Benazir Bhutto Hospital and Rawalpindi Medical College;**Department of Pathology, Benazir Bhutto Hospital and Rawalpindi Medical College, Rawalpindi

Abstract
Background: To determine the etiological spectrum of pancytopenia / bicytopenia in children aged 2 months to 12 years.
Methods: In this cross sectional descriptive study patients from 2 months to 12 years of age presenting with different cytopenias were included. Demographic profile and clinical findings were noted. Degree of malnutrition was assessed according to Gomez classification. Blood complete picture and peripheral smear were carried out for every patient having pancytopenia(leucopenia, anaemia and thrombocytopenia) or bicytopenia (if only two parameters from the full blood count are low) were further subjected to bone marrow aspiration and trephine biopsy
Results: A total of 105 patients were included in the study. More than half of the patients (61%) were 2 - 60 months of age. Out of these 64 patients, 71% were malnourished (second and third degree malnutrition according to Gomez classification) and it was statistically found to be significant (p value 0.004). Fever (82.9%) was the commonest presentation. Inadequate dietary history was present in 51.4%. About half of the patients (56.2%) received blood transfusion before bone marrow examination. Forty eight (36.3 %) patients had features of infection at presentation. Pneumonia was the leading cause of infection. Hepatosplenomegaly was seen in 27.6% and isolated splenomegaly in 4.8%, while 5.7% had generalized lymphadenopathy. Severe anemia (Hemoglobin < 5gm %) was found in 25.7%, leucopenia (TLC < 4000/cmm) in 45.7%, severe thrombocytopenia (platelet count ≤ 20,000/cmm) in 31.4%. Approximately half of the patients (62.9%) had bicytopenia and 37.1% had pancytopenia on blood complete picture. More than one third(41.9%) patients were diagnosed. Megaloblastic anemia on bone marrow examination and it was the leading cause of bicytopenia / pancytopenia in patients aged 13-60 months. Out of 40 patients of this age group 20 had Megaloblastic anemia and 18 out of these 20 patients (90%) were with grade II – III malnutrition (p value 0.02). Infective etiology was the cause of bicytopenia / pancytopenia in 19%, aplastic anemia in 13.3% and acute leukemia in 10.5% patients.
Conclusion: Megaloblastic anemia was the commonest cause of pancytopenia / bicytopenia followed by infective etiology, aplastic anemia and acute leukemia. Malnutrition was seen in majority of patients with megaloblastic anaemia
Key Words: Pancytopenia, bicytopenia, megaloblastic anaemia

Introduction
Pallor is an important and common symptom encountered in pediatric practice. It may on one hand be due to simple entity like nutritional anemia but on the other hand it may be the first manifestation of a life threatening condition like leukemia. Blood complete picture usually done as the initial investigation of a patient with pallor may reveal pancytopenia (Anaemia, thrombocytopenia, leucopenia), or bicytopenia (If only two parameters from the full blood count are low). A comprehensive workup is required to identify the etiology of pallor. This workup is very challenging as the etiologies are diverse. Bone marrow aspiration and trephine biopsy in these patients is indispensible. It is quite a safe procedure but yields tremendous information about hematopoietic disorders. To know the exact etiology is extremely important for specific treatment and prognosis. Early diagnosis in these patients helps in reducing morbidity and mortality.

Patients and Methods
This was a cross sectional descriptive study carried out for one year (Jan-Dec2012) in Department of Paedaitrics, Benazir Butto Hospital Rawalpindi. Patients from 2 months to 12 years of age of both sexes with pallor were included. Already diagnosed patients of hemolytic anemia, malignancy and those on
immunosuppressive medications were excluded. Demographic profile (name, age, sex, address), symptoms (fever, anorexia, bleeding manifestations, irritability, Lethargy, pica, jaundice, nutritional history and previous history of blood transfusion) were noted. Pertinent examination for lymphadenopathy and hepatosplenomegaly was carried out in detail. Degree of malnutrition was assessed according to Gomez classification. Blood complete picture and peripheral smear were carried out for every patient and patients having bicytopenia or pancytopenia (leucopenia, anaemia,thrombocytopenia).Inclusion criteria were presence of all 3 of the following: haemoglobin, <9 g/dl; total leukocyte count (TLC), <4,000 / µL; platelet count, <100,000/ µL), or bicytopenia if only two parameters from the full blood count are low).3,4,5,6 were further subjected to bone marrow aspiration and trephine biopsy by consultant pathologist after obtaining written consent from the parents.

