

# ETIOLOGICAL CONTINUUM OF PANCYTOPENIA IN NORTH WEST REGION OF PAKISTAN

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## ABSTRACT

**Objectives:** To find out the frequencies of different diseases causing pancytopenia based on bone marrow aspirate and biopsy.

**Material and Methods:** Total of 126 cases were studied by examining their medical records, basic hematological investigations like Complete Blood Count (CBC), reticulocyte count, peripheral smears, bone marrow aspirates and biopsy findings. Patients were included irrespective of age groups and gender while patients on cytotoxic drugs or radiotherapy were excluded.

**Results:** Among the 126 cases studied, age of the patients ranged from six months to 90 years with male to female ratio of 2.7:1. The maximum number 88 (70%) cases occurred below the age of 40 years, with majority of cases occurring in 2nd and 3rd decades. The most common presenting symptoms were pallor in 32 cases (25.4%) and fever in 20 cases (16%) followed by bleeding manifestations. Non-malignant etiology was seen in 85 (67.5%) patients and malignant causes were seen in 41 (32.5%) cases. Hypoplastic bone marrow was the most common cause seen in 33 (23.9%) patients, followed by megaloblastic anemia in 26 (20.63%) patients and acute leukemia in 20 (15.87%) of cases. Mean hemoglobin was  $6.86 \pm 1.98$ . Mean Total leucocyte count was  $2.30 \pm 0.948$ , whereas the mean platelet count was  $39.40 \pm 31.37$ .

**Conclusion:** The present study concludes hypoplastic bone marrow as the commonest cause of pancytopenia followed by megaloblastic anemia.

**Key Words:** Pancytopenia, Hypoplastic bone marrow, Myelodysplastic syndromes, Hemophagocytic syndromes.

## INTRODUCTION

Pancytopenia is a very common condition frequently encountered by hematologists in practice.<sup>1</sup> Frequency of pancytopenia in clinical settings is approximately 1%.<sup>2</sup> There is less than normal levels of all three elements of blood leading to concurrent presence of anemia, leucopenia and thrombocytopenia. Pancytopenia is not a disease itself but a serious hematological problem as the patients become prone to manifestations of anemia, recurrent infections and bleeding tendencies.<sup>3,4</sup>

Presenting symptoms of Pancytopenia are often attributable to anemia or thrombocytopenia. Leucopenia

is usually an uncommon initial presentation.<sup>5</sup> Wide variety of hematopoietic and non hematopoietic diseases manifest with symptoms of pancytopenia.<sup>6</sup> Among them bone marrow failure syndromes and malignancies are important causes but certain non-malignant conditions such as infection and nutritional anemia are equally important as well.<sup>7</sup> The severity and the underlying pathology of pancytopenia is important for the management and prognosis of the patients.<sup>8</sup>

Bone marrow examination is required for evaluation of Pancytopenia. Complete assessment of marrow architecture and the pattern of distribution of any abnormal infiltrate can be performed through it.<sup>6</sup> Although bone marrow examination often reveals an underlying condition causing pancytopenia, but it may not be always conclusive. Therefore workup of pancytopenia should also include a detailed clinical, drug, and environmental exposure history.<sup>9</sup>

The incidence of disorders causing pancytopenia vary in different populations depending on the

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differences in age patterns, nutritional status, climate and the prevalence of infections.<sup>4</sup> Various other factors like geographical distribution and genetic disturbances may also have some influence.<sup>1</sup> This study has been therefore undertaken to evaluate the various pattern of presentation clinical feature and causes of pancytopenia in north western region of Pakistan. This data might prove helpful in planning the diagnostic and therapeutic approach in local patients with pancytopenia.

## MATERIAL AND METHODS

This retrospective study was carried out by looking through the records of Rehman Medical Institute and Combined Military Hospital, Peshawar from January 2012 to December 2013. These tertiary care hospital exclusively provide medical services to the population of Khyber Pakhtunkhwa (KPK) Province.

All the patients who were referred to the laboratory of the hospitals for routine complete blood count (CBC) and peripheral smear (PS) examination, from the outpatient and the inpatient departments were screened for pancytopenia and a total number of 126 cases were selected, based on the following criterias: hemoglobin, <10 g/dL; total leukocyte count (TLC), <4,000 / L; platelet count, <100,000/L. Patients were included irrespective of age groups and gender in this study. Patients on cytotoxic drugs, chemotherapy or radiotherapy were excluded.

