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Original Article

Bone marrow evaluation in a pediatric population with pancytopenia in a tertiary care children's hospital in Nepal

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ABSTRACT

Background: Pancytopenia, which is characterized by a triad of anemia, leukopenia, and thrombocytopenia, is frequently observed among the pediatric population. This study was carried out to determine the common etiologies of pancytopenia in children through bone marrow aspiration examination.

Materials and methods: A one-year retrospective cross-sectional study of 64 cases of pancytopenia in the pediatric population was conducted at the Department of Pathology, Kanti Children's Hospital, from July 2019 to June 2020.

Results: 64 (35.55%) cases underwent bone marrow examination for pancytopenia. The patients' age ranged from 4 months to 14 years, with a median age of 6.24±1.12 years. The majority of the patients fell into the age group of 1-5 years. The most common cause of pancytopenia was acute leukemia and hypoplastic bone marrow followed by erythroid hyperplasia, leishmaniasis, and megaloblastic anemia.

Conclusions: Bone marrow examination is the fundamental diagnostic modality to diagnose the majority of cases of pancytopenia. It is important to consider acute leukemia, hypoplastic bone marrow, and leishmaniasis into account when evaluating pancytopenia in pediatric patients.

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INTRODUCTION

Pancytopenia is an important clinical-hematological entity characterized by a triad of anemia, leukopenia, and thrombocytopenia. Bone marrow examination is an established diagnostic modality in evaluating pancytopenia in patients across all age groups. It is useful, especially where first-line investigations such as full blood count and peripheral blood film are not sufficient for establishing a diagnosis.[1] The ultimate aim of bone marrow examination is to achieve a definite diagnosis with reasonable accuracy using a minimally invasive technique. Aspiration of the marrow has been primarily utilized for cytologic assessment,

with analysis directed toward assessing the morphology and obtaining a differential count. In addition to the microscopic evaluation of the cells and the structure, additional tests, like flow cytometry, cytogenetic and molecular studies, can be performed depending on the purpose.[2,3]

A spectrum of primary and secondary disorders that affect bone marrow may manifest with pancytopenia. It can be due to reduced hematopoietic cell production in the marrow by infections, malignant cell infiltrations or marrow suppression, vitamin B12 deficiency, chemotherapy, radiotherapy, parasitic infestation, and genetic disorders.[4] With a growing number of children, an increased incidence of anemia, infectious disease, leukemias, and thrombocytopenia is being observed. Hence the number of pediatric patients undergoing bone marrow examination has also increased.[5] Although many studies and literature are there on bone marrow examinations, not many studies have been conducted on the pediatric population.

The main aim of this study is to evaluate common bone marrow findings in pediatric patients presenting with pancytopenia.

MATERIALS AND METHODS

The descriptive cross-sectional study was conducted in Kanti Children's Hospital, a tertiary care hospital offering outpatient and inpatient services in Kathmandu. The study involved the analysis of data from medical records of patients aged between 1 month and 16 years who were diagnosed with pancytopenia and underwent bone marrow examination during the period from July 2019 to June 2020. Pancytopenia was confirmed based on complete blood count and peripheral blood smear. The criteria for defining pancytopenia were as follows: hemoglobin levels less than 10gm/dl, platelet counts less than 150 x 10^9/L, and total leukocyte count less than 4 x 10^9/L.

The details of the patient profile and hematological parameters were recorded at the time of examination. Bone marrow aspiration was done using a Salah needle from the posterior superior iliac spine under local anesthesia using lignocaine. Sudan Black B and PAS stain was used in acute leukemia cases to differentiate between acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL). We could not interpret the bone marrow biopsy findings since the histopathology service was not available at our center.

RESULTS

A total of 180 patients underwent bone marrow evaluation with aspiration during the study period. Pancytopenia was the indication in 64 (35.55%) cases, and bone marrow aspiration was performed. Five cases were excluded from the study due to the inadequacy and dilution of the sample. The total number of cases enrolled in our study was 59, of which 43 (72.88%) were males, and 16 (27.12%) were females. The patients' ages ranged from 4 months to 14 years, with a median age of 6.24±1.12 years. The age-wise distribution of the participants in the study is summarized in Table 1.

Table 1: Age-wise distribution of cases of pancytopenia

Age (in years)	Number of cases	Percentages
0-1	6	10%
1-5	25	42%
5-10	16	27%
10-16	12	20%
Total	**59**	**100%**

On bone marrow aspiration, normal hematopoiesis was seen in 15.25% of cases. In the remaining cases, the main etiology was hypoplastic bone marrow and acute leukemia seen in 16.94% of patients followed by erythroid hyperplasia in 13.55% of patients (Table 2). The miscellaneous group included two patients each from hemophagocytic lymphohistiocytosis and megakaryocytic thrombocytopenia and one patient each from bone marrow eosinophilia and metabolic causes.

