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A Prospective and Retrospective Study of Bone Marrow in Patients with Pancytopenia– A Study of 150 Cases

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ABSTRACT

BACKGROUND : The bone marrow is widely distributed organ and is the principle site for blood cells formation. The broad spectrum of disorders affects the marrow primarily or secondarily with presentation of peripheral pancytopenia. Hence, bone marrow examination is extremely helpful in evaluation of pancytopenia. This study emphasizes the different causes of pancytopenia and bone marrow morphology in cases of pancytopenia.

MATERIALS & METHODS: The present study is a retrospective and prospective study done in the department of Pathology, for a period of two years. All the relevant history, clinical details, radiological details, and biochemistry parameters were considered.

RESULTS: Out of 150 cases,96 were males and 54 were females. Majority of the patients were in the age group of 41-60 years (54%) amongst whom Megaloblastic anaemia was the most important cause of pancytopenia.

CONCLUSION: Bone marrow aspiration is relatively a very safe invasive procedure and primarily permits cytological assessment since the underlying pathology determines the management and prognosis of the patients.

KEYWORDS: Bone marrow aspiration, pancytopenia, Megaloblastic anaemia.

INTRODUCTION

The bone marrow is widely distributed organ and is the principle site for blood cells formation. In the normal adult, its daily production and export of blood cells amounts to about 2.5 billion red cells,2.5 billion platelets and 1.0 billion granulocytes per kilogram of body weight. [1]The broad spectrum of disorders affect the marrow primarily or secondarily with presentation of peripheral pancytopenia.Pancytopenia is defined as the presence of anaemia, leukocytopenia, and thrombocytopenia, when the haemoglobin is <13 gm/dl in males, 11gm/dl in females, WBC count <4000 cells/cu mm and platelet count < 1.5 lakhs/cu mm.

Anaemia leads to fatigue, dyspnoea and cardiac symptoms. Thrombocytopenia manifests as bruising, mucosal bleeding and neutropenia manifests as increased susceptibility to infections.

Varieties of hematopoietic and non-hematopoietic conditions manifest with features of pancytopenia. The different etiological causes contributing to pancytopenia can be classified as central type which include disorders in hematopoietic cell production, and peripheral type which includes disorders of increased destruction and bone marrow replacement or infiltration by malignant cells.Pancytopenia is a haematological disorder, where the etiological cause is varied by several factors like geographical region, age, gender, and genetic distribution. The underlying cause of pancytopenia is therefore best studied by bone marrow aspirate and biopsy as a diagnostic tool.

In India, the causes of pancytopenia are not well delineated. The present study has been undertaken to evaluate the various causes of pancytopenia and correlate the peripheral blood smear findings with the bone marrow aspirate morphology.

MATERIALS AND METHODS:

The present study is a retrospective and prospective study done in the department of Pathology, for a period of two years. All the relevant history, clinical details, radiological details and biochemical parameters were considered. Patients between age group of 5-65 years who are showing parameters as Hb less than 10 gm/dl, WBC count less than 4000 cells /cu mm, Platelet count < 1.5 lakhs/cu mm were included and patients of age group <5 years and >65 years were excluded in our study.Investigations like haemoglobin estimation, RBC count, WBC count, platelet count, reticulocyte count and haematocrit were carried out. Parameters like red cell indices were considered along with bleeding and clotting time tests were done when required, followed by peripheral smear study and bone marrow aspiration study. Three ml of anticoagulated blood was collected

by venepuncture in all cases for complete blood count investigation.Blood counts were again cross-checked with peripheral smear manually in all cases of pancytopenia. Peripheral smears were prepared, the films were air dried and stained with Leishman's stain. Smears were examined under microscope for following features-

RBC morphology- to type morphological anaemia, immature RBC's, any inclusions if any.

WBC morphology-for differential count, morphology of each cell, immature cells if any.

Platelet count-its morphology and for any hemoparasites.