A detailed history and physical examination was also taken from records of each patient. Basic hematological investigations like CBC, reticulocyte count, and Peripheral Smear examination findings were obtained. Blood counts in RMI were performed by Cell Dyn Ruby whereas in CMH they were performed by semi automated electronic cell counter (Sysmex KX – 21). Peripheral smears were examined using Leishman stain. Bone marrow aspiration and trephine biopsy findings of the patients were also noted wherever it was indicated. All the data was analyzed on SPSS 22 on the basis of etiology, clinical and hematological findings and expressed as frequency and percentages.

## RESULTS

A total of 126 patients with pancytopenia were included in study. They consisted of 92 males (73.02%) and 34 females (26.98%) with a male-to-female ratio of 2.7:1. The ages of patients varies from six months to 90 years. Table 1 display the Stratification of various age groups with gender distribution of each group at

the time of presentation. The maximum number i.e., 88 (70%) cases occurred below the age of 40 years, with majority of cases occurring in 2nd and 3rd decades.

The most common presenting symptoms were pallor in 32 cases (25.4%) and fever in 20 cases (16%). Next most common complaint was bleeding from different sites (purpuric spots on the body, epistaxis,

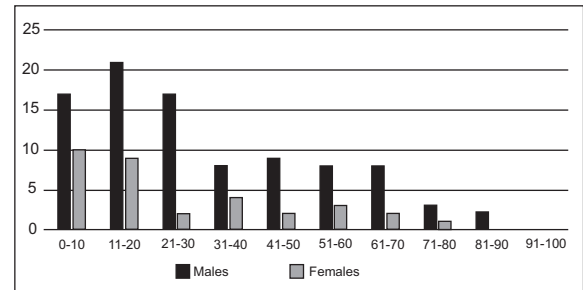


Figure 1: Age and sex distribution of cases studied at the time of their presentation Age in years on x-axis and number of patients of y axis

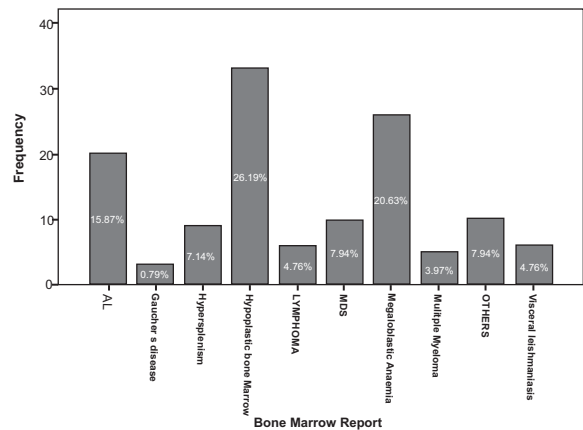


Figure 2: Percentage of etiological causes of pancytopenia

Table 1: Common presenting clinical features of pancytopenia (n=126)

Clinical Features	Number of patients & Percentage
Pallor only	32(25.4%)
Fever only	20(16%)
Bleeding only	19(15.1%)
Bleeding, fever	15(12%)
Pallor, fever	14(11.1%)
Generalized body pain/ weakness	12(9.5%)
Bleeding, pallor	7(5.6%)
Hepat/splenomegaly	7(5.6%)
Total	126(100%)

**Table 2: Frequency of pancytopenia among both genders according to causative disease**

Gender	No. of patients	Common causes of pancytopenia					
		Hypoplastic marrow	Megaloblastic anemia	Visceral lieshmaniasis	Hypersplenism	Malignant causes	Others
Male	92	22(24%)	21 (22%)	6 (7%)	9 (10%)	26 (28%)	8 (9%)
Female	34	11(32%)	5 (15%)	0	0	15(44%)	3 (8%)

**Table 3: Frequency of different etiologies of pancytopenia according to age groups**

Age in years	Hypoplastic marrow	Megaloblastic anemia	Visceral Lishmaniasis	Hyper-splenism	Malignant causes	Others*	Total
0-10	10 (37.0%)	3 (11.1%)	4(14.8%)	2(7.4%)	7(25.9%)	1(3.7%)	27
11-20	12(40%)	4(13.3%)	0	3(10%)	10(33.3%)	1(3.3%)	30
21-30	4(21.0%)	6 (31.5%)	1(5.2%)	0	4 (21.0%)	4(21.0%)	19
31-40	2(16.6%)	5(41.6%)	0	1(8.3%)	3(25%)	1(8.3%)	12
41-50	1(9.0%)	2(18.1%)	1(9.0%)	2(18.1%)	4(36.3%)	1(1.0%)	11
51-60	2(18.1%)	2(18.1%)	0	0	5(45.4%)	2(18.1%)	11
61-70	1(10.0%)	2(20.0%)	0	0	6(60.0%)	1(10.0%)	10
71-80	0	1 (25.0%)	0	1 (25.0%)	2 (50.0%)	0	4
81-90	1 (50.0%)	1 (50.0%)	0	0	0	0	2

