Clinico-hematological Profile of Childhood Pancytopenia with Special References to Non Malignant Presentation

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ABSTRACT:

Background: Pancytopenia refers to a reduction in all the three formed elements of blood: red blood cells, white blood cells and platelets. There is scarcity of such data on pediatric patients, and to the best of our knowledge, no study has analyzed adult or pediatric bicytopenic patients. **Aims:** The aim of this study was to evaluate the clinico-hematological profile of children with bicytopenia/pancytopenia. **Material & Methods:** Patient's age group between 6 months to 15 years from 1st September 2014 to 31st August 2015 admitted in children hospital, S.P. Medical College, Bikaner was selected for this study. Pancytopenia was reported by automated cell counter "Symex CBC 18PAR KX-21". Hemoglobin <10gm%, TLC <4000mm^3 and Platelet count <1 Lac/mm^3 were taken as criteria of pancytopenia. Platelet count was confirmed by PBF manually. **Results:** The majority of patients belonged to age group 1-5 years (51.6%) in non-malignant etiology in pancytopenia patients from a rural area (77.1%) and lower upper socioeconomic status (41.2%). According to PBF expert, the majority of the patients had pancytopenia with dimorphic anemia (32%). **Conclusion:** Dimorphic anemia in PBF examination was the most common finding in cases of pancytopenia due to severe malnutrition. 18.2% cases of pancytopenia were of malignant etiology, out of them maximum were of ALL.

Key-words: Pancytopenia, Hematological examination, Peripheral blood film, Hemoglobin.

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INTRODUCTION:

Pancytopenia has either cellular, hypocellular or hypercellular bone marrow morphology. There are very few studies in the literature that explore the various etiological factors of pancytopenia with hypocellular and cellular marrows. The common causes of pancytopenia vary in different studies.[1-3] Pancytopenia is a problem in which there is a reduction of all the three cellular elements of blood up to a significant level, hemoglobin (Hb) <10g%, absolute neutrophil count (ANC) <1.5*109/L, platelet count <100*109/L. In pancytopenia the bone marrow is usually hypocellular as a result of primary

production defects and it can be due to diminution of hematopoitic stem cell production, ineffective haematopoiesis or due to peripheral destruction of cells. The production of hematopoitic cell can be hampered in the bone marrow either by infections, toxins, and malignant cell infiltration leading to hypocellular marrow. Other causes like ineffectual hematopoiesis and dysplasia, maturation arrest of all the cell lines and peripheral sequestration or destruction of blood cells can also be the cause of pancytopenia.[4-6] Peripheral cytopenia is defined as reduction in any one of the cellular elements of blood, i.e., red cells, white cells or platelets while bicytopenia is the reduction in any of the two cell lines and reduction in all the three cells is known as pancytopenia.[7] There is considerable overlap between the causes and diagnostic approach of bicytopenia and pancytopenia. The etiology of bicytopenia and 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. In the year 1990, Bello-González and Bergés-García[8] described that peripheral pancytopenia is a syndrome which allows for an early diagnosis, and although it may cover a large number of pathological entities, it can be clearly defined into three groups of illnesses which evolve with this syndrome manifestation. The first group includes non-neoplastic illnesses which include aplastic anemia, hemophagocytic syndrome associated with infection, immunological diseases and the deficiency of folates or vitamin B12. The second group includes neoplastic diseases as acute leukemia, non-Hodgkin lymphoma, and Hodgkin's lymphoma with myelofibrosis, malignant histiocytosis and non-hematological neoplasms, like the neuroblastoma and the embryonal rhabdomyosarcoma. The third group is formed by illnesses which have some similarity with neoplasms. The aim of this study is to identify the clinical profile and bone marrow morphology of pancytopenia patients.

MATERIAL & METHODS:

The present study was conducted in the Department of Pediatrics, S.P. Medical College and P.B.M. Associated Group of Hospitals, Bikaner (North West Rajasthan).

Source of Data

Patient's age group between 6 months to 15 years from 1st September 2014 to 31st August 2015 admitted in a children hospital, S.P. Medical College, Bikaner. Pancytopenia was reported by automated cell counter "Symex CBC 18PAR KX-21". Hemoglobin <10gm%, TLC <4000mm^3 and Platelet count <1 lac/mm^3 were taken as criteria pancytopenia. Platelet count was confirmed by PBF manually.