Based on these basic haematological investigations in suspected cases, clinical details like age, sex and symptoms like bone pain, fever, night sweats, malaise, weight loss and pruritis were taken. A thorough physical examination was done to see for the presence of pallor, lymphadenopathy, sternal tenderness, gum hypertrophy, evidence of hepatomegaly, splenomegaly, hypersplenism and any malignant neoplasm presentation if any. Further bone marrow aspiration was carried out in all these cases. Bone marrow aspiration smears stained with Leishman's stain were examined thoroughly for cellularity, M:E ratio, erythropoiesis, myelopoiesis, megakaryopoiesis, plasma cells, lymphocytes, mast cells, abnormal cells, extraneous deposits and hemoparasites if any.

Considering all the clinical details, haematological parameters and peripheral blood and bone marrow aspiration smears, the cases were studied accordingly as per age and sex distribution to evaluate the cause for pancytopenia.Bone marrow aspiration was performed in all the patients using Salah bone marrow needle after obtaining written consent for the procedure either from the patient or the guardian. The aspiration site was done at the posterior iliac crest or sternum.

RESULTS:

One hundred and Fifty patients with a haematological diagnosis of pancytopenia were studied during retrospective and prospective study. The following data was recorded and analyzed.The sex distribution of pancytopenia showed a male preponderance-Table 1 The male to female ratio was 1.8:1. Most of the patients were in the group of 16-25 years (32.7%) and least occurrence was seen in the age group of 46-55 years (7.3%)-Table 2

The commonest symptom was generalized weakness (86%). The other main symptoms were fever (59.3%), dyspnoea (44.7%), and bleeding (2.7%). Pallor being the commonest finding in 83.3% cases. Varying degrees of hepatomegaly (24%) and splenomegaly (18%) were also noted.9.3% of patients had lymphadenopathy. Pancytopenia is a haematological condition with clinical manifestations as anaemia, infections and bleeding tendency. Underlying it are many causes which are diagnosed by means of bone marrow aspiration and biopsy.

Sl No	SEX	NO OF CASES (%)	PERCENTAGE (%)
1	MALE	96	64
2	FEMALE	54	36
	TOTAL	150	100

Table 1: 1: Incidence of Pancytopenia among both Sexes

In the present study, megaloblastic anaemia was studied to be the commonest cause of pancytopeniaTable 3

In megaloblastic anaemia, peripheral smear may show pancytopenia. Moderate degree of anisopoikilocytosis, macro ovalocytes usually are the main features seen in peripheral smears. Mean corpuscular volume (MCV) is >100 fl. Polychromatophilic cells are reduced. Reticulocyte count may be less than 1%. The leucocyte count is reduced due to reduction of both neutrophils and lymphocytes. Hyper segmented neutrophils are usually seen. A minimum of five to six lobed neutrophils are considered significant. Thrombocytes are reduced in number. Both macrocytosis and hyper segmented neutrophils strongly suggest towards megaloblastic haematopoiesis.

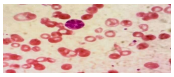

Figure 1: Peripheral smear showing macro ovalocytes and hyper segmented neutrophils(Leishman -100x)

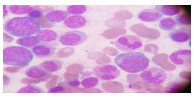

Figure 2: Bone marrow aspiration shows hypercellular smears with predominance of megaloblastic changes with giant metamyelocytes.(Leishman -100x)

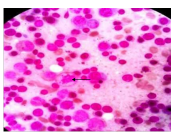

Figure 3: Mixed deficiency anaemia- BMA showing Megaloblastic and Micro normoblastic reaction with mitotic figure(arrow), (Leishman'sstain-100x)

DISCUSSION

The present study was conducted to analyze the various causes of pancytopenia, its age distribution with their clinical manifestations. The statistical data obtained were compared to the previous studies published in the literature. In

Age (in years)	Sex				Total	%
	Male	%	Female	%		
5 to 15	15	15.6	13	24.1	28	18.7
16 to 25	32	33.3	17	31.5	49	32.7
26 to 35	19	19.8	10	18.5	29	19.3
36 to 45	13	13.5	4	7.4	17	11.3
46 to 55	6	6.3	5	9.3	11	7.3
56 to 65	11	11.5	5	9.3	16	10.7
Total	96	100.0	54	100.0	150	100.0

