

# RESULTS OF BONE MARROW EXAMINATION IN PATIENTS PRESENTING WITH PANCYTOPENIA AND HIGH MEAN CORPUSCULAR VOLUME

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## ABSTRACT

**Background:** Most of the causes of pancytopenia are associated with normocytic normochromic red cell indices but certain causes are associated with high mean corpuscular volume. This study aimed to determine the frequency of causes of pancytopenia with high mean corpuscular volume. **Methods:** This cross-sectional study was conducted at Pathology Department, King Edward Medical University Lahore and included all the cases from affiliated hospitals from 30<sup>th</sup> January 2011 to 30<sup>th</sup> June 2011. The calculated sample size was 150 cases. Patients having pancytopenia and macrocytosis were included in the study. The data was analyzed on SPSS 13 to determine the frequencies and percentages. **Results:** Results of bone marrow biopsy showed aplastic anemia in (50.67%), megaloblastic anemia (36.6%), leukemia (7.3%) and myelodysplastic syndrome in (5.3%) of these patients. **Conclusion:** Aplastic and megaloblastic anemia are the commonest causes of pancytopenia with high mean corpuscular volume.

**KEY WORDS:** Pancytopenia, Mean corpuscular volume, Megaloblastic anemia, Aplastic anemia.

## INTRODUCTION

Pancytopenia is defined as a decrease in all the three cell lines of blood. It is not a disease entity but a triad of findings that may result from a number of disease processes, the important ones of which are myelodysplasia, leukemia, megaloblastic anemia, aplastic anemia, infiltration of bone marrow due to lymphoma and solid tumors.<sup>1</sup> Pancytopenia can present with moderate to severe symptoms like anemia manifested by pallor, fatigue and breathlessness on exertion, infections due to neutropenia e.g. sore throat or chest or soft tissue infections, or thrombocytopenia leading to petechial hemorrhages in skin and mucous membranes like epistaxis, hematuria, gastro-intestinal bleeding and menorrhagia.<sup>2</sup>

Red blood cell indices help us to classify anemias as microcytic, normocytic, and macrocytic depending on low, normal or high MCV.<sup>3</sup> Most of the causes of pancytopenia present with normal RBC indices,<sup>4</sup> but causes like megaloblastic anemia, aplastic anemia, myelodysplastic syndrome and paroxysmal nocturnal hemoglobinuria present with high MCV.<sup>5</sup>

Out of these causes megaloblastic anemia is one of the most common causes of pancytopenia which is easily preventable as well as treatable with timely treatment with Folic acid and Vitamin B12.<sup>6</sup> Other causes not only carry a grave prognosis but

also require aggressive treatment in terms of immunosuppressive drugs, and stem cell replacement therapy.<sup>7</sup> Workup for pancytopenia requires peripheral smear, reticulocyte count and bone marrow biopsy as a part of basic investigations.<sup>8</sup>

The present study aims at identifying the causes of pancytopenia associated with high MCV. This will help the clinicians in formulating a list of differential diagnosis when patients presenting with pancytopenia and the RBC indices showing a high MCV are encountered.

## MATERIAL AND METHODS

Pancytopenia was taken as blood count showing subnormal values; Hemoglobin (Hb) less than 13 in adult males and less than 11 in females, TLC less than  $4.0 \times 10^9$  x/L and platelet count less than  $150 \times 10^9$ /L. High MCV was taken as an MCV of more than 100 fl. Patients of both genders and all ages and those with evidence of pancytopenia and High MCV were included in the study. Exclusion criteria were patients being treated with iron, folic acid, vitamin B<sub>12</sub> or blood transfusions, presence of blast cells on peripheral smear, alcoholic patients, and those getting radiotherapy or chemotherapy.