### Results

A total of 105 patients with pallor were included in the study. There were 56 (53.3%) male and 49 (46.7%) female patients with ratio of 1.2:1. Patients were from 2 months to 12 years of age with mean age 4.9±4.1 year(Table 1). More than half of the patients (61%) were 2 - 60 months of age at presentation. Out of these

#### Table 1: Age of patients in months

<table>
<thead>
<tr>
<th>Age</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>2months-12months</td>
<td>24</td>
<td>22.9</td>
</tr>
<tr>
<td>13-60 months</td>
<td>40</td>
<td>38.1</td>
</tr>
<tr>
<td>More than 60 months</td>
<td>41</td>
<td>39.0</td>
</tr>
</tbody>
</table>

#### Table 2: Correlation of Nutritional history and age of patients

<table>
<thead>
<tr>
<th>Nutritional History</th>
<th>Age of patients in months</th>
<th>Total</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2-12 months</td>
<td>13-60 months</td>
<td>More than 60 months</td>
</tr>
<tr>
<td>Well nourished</td>
<td>10</td>
<td>13</td>
<td>28</td>
</tr>
<tr>
<td>Malnutrition II-III degree</td>
<td>14</td>
<td>27</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>49</td>
<td>41</td>
</tr>
</tbody>
</table>

64 patients, 71% were malnourished (second and third degree malnutrition according to Gomez classification) and it was statistically found to be significant (p value.004) (Table 2). Fever (82.9%) was the commonest presentation. Inadequate dietary history was present in 51.4%. About half of the patients (56.2%) received blood transfusion before bone marrow examination (Table 3). Forty eight (36.3%) patients had features of infection at presentation. Pneumonia was the leading cause of infection. Hepatosplenomegaly was seen in 27.6%, and isolated splenomegaly in 4.8%, while 5.7% patients had generalized lymphadenopathy. Severe anaemia (Hemoglobin < 5gm %) was found in 25.7%, leucopenia (TLC < 4000/cmm) in 45.7%, severe thrombocytopenia (platelet count ≤ 20,000/cmm) in 31.4% patients. Approximately half of the patients 62.9% had bicytopenia and 37.1% had pancytopenia on blood complete picture (Table 4). More than one third (41.9%) patients were diagnosed Megaloblastic anaemia on bone marrow examination and it was the leading cause of bicytopenia / pancytopenia in patients aged 13-60 months. Out of 40 patients of this age group 20 had Megaloblastic anaemia and 18 out of these 20 patients (90%) were with grade II – III malnutrition (p value 0.02) (Table 5). Infective etiology was the cause of bicytopenia/pancytopenia in 19%, aplastic anaemia in 13.3% and acute leukemia in 10.5% (Table 6).

### Discussion

Bicytopenia / Pancytopenia is a feature of many life threatening conditions. The frequency of pattern of diseases causing them varies in different populations.12 In the present study the patients were from 02 months
to 12 years of age with the mean age of 4.9 ± 4.1 year. More than half (61%) of the patients were under 5 years of age which correlates with the results of the studies done by Chandra et al. in 2002 stating that malnourished children of tropical and subtropical countries commonly suffer from nutritional megaloblastic anemia.19 In another study Borelli et al. in 2009 concluded that protein energy malnutrition causes depletion and changes in cellular development of progenitor hemopoietic cells which result in pancytopenia.20 Both these studies support the current study results which state that 90% of 1-5 years of age children having bicytopenia / pancytopenia are malnourished.

Tilak V in his study “Pancytopenia- A clinic-hematological analysis of 77 cases” states that he found aplastic anemia as the commonest cause of pancytopenia in various studies conducted previously.21 Gupta at el in their study found aplastic anemia as the commonest cause followed by acute leukemia and infections.22 In another study done by Memon et al. reported the common causes of pancytopenia as aplastic anemia, megaloblastic anemia, leukemia and infections respectively.23 Aplastic anemia was the most common cause of pancytopenia followed by myelodysplastic syndrome and acute leukemia in a study conducted by WU Jun et al.24 In another study done in 2010, aplastic anemia was identified as the leading cause and megaloblastic anemia being the second most common disorder.25 The results of above mentioned studies are contrary to the results of our study where the commonest cause found is megaloblastic anemia. In a study conducted by Pine M et al. the commonest cause was infections (64%) followed by hematological disorders (28%) which is also in contrast to our study results.26 Jha A et al. found hypoplastic bone marrow (29%) followed by megaloblastic anemia (24%) as the common causes in their study.11 It can be ascribed to malnutrition rampant in our society, especially in underprivileged

**Conclusion**

Commonest cause of bicytopenia / pancytopenia in pediatric patients is megaloblastic anemia which is found to be statistically significant in malnourished children aged 1-5 years. We should suspect such conditions in children presenting with pallor and employ appropriate diagnostic modalities to establish the underlying aetiology without delay, as early diagnosis and management results in better prognosis.

**References**