Original Research Article

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Bicytopenia/pancytopenia in children - clinico etiological profile and importance of bone marrow evaluation in a tertiary care centre

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ABSTRACT

Background: Peripheral cytopenia is a common hematological problem in our day-to-day clinical practice resulting from various diseases ranging from transient infection induced bone marrow suppression to life threatening hematological malignancies. The objective of this study was to know the clinicoetiological profile,hematological analysis and importance of bone marrow evaluation of bicytopenia/pancytopenia in children in a tertiary care teaching hospital.

Methods: This was a retrospective, observational study, conducted in pediatric department, NRIIMS, Visakhapatnam, Andhra Pradesh from May 2019 to May 2020. All children in the age group of 1-18yrs of age admitted with new onset bicytopenia/pancytopenia who underwent hematological analysis and bone marrow examination in our hospital were included in this study. Children with bicytopenia/ pancytopenia evaluated outside/treated in other hospitals were excluded from our study. Data was obtained from bone marrow biopsy register from pathology department, admission register of pediatric ward and hospital medical records.

Results: Out of the 31 children studied, males were (54.8%), females were (45.2%).11-18 years of age were (51.6%), 1-5 years of age were (38.7%). Fever (77.4%), pallor (74.1%), hepatosplenomegaly (41%) was the most common clinical feature noted in these patients. ALL (52.3%), followed by ITP (9.52%) was the most common etiology for bicytopenia. Aplastic anaemia (40%), megaloblastic anaemia (20%) were most common etiology noted for pancytopenia. Bicytopenia (67.7%) was more common than pancytopenia (32.2%). Peripheral smear examination picked up only 11 out of 14 cases of haematological malignancy, identified by bone marrow examination. Most common bone marrow finding noted was ALL (38.7%), followed by hypocellular bone marrow (22.5%).

Conclusions: When there is high index of clinical suspicion and peripheral smear is unable to pick up these cases, it is advisable to do bone marrow examination at the earliest for early confirmation.

Keywords: Bone marrow evaluation, Bicytopenia, Clinical profile, Etiology, Pancytopenia

INTRODUCTION

Peripheral cytopenia is defined as the reduction of blood cells (erythrocytes, leucocytes or thrombocytes). Bicytopenia is defined as the reduction of 2 cell series, Pancytopenia as the reduction of 3 cell series. Etiology of Bicytopenia and Pancytopenia has a broad distribution in

children.¹ Criteria for diagnosis is: hemoglobin <10gms, total leucocyte count <4000 and platelet count <1 lac/cubic millimeter of blood. In order to establish the cause of Pancytopenia, bone marrow aspiration is needed which can be done from Manubrium sterni, Iliac crest or upper end of Tibia in case of children. Needless to say that bone marrow aspiration is a good standard as far as

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the diagnosis of the cause of Pancytopenia is concerned, if applied using proper discretion.2 The etiology of Pancytopenia varies widely in children ranging from transient marrow suppression due to viral infection to marrow infiltration by life threatening malignancy These may also be caused iatrogenically, secondary to certain drugs, chemotherapy or radiotherapy for malignancy.³ To know the exact etiology is extremely important for specific treatment and prognosis. Early diagnosis in these patients helps in reducing morbidity and mortality. BMA and Trephine biopsy in these patients is indispensable.⁴ BMA is not helpful in those with Aplastic anemia or marrow infiltrations even if fragments were aspirated. In such cases bone marrow biopsy is helpful. Bone marrow aspirate specimens are superior for morphological detail over biopsy specimens, while biopsy specimens provide a more reliable index of cellularity and often reveal marrow infiltration, fibrosis and granulomas which are not detected on aspiration.⁵ The incidence of various disorders causing Pancytopenia varies according to geographical distribution and genetic mutations. 6 Marrow cellularity and composition differ in relationship to the cause. The marrow is generally hypocellular in cases of Pancytopenia caused by primary production defects. Cytopenias resulting from ineffective hematopoiesis, increased peripheral utilization or destruction of cells and bone marrow invasive processes are usually associated with a normocellular or hypercellular marrow. 7 Anaemia results in FTT, respiratory distress, and cardiac failure. Leucopenia can present with recurrent fever, mouth ulcers and gingivitis. Thrombocytopenia presents with skin petechiae and mucosal bleeds. The objective of this study was to know the clinicoetiological profile, hematological analysis and importance of bone marrow evaluation of bicytopenia/pancytopenia in children in a tertiary care teaching hospital.

METHODS

This was a retrospective study, done on children aged 1 to 18 years of age, admitted with bicytopenia/pancytopenia in pediatric department and referred for bone marrow aspiration and biopsy to pathologist of Anil neerukonda hospital, NRIIMS, Visakhapatnam, Andhra Pradesh, from May 2019 - May 2020. The patients needed for this study were taken from the bone marrow register in pathology department and the details were confirmed from the admission register in paediatric department. Thereafter, complete patient information was collected from medical records department.