## RESULTS

In this study 150 patients of pancytopenia and high mean corpuscular volume

were taken. The age range was from 1-70 years with mean age of 26.04 years. Out of these, 98 (65.33%) were males and 52 (34.67%) females. (Table 1)

**Table 1: Age distribution of patients with pancytopenia (n=150).**

Age (years)	Patients with pancytopenia Number (%)	Males Number (%)	Females Number (%)
1-10	6 (4)	3 (2)	3 (2)
11-20	37 (24.67)	26 (17.36)	11 (7.3)
21-30	58 (38.67)	39 (26)	19 (12.6)
31-40	25 (16.67)	12 (8)	10 (6.7)
41-50	13 (8.67)	7 (4.7)	6 (4)
51-60	8 (5.33)	9 (6)	2 (1.3)
61-70	3 (2)	2 (1.38)	1 (0.66)
Total	150 (100)	98 (65.44)	52 (34.56)

In cases of pancytopenia 149 (99.3%) patients presented with pallor, 86 (57.3%) with epistaxis, 94 (62.6%) with gum bleeding, 11 (17.3%) with mild jaundice, 78 (52%) with fever due to upper respiratory tract infections, and 7 (4.6%) with impaired

wound healing. Among 52 female patients 24 (46%) presented with menorrhagia. (Fig. 1)

All the patients were subjected to bone marrow biopsy. The results revealed four diseases; aplastic anemia, megaloblastic anemia, myelodysplastic syndrome and leukemia. Out of 150 patients, 76 (50.8%) were of aplastic anemia, 55 (36.6%) megaloblastic anemia, 8 (5.8%) myelodysplastic syndrome, and 11 (7.3%) leukemia. (Table-2)

**Table 2: Bone marrow biopsy results and gender distribution.**

Results of bone marrow biopsy	Total patients number (%)	Males number (%)	Females number (%)
Aplastic anemia	76 (50.67)	53 (54.08)	23 (44.23)
Megaloblastic anemia	55 (36.60)	32 (32.65)	23 (44.23)
Leukemia	11 (7.30)	7 (7.1)	4 (7.69)
Myelodysplastic syndrome	8 (5.30)	6 (6.12)	2 (3.84)
Total	150 (100)	98 (65.33)	52 (34.67)

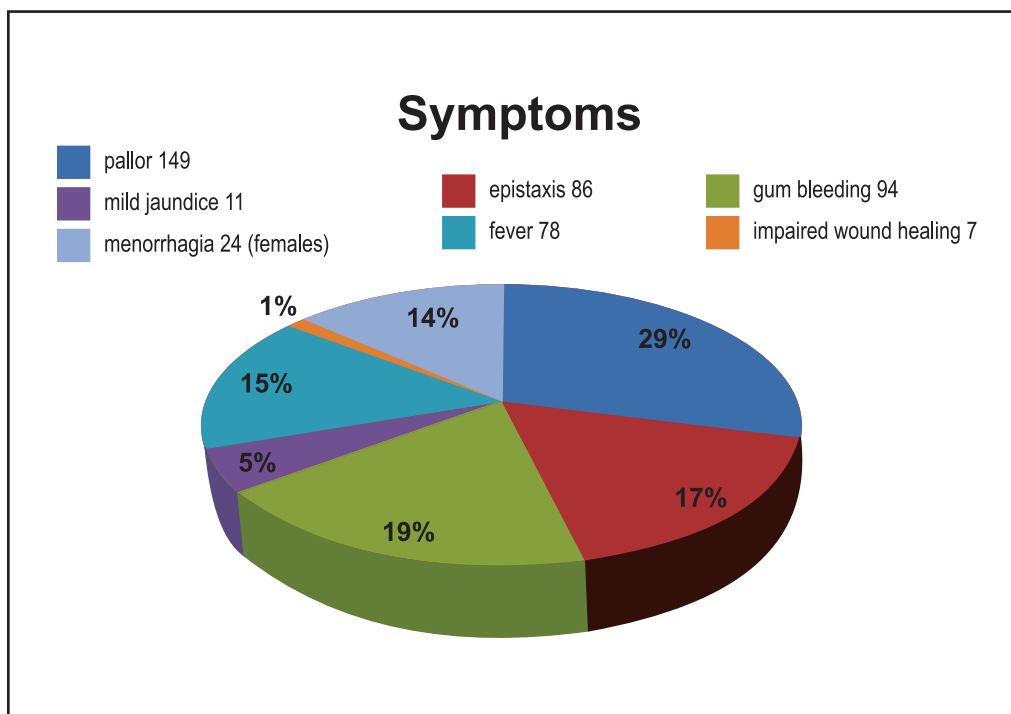


Fig 1: Symptoms of patients with pancytopenia.

