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Clinical and etiological profile of pancytopenia in children

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Abstract
Introduction: The etiology of pancytopenia varies widely in children, ranging from transient marrow viral suppression to marrow infiltration by fatal malignancy. Prompt intervention is required to avoid complications. The aim of this study was to evaluate the etiology and clinical profile of pancytopenia in children.
Methods: A retrospective descriptive study was carried out at a tertiary pediatric care centre of Gwalior district in children aged 6 months to 18years.The details of complete clinical profile and hematological parameters at presentation were recorded.
Results: Ninety four children with a mean age of 4.2 years with a male preponderance were included in the study. Common presenting complaints were pallor, fever and bleeding. Megaloblastic anemia was the commonest cause that was observed in 38.29% cases followed by aplastic anemia (23.4%) and acute leukemia (22.34%) cases, respectively. Infections were the next most common cause of which malaria was the commonest.
Conclusion: Detailed primary hematological investigations along with bone marrow aspiration in cytopenic patients are helpful for understanding the etiology and planning further management. Megaloblastic anemia is commonest cause of pancytopenia in most Indian studies and respond rapidly to effective therapy.

Keywords: Bone marrow examination, children, Megaloblastic anemia, pancytopenia

1. Introduction
Pancytopenia is a deficiency of all three cellular elements of blood (red blood cells, white blood cells and platelets) prevailing when hemoglobin (Hb) <10g%, absolute neutrophil count (ANC) <1.5*109/L, platelet count <100*109/L. The pancytopenia is labelled as severe if patient had two or more of the following: Hb <7 gm%, ANC <0.5*109/L, and platelet count <20*109/L.[1] Depending on the degree and duration of the impairment it can lead to serious illness and death. The etiology of pancytopenia varies widely in children, ranging from transient marrow viral suppression to marrow infiltration by life-threatening malignancy. These may also be caused iatrogenically, secondary to certain drugs, chemotherapy or radiotherapy for malignancies. The bone marrow picture may vary depending on the etiology, from normocellular with non-specific changes to hyper cellular being replaced completely by malignant cells. According to etiology, degree and duration of the impairment, clinically these can lead to fever, pallor, infection, or serious illness and death. Knowing the exact etiology is important for specific treatment and prognostication. Few studies have analyzed adult patients with pancytopenia.[2-4]There is scarcity of such data on pediatric patients. The aim of this study was to evaluate the clinico-hematological profile of children with pancytopenia.

2. Methods
Records of children aged 6 months to 18 years, admitted in a tertiary pediatric care centre with pancytopenia were retrieved and analyzed. The details of complete clinical profile and hematological parameters at presentation were recorded. Cases with history of blood transfusion in recent past were excluded. Hematological profile included hemoglobin, red cell indices, total and differential leukocyte counts, platelet count, peripheral blood smear morphology and bone marrow examination (BMA). Only those cases in which the diagnosis could be confirmed were included for final analysis.

3. Results

Ninety four cases fulfilling the inclusion criteria and with a definite diagnosis were studied for the etiology of pancytopenia. Mean age was 4.2 years (range: 0.5- 18 years). Maximum number of patients 41 (43.61%) were in the age group of 6 month to 5 years, followed by 31 (32.97%) in the 6 to 11 years age group while minimum number 22 (23.42%) were those exceeding 12 years of age (Table 1), all age group had a male predominance. Over all, male: female ratio was 1.29:1.

Table 1: Age and Gender Distribution

Age	Male (n=53)	Female (n=41)	Total(n=94)
6 month - 5 years	22	19	41 (43.61 %)
6 years - 11 years	18	13	31 (32.97 %)
12 years – 18 years	13	9	22 (23.42 %)

Frequency of common causes leading to pancytopenia are shown in Table 2. Megaloblastic anemia was the commonest cause that was observed in 36 (38.29%) cases followed by aplastic anemia and acute leukemia with 22(23.4%) and 21(22.34%) cases, respectively. Acute lymphoblastic leukemia (ALL) contributed to majority (15.95%) of acute leukemias with less common causes being Acute myeloid leukemia (AML) (4.25%) and myelodysplastic syndrome (MDS). Infections such as malaria, enteric fever, disseminated tuberculosis (TB) and kala-azar caused pancytopenia in 11 (11.7%) of our patients. In 2 cases, cause of pancytopenia was concluded to be iatrogenic (chemotherapy). Miscellaneous group included one patient each with Gaucher's Disease and Non Hodgkins Lymphoma (NHL).

Table 2: Etiology of Pancytopenia

	n	(%)
Megaloblastic Anemia	36	38.29
Aplastic Anemia	22	23.4
Acute Leukemia	21	22.34
ALL	15	15.95
AML	4	4.25
MDS	2	2.12
Infections	11	11.7
Malaria	5	5.31
Enteric Fever	3	3.19
Disseminated TB	2	2.12
Kala Azar	1	1.06
Iatrogenic	2	2.12
Miscellaneous	2	2.12
Gaucher's disease	1	1.06
NHL	1	1.06

Table 3 shows that pallor was the most common complaint presented in almost all cases (97.87%) followed by fever (72.34%). Skin bleeding manifestations in form of petechiae, bruises and ecchymosis were seen in 54(57.44%) children, while 43 cases (45.74%) showed mucosal bleeds (epistaxis, gum bleed, melena, etc.). On examination, hepatomegaly, splenomegaly and lymphadenopathy were found in 34, 29 and 9 cases, respectively. Few children (12.76%) presented with other symptoms like bone pain, fatigue, weight loss, etc.