Inclusion criteria

1. All admitted cases from 6 months to 15 years of age in Department of Pediatrics, S.P. Medical College and

P.B.M. Associated Group of Hospitals, Bikaner with pancytopenia.

2. Informed consent by guardian.

Exclusion criteria: The patients on Chemotherapy, radiotherapy and known cases of hematological malignancy.

A systematic review of causes, detailed history, clinical examination and laboratory parameters for etiology causing cytopenia were recorded in preset proforma. Hematological profile included hemoglobin, red cell indices, total and differential leukocyte counts, platelet count, peripheral blood smear morphology and bone marrow aspiration or biopsy were done. Relative test was done to establish the diagnosis of various diseases appropriately. PBF was prepared with standard staining method and seen and counter checked by a pathologist. Bone marrow aspiration and trephine biopsy were carried out as per the clinical indication. The bone marrow procedure and further staining were carried out by standard methods.[9-11] Appropriate statistical analysis was applied as and when required using SPSS statistical software version 10.0. A p-value <0.05 was taken as significant.

RESULTS:

In the present study, in our institution during our study period, total 16936 patients were admitted, out of them 68% patients were between 6 months to 15 years (table 1) and only 18.2% cases have malignant etiology in pancytopenia patients. The majority of patients belonged to age group 1-5 years (51.6%) in non-malignant etiology in pancytopenia patients (table 2). The our study shows the most common presenting complaint was fever (71.9%), followed by pallor (33.35%) (table 3). Clinically observed that the spleen was not palpable in 26.1%, while majority of patients had mild (just palpable – 3cm) (54.9%) (table 4). On hematological examination the complete blood count seen in (table 5). According to PBF expert, Majority of patients had pancytopenia with dimorphic anemia (32%) followed by Macrocytic anaemia (22.5%), Malignant Cells (18.2%), Microcytic anaemia (16.6%) and Normocytic anaemia (10.75) (table 6).

DISCUSSION:

We studied the eligible candidates (6 months to 15 years patients with informed consent). Total 10040 patients were analyzed, out of them 187 patients CBC and PBF reports were showing pancytopenia during 1st September 2014 to 31st August 2015. The our results show that out of 187 patients of pancytopenia there were 34(18.2%) cases of malignant etiology. Further evaluation of these pancytopenia cases of malignant etiology shown that out of 34 cases there were 19(55.8%) cases of ß-cell ALL, 6 cases of T cell ALL (17.7%), 7 cases of AML (20.7%), 1 case each (2.9%) of the NHL and MDS. The pattern of leukemia was in accordance to the Gruchy's Clinical Hematology in Medical Practice (6th adapted edition)[12]. According to Naseem[13] in 2008, a similar pattern was present ALL was present in 84.7%, AML was present in 15.2% and one

case of myelodysplastic syndrome 0.7%. Zeb Jan[14] in 2013 also shown that malignancies 48.9% was of ALL, AML was present in 32.6% and MDS in 18.4%.

Our study result is in line with the results of studies previously done by Zeb Jan[14] in 2013 in which maximum number of patients were in the age group of 6 months to 5 years 42.44% followed by 35.13% in the age group 6-10 years. Study done by Sharif[15] 2012 also shown that maximum number of patients belong to the age group 2 months to 5 years (61%)., Gupta et al[39] also shown similar results 1 years to 5 years cases while 58% of total cases. Study done by Rathod et al[16] 2015 also show that maximum number, 39% was in the age group of 6 months to 5 years. Our study male outnumbers the female patients with a male to female ratio 1.1:1. These results are comparable with Sharif[15] in 2012 in Pakistan in which male and female population was 1.2:1. A study done by Santra[17] in 2010 also show male to female ratio 1.47:1. Study done by Goel et al[18] in 1981 reported 1.76:1 male to female ratio and Chhabra[19] in 2012 show male predominance 55:36 (1.64:1). Study done by Gayatri[20] in the year 2014, in Devenagre Karnataka had similar results of 1.2:1. As India is a country in which majority of the population resides in rural areas. In our hospital total indoor patient when evaluated for residential area 80% cases were from rural areas, this is in accordance with total hospital admissions. India is “rural country” mainly population in the study area, living in the village, government of India data shows rural : urban ratio 72:28 for this study was conducted in a government hospital having predominantly poor rural population. Study done by Santra[17] in 2010 in Kolkatta shows that middle class patients predominantly 57%, followed by lower class 30%.