## DISCUSSION

In our study 150 patients of pancytopenia were taken, out of these 65.3% were males and 34.67% females. So there was preponderance of male patients and male to female ratio was 1.9:1. Balgir<sup>9</sup> in his study concluded socioeconomic status as taboo to treatment of female child and more care for male child. This limited care for females was blamed because of male dominating society. This might be a cause of more males presenting to us with pancytopenia.

The age of patients ranged from 1-70 years with mean age of  $26.04 \pm 11.97$  years. The maximum number of patients presented in the age range of 21-30 years. Niazi & Raziq<sup>10</sup> in their study found the maximum presentation of pancytopenia as well as megaloblastic anemia in the same age group i.e. 21-30 years.

In our study 99.3% patients presented with pallor, 57.3% with epistaxis, 62.6% with gum bleeding, 17.3% with mild jaundice, 52% with fever due to upper respiratory tract infection. Impaired wound healing was observed in 4.6% patients. Out of 52; 24 females (46%) presented with menorrhagia. Whereas in a study by Raziq<sup>10</sup> the majority of the patients presented with bruising, gum bleeds, epistaxis and fever, malabsorption (diarrhea) was seen in 33.7% of patients. In the present study aplastic anemia was found to be the commonest cause of pancytopenia associated with High MCV but according to a study by Tahir & Khan.<sup>11</sup> Megaloblastic anemia is the commonest cause of pancytopenia. A study conducted by Aziz et al<sup>12</sup> also concluded that Megaloblastic anemia is still the commonest cause of pancytopenia despite the appropriate therapy and diagnostic facilities available.

In a study conducted by Ishtiaq et al<sup>13</sup> majority of the patients with pancytopenia presented with megaloblastic anemia. So our study was in contrast to all the above studies that tried to find out the commonest causes of pancytopenia. We took into account all the age groups, all the geographical areas of Pakistan and pancytopenia associated with High MCV only. Whereas the above studies were restricted to their respective local areas, and did not take into account high MCV as an inclusion criterion.

In our study, 44.2% females and 32.6% males with pancytopenia were found to have megaloblastic anemia. In our study the male to female ratio for pancytopenia was found to be 1.7:1. While the male to female ratio for megaloblastic anemia in our study was 1:1.4; while Niazi & Raziq<sup>10</sup> showed male to female ratio of 1.7:1 that differs from our study. The reason for this female prepon-

derance seems to be the physiological stresses associated with reproductive age group in females. Khan et al<sup>14</sup> in their study considered physiological stresses e.g. pregnancy, lactation as one of the causes of female preponderance in reproductive age group. Such a pattern is seen in other developing countries too suggesting significant role of geographical, socioeconomic, personal (nutritional status) and immunological factors. These factors lead to high incidence of megaloblastic anemia in ages less than 40 years and a female preponderance. According to Zengin et al<sup>15</sup> causes for female preponderance include exclusive breast feeding, lower maternal folic acid and vitamin B12 reserves, poor socioeconomic status in western countries.

Our study showed aplastic bone marrow to be the most frequent cause of pancytopenia, followed by megaloblastic bone marrow, leukemia and myelodysplastic syndrome. Similar results were shown in a study by Niazi & Raziq<sup>10</sup> where aplastic anemia was more common in paediatric age groups and male gender, megaloblastic anemia in 21-30 years age males, leukemia in paediatric age group while MDS in elderly.

The value of bone marrow biopsy is irreplaceable in diagnosing the cause of pancytopenia. a single bone marrow biopsy should be adequate in diagnosis in most instances. Khodke et al<sup>16</sup> did simultaneously bone marrow aspirate and trephine biopsies in 50 cases of pancytopenia. Megaloblastic anemia was seen in 44% of the cases. Most cases that yielded diluted bone marrow aspirate were leukemias and that showed dry tap were Aplastic anemias. Shimamura<sup>17</sup> showed the importance of bone marrow biopsy in megaloblastic anemia and this study showed bone marrow biopsy to be imperative in determining the cause of pancytopenia.

In our study of all the cases, 63 (42%) were diagnosed on bone marrow aspirate of which 55 were megaloblastic anemia 6 were leukemias and 2 were MDS. The remaining 87 (58%) were diagnosed on trephine biopsy of which 76 were aplastic anaemia.

## CONCLUSION

The current study shows that when pancytopenia is associated with a high MCV it has a number of reasons, the commonest being aplastic anemia followed by megaloblastic anemia, leukemia and myelodysplastic syndromes.

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