**Table 4: Mean and Standard deviation of Hemoglobin, Total leucocyte count and platelets of both genders**

	Mean ± SD	Range
Hemoglobin level	6.86±1.98g/dL	2.5-9.9g/dL
Total leucocyte count	2.30±0.948	0.44-3.93
Platelet count	39.4±31.7	1.0-99.0

haemetemesis, malena, petechial hemorrhages). Combinations of different symptoms were also reported. (Table 2). Figure 2 represent the etiological basis of pancytopenia seen in 126 patients. Non-malignant etiology was seen in 85 (67.5%) patients. Among them hypoplastic bone marrow was the most common cause seen in 33 (23.9%) patients, followed by megaloblastic anemia in 26 (20.63%) patients. Other common non-malignant causes were hypersplenism and visceral lieshmaniasis. (Figure 2)

Malignant causes acute leukemia, lymphoma, MDS and multiple myeloma) were seen in 41(32.5%) patients. Among the malignant hematological disorders, acute leukemia was the most common seen in 20 (15.87%) cases. Table 4 displays the distribution of the etiological causes for pancytopenia with stratification of age groups. Table 4, however presents the distribution of diseases causing pancytopenia among both genders.

## DISCUSSION

Pancytopenia has multiple causes and evaluation of underlying pathology requires detailed history, physical examination and various laboratory tests including hematological, biochemical and histopathological investigations.<sup>10</sup> Differences in the frequencies of various diagnostic entities causing pancytopenia in different population groups has been reported. This could be due to disparity of geographic area, age pattern, nutritional status, prevalence of infective disorders, genetic differences, and varying exposure to agents causing pancytopenia.<sup>3</sup>

Outstanding male predominance (male to female ratio 2.7:1) was observed in our study (Figure 1). Higher incidence of pancytopenia in males has been reported by many other studies carried out in Pakistan and India previously.<sup>1,3,11</sup> This could be due to gender discrimination in developing countries like ours, where men have increased access to hospitals as compared to women especially in rural areas. We have also observed in our study that majority n = 88 (70%) cases presented below 40 years of age (Table 1). In our study 24.8% presented in 2nd and 3rd decade (Table 1) which is in accordance with previous studies<sup>8,12</sup> however a study conducted earlier in India showed highest number of patients in 3rd and 4th decade.<sup>2</sup>

In the present study, amongst 126 cases, 26.19% were diagnosed as hypoplastic bone marrow making it the most common cause of pancytopenia. Megaloblastic anaemia (21%) was second most evident etiology followed by acute leukemia (16%). Almost similar results have been reported in study done previously in different provinces of Pakistan<sup>13-19</sup> and in Nepal.<sup>19</sup> However studies showing contradicting results were conducted in Karachi and India previously indicating Megaloblastic anaemia to be a most common etiology of pancytopenia.<sup>6,11,15,20-23</sup> Jain and Naniwadekar in their study in India and Hamid et al in their study in Yemen found hypersplenism as a most common cause of pancytopenia.<sup>3,19</sup> Whereas study carried out to determine the frequent causes in different ethnic groups (Pakistani and Afghan) living in Baluchistan Province reports malaria to be the most common cause.<sup>7</sup>

The most common clinical presentation in our study was found out to be progressive pallor (25%), followed by fever in (16%) and bleeding (15%). Combination of these feature and other non-specific features like generalized body aches were also observed. These results are in accordance with other studies carried out previously which report pallor as a universal feature in all the cases.<sup>14,19,23</sup>

Hypoplastic bone marrow was found to be the most common cause of pancytopenia in younger patients (below 40 years) in our study. However we found no significant variation in different age groups of megaloblastic anemia and other diseases as the most important cause of pancytopenia. Similar finding of hypoplastic marrow as the most common cause of pancytopenia in younger age groups is comparable with other studies also.<sup>13,15</sup> However few studies report no significant variation in the age groups of various diseases contributing to pancytopenia.<sup>11,19</sup> We studied the frequency of pancytopenia among both genders according to causative disease but found no significant differences between male and females. Previous study also support this finding.<sup>20</sup>

## CONCLUSION

Hypoplastic bone marrow is the most common cause of pancytopenia followed by megaloblastic anemia, acute leukemia and hypersplenism in our study participants. Higher frequency of pancytopenia was observed in younger patients. No significant difference was observed in frequency of different diseases leading to pancytopenia among both genders.

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### **AUTHOR'S CONTRIBUTION**

Following authors have made substantial contributions to the manuscript as under:

**Batool Z:** Concept and idea.

**Amin H:** Manuscript writing.

**Durrani SH:** Statistics and followup.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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