Inclusion criteria

Presence of all 3 (pancytopenia) or any 2 (bicytopenia) of the following parameters: hemoglobin < 9g/dl, total leucocyte count < 4000, platelet count <100,000. 1 to 18 years old children admitted with new onset bicytopenia/ pancytopenia for evaluation to the pediatric department, complete patient information along with clinicoetiological profile, complete blood counts, peripheral

smear and bone marrow aspiration and biopsy report in the medical records were included in the study.

Exclusion criteria

Children with bicytopenia/ pancytopenia with incomplete information in medical records, had bone marrow examination done in other hospitals/already received treatment outside before admission in our hospital were excluded from study.

The following data was collected from the medical records department (MRD) about the children included in this study *Age, sex, clinical profile and etiology of these patients at admission and *complete blood count, peripheral smear, bone marrow aspiration and biopsy report.

RESULTS

A total of 31 cases that fulfilled the inclusion criteria were studied and the results were analysed as below.

Table 1: Distribution of cases according to demographic data.

Demographic data	N (%)
Gender	
Male	17 (54.83)
Female	14 (45.17)
Age group (in years)	
1-5	12 (38.70)
6-10	3 (9.67)
11-18	16 (51.61)

Table 2: Distribution of cases according to clinical profile.

Clinical profile	N (%)
Symptom	· /
Fever	24 (77.41)
Anorexia	9 (29.03)
Bleeding	8 (25.80)
Fatigue	7 (22.58)
Weight-loss	6 (19.35)
Joint-pains	3 (9.67)
Parotitis	2 (6.45)
Respiratorydistress	2 (6.45)
Healed varicella lesions	1 (3.22)
Signs	
Pallor	23 (74.19)
Hepatosplenomegaly	13 (41.93)
Lymphadenopathy	5 (16.12)
Hepatomegaly	3 (9.67)
Icterus	2 (6.45)
Pedal-edema	2 (6.45)
Pleural-effusion	2 (6.45)
Splenomegaly	2 (6.45)

In Table 1, it was seen that, out 31 cases studied, male children (54.83%), female children (45.17%). Maximum numbers of bicytopenia/ pancytopenia cases were seen among 11-18 years of age. 16 cases (51.61%), followed by 12 cases in (38.70%) in 1 to 5 years of age, 3 cases (9.67%) in 6 to 10 years of age.

It was seen that according to Table 2, the most common symptom was fever seen in 24 cases (77.41%), followed by anorexia in 9 cases (29.03%), bleeding manifestations in 8 cases (25.80%), fatigue in 7 cases (22.58%), weight loss in 6 cases (19.35%), joint pains in 3 cases (9.67%), parotitis in 2 cases (6.45%), respiratory distress in 2 cases (6.45%), healed varicella lesions in 1 case (3.22%)

The most common sign was pallor in 23 cases (74.19%), followed by hepatosplenomegaly in 13 cases (41.93%), lymphadenopathy 5 cases (16.12%), hepatomegaly 3 cases (9.67%), icterus, pedal edema, pleural effusion, splenomegaly, is 2 cases each (6.45%).

Table 3: Distribution of cases according to etiology.

Etiology	N (%)
Total no. of patients with bicytopenia	(n=21)
Acute-leukemia	11 (52.38)
ITP	2 (9.52)
Aplastic-anaemia	1 (4.76)
Thalassemia-with-hypersplenism	1 (4.76)
SLE	1 (4.76)
Megaloblastic-anaemia	1 (4.76)
Neuroblastoma	1 (4.76)
Hemophagocytic-syndrome	1 (4.76)
Hodgkins-lymphoma	1 (4.76)
Unknown	1 (4.76)
Total no. patients with pancytopenia	(n=10)
Aplastic-anaemia	4 (40)
Megaloblastic-anaemia	2 (20)
AML	1 (10)
ALL	1 (10)
Varicella	1 (10)
Portal hypertension with hypersplenism	1 (10)

According to Table 3 it was seen that, out of the 21 cases of bicytopenia the most common etiology was ALL in 11 cases (52.38%). This was followed by ITP in 2 cases (9.52%), 1 case (4.76%) each of Aplastic Anaemia, Thalassemia With Hyperspenism, SLE, Megaloblastic Anaemia, Neuroblastoma, Hemophagocytic Syndrome, Hodgkins Lymphoma was seen as a cause of bicytopenia. The etiology was unknown in 1 case (4.76%). The etiology of Pancytopenia is as follows, Aplastic anaemia in 4 cases (40%), Megaloblastic anaemia in 2 cases (20%), AML in 1 case (10%), ALL in 1 case (10%, Varicella in 1 case (10%), Portal hypertension with Hypersplenism in 1 case (10%). According to Table 4, it was seen that Bicytopenia was seen in 21 cases (67.74%)

and Pancytopenia in 10 cases (32.25%). Abnormal cells in peripheral smear was seen in 11 out of 14 cases of hematological malignancy diagnosed by bone marrow examination.