In our study spleenomegaly was also present in 73.9% cases out of them 54.9% cases were of mild spleenomegaly just palpable to 3 cm moderate to severe spleenomegaly was present in 19% cases, hepatomegaly was also associated with spleenomegaly, Mild hepatomegaly (just palpable to 3 cm) was present in 77.1%, moderate to severe hepatomegaly was present in 14.4% cases. A patient having more than one clinical feature is counted in each category, hence the sum may be more than the total number of cases in the study. Our study results are comparable with previous studies done at various other centers by different authors. Accordance by Naseem et al[13] showed fever 65.5%, pallor 59%, petechiae rash 18%, bleeding 26.6%, hepatomegaly 51.8%, spleenomegaly 37.5% and lymphadenopathy in 15.5%. According to Nigam[21] in 2013 also show fever was more common, but Zeb Jan[14] in 2013 found pallor (82.9%) was the common symptom followed by fever (62.8%). The present study observed complete blood count, the results similar with Santra[17] where they found that mean Hb was 5.9 with SD 1.9gm%, mean TLC was 2633 with SD 670/mm^3 and mean platelet count was 42200 with SD 38600/mm^3. After proper methodology of PBF examination smear examined by us and counter checked by experienced pathologist the results show that the total number of

leucocyte and platelets were decreased in all patients. Leucocyte shown the malignant transformation as raised N:C ratio, chromatin tissue in 34(18.2%). Similar results were shown by Gayatri[20] 2014 dimorphic anaemia is most common in 37.5%, followed by macrocytic anemia 31.7%. According to Tilak[10] emphasized role of PBF expert in evaluation of pancytopenia and showed that 84.9% of cases of megaloblastic anemia.

CONCLUSION:

Dimorphic anemia in PBF examination was the most common finding in cases of pancytopenia due to severe malnutrition. 18.2% cases of pancytopenia were of malignant etiology, out of them maximum were of ALL. The majority of the patients were from lower socioeconomic status and rural area.

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Table 1: Show the distribution of Admission of cases

	No.	%
Total Number of Admission (01-09-14 to 31.08.15)	16936	100
Admission <6 months of age	5419	32.0
6 months to 15 years admission	11517	68.0
Total number of patients with CBC report	14765	87.2
CBC done in <6 months of age	4725	27.9
CBC 6 months – 15 years	10040	59.3
Rest (11517-10040=1477) CBC was not done due to short stay, early discharge or normal CBC from another source		

Table 2: Distribution of cases according to age group in non malignant causes of pancytopenia

Age Group	Frequency	%
6 month – 1 year	17	11.1
1 - 5years	79	51.6
>5 - 10 years	14	9.2
>10 years	43	28.1
Total	153	100

Table 3: Distribution of cases according to presenting complaints

Presenting Complaints	No.	%
Fever	110	71.9
Pallor	51	33.3
Weakness and Fatigue	46	30.1
Cough & Respiratory Distress	33	21.6
Edema	28	18.3
Rash	13	8.5
Epistaxis	5	3.3
Hemetemesis	1	0.7
Blood in stool	4	2.6
Menorrhagia	1	0.7
Loose Motion	17	11.1
Vomiting	6	3.9
Abdominal Distension	10	6.5
Joint Pain	11	7.2
Abscess	6	3.9

Table 4: Distribution of cases according to spleenomegaly

Spleenomegaly	Frequency	Percentage
Non Palpable	40	26.1
Mild (Just Palpable -3cm)	84	54.9
Moderate (>3-6cm)	22	14.4
Severe (>6cm)	7	4.6
Total	153	100

Table 5: Distribution of cases according to complete blood count

CBC	Mean	SD
Hb	5.97	2.12
TLC	2860.13	775.22
Platelet Count	51164.71	28814.31

Table 6: Distribution of cases according to PBF Expert

Pancytopenia with	Frequency	Percentage
Microcytic anaemia	31	16.6
Normocytic anaemia	20	10.7
Macrocytic anaemia	42	22.5
Dimorphic anaemia	60	32.0
Malignant Cells	34	18.2
Total	187	100