Table 3: Clinical profile of Pancytopenia at presentation

Signs/Symptoms	n	(%)
Pallor	92	97.87
Fever	68	72.34
Skin bleed (petechiae, bruises, ecchymosis)	54	57.44
Mucosal bleeds(epistaxis, melena, gum bleed, hematuria)	43	45.74
Hepatomegaly	34	36.17
Splenomegaly	29	30.85
Lymphadenopathy	9	9.57
Bone pain	13	13.82
Others(fatigue, dyspnea, weight loss, etc)	12	12.76

4. Discussion

Pancytopenia is a feature of many transient illnesses or serious life-threatening diseases. The frequency of pattern of diseases causing them varies in different population groups and this has been attributed to differences in age, methodology, geographic area, period of observation, nutritional status, prevalence of infections and varying exposure to myelotoxic drugs among others. In India, diseases leading to pancytopenia are less defined. Most cases reports are limited to adults. [2, 4] Few of them have included children. [5-8] in present study, patients were predominantly male in all age groups. Previous studies also had the some finding with male dominating female. [9-11]

In our study many disease entities other than malignancies, emerged as recognizable cause of pancytopenia. Megaloblastic anemia was the most common cause (38.29%) of pancytopenia followed by Aplastic anemia diagnosed on bone marrow accounting for 23.4 %of cases. Comparable results were reported by studies done by Savage *et al* in Zimbabwe [12] and Bhatnagar *et al* in India. [7] A study from Pakistan also found megaloblastic anemia as the most prevalent diagnosis and the major cause of bicytopenia and pancytopenia in the bone marrow aspirates performed in their pediatric unit. [13] The high prevalence of nutritional anemia in India has been cited for the increased frequency of Megaloblastic anemia. Because of geographical and social similarities, nutritional anemias may also be responsible for increased frequency of Megaloblastic anemia in northern region of Pakistan.

However, Gupta *et al* [8] reviewed 105 children aged 1.5-18 years with pancytopenia. In their study, aplastic anemia was the most common cause of pancytopenia (43%), followed by acute leukemia (25%). In another study 64 children were identified with diagnosis of pancytopenia. The most common cases were infectious in origin (64%), followed by hematological (28%) etiologies. [14] Megaloblastic anemia was seen in just 6.7% of the patients by Khodke *et al*. [15]

In our study, ALL in 15 (15.95%) cases was the most common malignant condition presenting as pancytopenia followed by AML (4.25%) and the least common was MDS 2 (2.12%) This finding of our study is almost consistent with a study done by Shazia *et al* [16] in which 40 cases presented with pancytopenia with malignant condition, the ALL (8.69%) was the most common haematological malignancy followed by AML (2.17%).

Various infections as cause of pancytopenia have been variedly documented. In this study, of 11 patients with infections, malaria caused by Plasmodium falciparum was implicated as causation of pancytopenia in 5 patients. Arya *et al*. [17] and Gupta *et al* [8] also reported pancytopenia due to P. falciparum malaria in children. Enteric fever accounted for 3.19% cases in this study. Varying degrees of cytopenias have been reported in many other series on enteric fever. [18-20] Disseminated TB is an uncommon cause of pancytopenia, but has been previously reported. [21] In present study, we found 2 cases of disseminated TB with pancytopenia.

The most common presenting complaint in current study was pallor (97.87%) and low-grade fever, followed by bleeding. The presenting symptoms were usually attributed to anemia or

thrombocytopenia. Leukopenia was an uncommon cause of the initial presentation of the patient but can become the most serious threat to life during the disorder. Similar to our findings, Gupta *et al* found fever and progressive pallor as the most common presenting complaints, being present in 81.4%, followed by bleeding manifestations in 72.9%.Fever is known to be a common symptom in pancytopenia in children as demonstrated by earlier studies. Also, frequency of bleeding manifestations in various other reported series ranges between 4-20 %. [22-24] Hepatosplenomegaly was present in more than 1/3rd of our patients. Marwaha *et al* reported hepatomegaly and splenomegaly in about 45% of pancytopenia cases.[25]

5. Conclusion

The present study concludes that detailed primary hematological investigations along with bone marrow aspiration in cytopenic patients are helpful for understanding the disease process; to diagnose, or to rule out the causes of cytopenia; and in planning further investigations and management of cytopenic patients. With wider availability of the electronic cell counters Megaloblastic anemia could be easily picked up using various indices like mean corpuscular volume. Emergency treatments with B12 or folic acid will immediately improve the affected bone marrow and halt the associated complications. Early recognition of these conditions will certainly have impact on the morbidity and mortality in vulnerable pediatric patients.

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