Table 4: Distribution of cases according to hematological analysis.

Complete blood counts and peripheral smear	N (%)
Bicytopenia	21 (67.74)
Pancytopenia	10 (32.25)
Presence of abnormal cells in peripheral smear (blast cells/ atypical lymphocytes/ activated lymphocytes)	11 (35.48)

Table 5: Distribution of cases according to bone marrow findings.

Bone marrow findings	N (%)
Acuteleukemia of-lymphoidseries	12 (38.70)
Hypocellular-bonemarrow	7 (22.58)
Normocellular-bonemarrow	3 (9.67)
Megaloblastic-anaemia	3 (9.67)
Megakaryocyticthrombocytopenia	2 (6.45)
Hodgkins-lymphoma	1 (3.22)
Hemophagocytic-syndrome	1 (3.22)
Blue round cell tumor	1 (3.22)
Acute leukemia of myeloid series	1 (3.22)

According to Table 5, it was seen that the most common bone marrow finding in our study was malignant cell of lymphoid series (ALL) in 12 cases (38.70%), followed by Hypocellular bone marrow in 7 cases (22.58%), Normocellular bone marrow in 3 cases (9.67%), Megaloblastic marrow in 3 cases (9.67%), Megakaryocytic thrombocytopenia in 2 cases (6.45%), one case (3.22%) each of Hodgkins lymphoma, Hemophagocytic syndrome, Blue round cell tumor, Acute leukemia of myeloid series (AML)

DISCUSSION

In our study it was seen that males were (54.83%), and outnumbered females (45.17%). Similar finding was reported by Sharif et al, in which males were (53.3%), and females were (46.7%).⁴ The age group most commonly affected in our study was 11 - 18 years of age (51.61%), followed by 1 - 5 years of age (38.70%), then 6 - 10 years (9.67%). In contrast, a study conducted by rathod etal14, it was seen that 6 months to 6 years were most commonly affected (39%), followed by 7 to 10 years of age (34%).¹⁴ Similar to our study, Sharif etal4 has observed that children more than 5yrs of age were most commonly affected (39%).⁴

Our study observed that, in children with bicytopenia/ pancytopenia, most common symptom was Fever (77.41%), followed by Anorexia (29.03%), Bleeding (25.80%). Most common sign noted was Pallor (74.19%), followed by Hepatosplenomegaly (41.93%). Similarly many studies have revealed fever and pallor as the most common clinical feature among patients with bicytopenia / pancytopenia. 4,10-15

Our study observed that the most common cause for bicytopenia was ALL (52.38%), followed by ITP (9.52%). Yalaki et al has noted that in bicytopenia patients the most common etiology was infection (64.2%), followed by ALL (14.2%), ITP (7.1%). Aplastic anaemia (40%) followed by Megaloblastic anaemia (20%) was the most common etiology of Pancytopenia observed in our study. But in contrast the etiological pattern noted for Pancytopenia in children by various others authors were Megaloblastic anaemia followed by Aplastic anaemia. 11.12,14

Our study has noted that Bicytopenia (67.74%) was more common than Pancytopenia (32.25%) in these patients. Similar findings were noted by Sharif et al in which Bicytopenia was seen in (62.9%) and Pancytopenia in (37.1%).⁴ It was seen that out of the 14 cases of hematological malignancy identified by bone marrow examination in our study, only 11 cases were picked up by peripheral smear examination. In a study done by thiagarajan etal9, it was seen that peripheral smear was able to pick up only 7 out of 11 cases of hematological malignancy.⁹

It was observed that in our study the most common bone marrow findings were that of Acute leukemia of lymphoid series (38.70%), followed by Hypocellular bone marrow (22.58%), Megaloblastic anaemia (9.67%). In contrast, in a study done by Sharif et al, it was noted that Megaloblastic anaemia (41.9%), as the most common bone marrow finding followed by Infection (19%), Aplastic anaemia (13.3%) and Acute leukemia in (10.5%)of cases in children Bicytopenia/Pancytopenia.4 Mallik et al has observed that Megaloblastic anaemia (47.67%) and Hypoplastic bone marrow (33.72%) as the most common bone marrow finding in children with Pancytopenia.¹⁶

Limitation

Small sample size. We recommend more studies with larger sample sizes.

CONCLUSION

Bone marrow examination can diagnose the etiology for majority of cases of Bicytopenia/Pancytopenia. So, whenever there is high index of clinical suspicion of hematological malignancy and peripheral smear is unable to pick up the findings, it is advisable to do bone marrow examination at the earliest, so that unnecessary delay in diagnosis and treatment can be avoided.

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