Table 2: Bone marrow findings in cases of pancytopenia

Bone marrow findings	Number	Percentages
Normal Marrow findings	9	15.25%
Hypocellular Marrow	10	16.94%
Acute leukemia	10	16.94%
Erythroid Hyperplasia	8	13.55%
Infective cause (Leishmaniasis)	6	10.16%
Megaloblastic Anemia	5	8.47%
Metastatic Disease	5	8.47%
Miscellaneous	6	8.47%
Total	**59**	**100%**

DISCUSSION

The sex ratio in our study was found to be 2.6 with a preponderance of male patients. These findings were consistent with studies conducted in India and Pakistan.[5-8] However, other studies conducted in Pakistan showed female preponderance with a sex ratio of 0.88 and 0.76.[11,12]

The mean age in our study was 6.24±1.12 years, which was lower compared to similar studies.[8,9] The majority of the patients fell into the younger age group of 1-5 years which was similar to the results found by Zubair et al.[10] On the contrary, studies conducted in India and Pakistan showed the highest prevalence of pancytopenia among adolescents.[8,9]

Hypoplastic anemia and acute leukemia were the most common causes of pancytopenia in our study, which were also observed in other studies.[7,11-13] It is important to note that

due to the lack of histopathology service, we were unable to interpret the bone marrow biopsy findings, and the diagnosis of hypoplastic anemia was made based on bone marrow aspiration findings. Some cases of hypoplastic marrow may have cellular marrow due to regenerating focus called 'hot spot'. In such cases, bone marrow biopsy is diagnostic.

A high incidence of acute leukemia in our center can be attributed to the availability of a separate cancer treatment unit. While bone marrow findings in acute leukemia typically present with the hypercellular marrow, the reason for pancytopenia in acute leukemia is the suppression of normal marrow function by rapidly proliferating neoplastic cells. Additionally, some cases included in our study were undergoing chemotherapy. Among cases of acute leukemia, the male-to-female ratio was 5:1, and the average age at diagnosis was 5.19±3.37 years, ranging from 10 months to 11 years. Out of 10 cases of acute leukemia, 80% (8/10) of cases account for ALL, and 20%(2/10) of cases account for AML. These findings support the fact that ALL is the most common cancer in the pediatric population in terms of prevalence and mortality.[14]

Erythroid hyperplasia was the second most common cause of pancytopenia in our study, which was also observed in a study from Nepal.[12] The pathogenesis of erythroid hyperplasia leading to pancytopenia remains unknown but is believed to represent one phase in the evolution of hypoplasia and occasionally represents cases of refractory anemia.[12] Further evaluation of these cases should involve bone marrow biopsy and other additional tests to guide the final diagnosis.

In our study, Leishmaniasis was seen in 10.16% of patients. Rathod et al also found leishmaniasis as one of the causes of pancytopenia in children, although it was reported in only 1.5% of cases. The higher incidence of Leishmanias is in our study can be attributed to the referral of cases from the endemic Terai regions of Nepal, as our center is the major referral center for the pediatric population. Megaloblastic anemia accounted for 8.47% of cases in our study and is one of the most common causes of pancytopenia in the Indian subcontinent as reported in various studies.[6,7,9-11,15] This finding highlights the high prevalence of nutritional deficiencies of Vitamin B12 and Folic acid in the region.

Metastatic disease was observed in 8.47% of cases in our study, which includes four cases of metastatic neuroblastoma and one case of metastatic retinoblastoma. These were diagnosed cases of solid tumors, and a bone marrow examination was done to evaluate the presence of metastasis. Hemophagocytic lymphohistiocytosis was identified in two cases in our study, diagnosed according to HLH-2004 (Updated 2007) criteria.[16]

The study has its limitations. It was conducted in a single hospital setting with a small sample size, which may limit the generalizability of the results. In most cases, it is recommended to perform both bone marrow aspiration and a biopsy at the same time to reach a final diagnosis. However, due to the unavailability of a histopathology facility in our center, the etiology of pancytopenia was determined based on peripheral blood smear and bone marrow aspiration findings. In our study, a significant portion of the cases have normal findings and erythroid hyperplasia. Similarly, hypoplastic bone marrow could be further investigated, and the differential diagnosis can be narrowed down. A bone marrow biopsy and other relevant additional tests would complement our diagnosis and make it more accurate.

CONCLUSIONS

Bone marrow examination is the fundamental diagnostic modality to diagnose the majority of cases of pancytopenia. In our study, we found that hypoplastic bone marrow, acute leukemia, and leishmaniasis were the major causes of pancytopenia in children. Therefore, it is crucial to consider these conditions into account when evaluating pancytopenia in pediatric patients. ALL is found to be the most important malignant cause of pancytopenia in children.

Conflict of interest: None

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