Table 2: Age and Sex wise distribution of incidence of Pancytopenia

Causes	Gayatri and Rao, et al. [2],	Rangaswamy N, et al. [3]	Sunkesula SB, et al. [4]	Present study
MA	77(74%)	33(33%)	70(58.3%)	96(64%)
NA (Mixed deficiency)	-	16(16%)	-	30(20%)
AA	19(19%)	14(14%)	22(18.3%)	11(7.3%)
Leukemia	4(3.8%)	5(5%)	11(0.2%)	9(6%)
MDS	-	2(2%)	4(3.3%)	2(1.3%)
MM	1(1%)	1(1%)	-	2(1.3%)

Table 3: Various causes of Pancytopenia compared to other studies

present study,16-25 years age group are most commonly affected group. Age distributions were comparable with Khunger JM, et al. [5]Gayatri and Rao, et al. [2]Nigam RK, et al. [6],Sunkesula SB, et al. [4]studies of pancytopenia. In all studies, males are affected more than females. Present study also shows male preponderance with male to female ratio-1.8:1.Sex distribution was comparable with Desalphine M, et al [7] (1.8:1) and Rangaswamy M, et al. [3](1.63:1) showing male preponderance.Common age group affected was 10-30 years in the studies done by Khodke K, et al. [8], Khunger JM, et al. [5] Niazi, et al. [9], Rangaswamy M, et al. [3] comparable to present study where 16-25 years age group was most affected. In the present study, most common clinical manifestation was generalized weakness (86%) followed by fever (59.3%) comparable with Gayatri and Rao, et al. [2]Sunkesula SB, et al. [4]Other clinical manifestations included dyspnoea (44.7%) and bleeding disorders (2.7%).The most common physical examination finding was pallor (83.3%) followed by hepatomegaly (24%) and splenomegaly (18%) comparable to Gayatri and Rao, et al. [2]Rangaswamy M, et al. [3], Nigam RK, et al. [6]

The variations in the frequency of various etiological factors causing pancytopenia has been attributed to difference in methodology, stringency of diagnostic criteria, geographic area, period of observation, genetic differences and any exposure to myelotoxic agents, etc. In the present study, Megaloblastic anaemia (MA) (64%) was the commonest cause of pancytopenia, followed by Nutritional (mixed deficiency) anaemia (20%), Aplastic anaemia (7.33%), leukaemia (6%),MDS(1.33%) and Multiple myeloma (1.33%) comparable with Gayatri and Rao et al. [2], Sunkesula SB, et al. [4]second most common cause of pancytopenia in our study was Nutritional anaemia (mixed deficiency) which was in sharp contrast with the studies done by other authors.

Pancytopenia is an important clinic haematological entity encountered in our clinical practice. The possible underlying aetiologies range from transient viral marrow suppression to life threatening malignant neoplasm. The etiological diagnosis is essential for the clinical management and prognosis of the patient. Evaluation of peripheral blood films reveals the most probable cause of anaemia, presence of immature myeloid cells may suggest marrow infiltration of hematologic disorder. Bone marrow examination -both aspiration and biopsy are important diagnostic tools in haematology to evaluate various causes of pancytopenia.

Bone marrow examination is accurate, reproducible, rapidly available information at an economical cost and with minimal discomfort to the patient. Bone marrow aspiration is sufficient in making diagnosis of megaloblastic anaemia, mixed nutritional anaemia, and initial diagnosis of leukaemia.

Megaloblastic anaemia was observed to be the commonest cause of pancytopenia in the present study, reflecting the higher prevalence of nutritional anaemia in Indian patients.

CONCLUSION:

A compilation of all physical findings, primary haematological investigations and bone marrow aspiration was done in diagnosed cases of pancytopenia. Megaloblastic anaemia (64%) was the most the commonscause of Pancytopenia followed by nutritional anaemia (mixed deficiency) (20%), Aplastic anaemia (7.33%), leukaemia (6%),MDS(1.33%) and Multiple myeloma (1.33%).Pancytopenia is a common haematological problem encountered in day-to-day practice commonly presenting as generalized weakness, fever, and bleeding manifestations.

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