



## Clinicohematological Evaluation of Patients Presenting with pancytopenia in Kashmir Valley

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### Abstract

**Introduction:** Pancytopenia, simultaneous presence of anemia, leucopenia and thrombocytopenia, is a common manifestation of a wide variety of diseases arising from or involving the bone marrow. Evaluation of hematological parameters including peripheral blood film examination and bone marrow evaluation helps in identifying the cause in most of the cases.

**Materials and Methods:** A total of 143 patients presenting with pancytopenia between Jan 2018 to Dec 2018 to the department of pathology were included in the study. Relevant clinical history and physical examination were taken. A complete Hemogram, peripheral blood film examination and bone marrow evaluation was done and results were observed and analyzed.

**Results:** The most of the patients were in age group of adolescents and young adults. There was a slight predisposition for female sex. On bone marrow aspiration, megaloblastic anemia was found to be the commonest cause of pancytopenia followed by dual deficiency anemia. Hematological malignancies constituted a significant cause with acute myeloid leukemia as the most common one. Aplastic anemia was seen in 5 cases. Bone marrow biopsy aided in diagnosis in a plastic anemia while in others it was concordant with aspiration findings.

**Conclusion:** Bone marrow evaluation is an important diagnostic tool in the evaluation of pancytopenia. Bone marrow aspiration gives diagnosis in majority of the cases; however, bone marrow trephine biopsy is helpful in many cases especially in cases of dry tap. Megaloblastic anemia is the commonest cause and a treatable one.

**Keywords:** Pancytopenia, Megaloblastic anemia, Bone marrow aspiration, Bone marrow trephine biopsy.

### Introduction

Pancytopenia, a clinical trial of anemia, leucopenia and thrombocytopenia, is a common manifestation of a wide variety of diseases either arising primarily from or secondarily involving the bone marrow. Evaluation of hematological parameters including peripheral blood film

examination and bone marrow evaluation helps in identifying the cause in most of the cases. Pancytopenia is defined based on the criteria's laid by de Gruchy as follows:<sup>1</sup>

- 1) Hemoglobin level – below 13.5 g/L for males and below 11.5 g/L for females.

2) Total Leukocyte Count (TLC) - below  $4 \times 10^9/L$ .

3) Platelet count – below  $150 \times 10^9/L$ .<sup>1</sup>

The cause of pancytopenia varies from hematopoietic to non-hematopoietic as well as from non-neoplastic to neoplastic conditions. There are a variety of underlying mechanisms involved like decreased hematopoietic cell production, increased destruction of marrow cells, replacement of marrow cells by abnormal cells, suppression of bone marrow growth and differentiation and ineffective hematopoiesis.<sup>2</sup>

Proper diagnostic evaluation requires detailed clinical history, physical examination and hematological assessment including careful peripheral blood smear examination and bone marrow evaluation. This study is aimed at evaluation of patients presenting with pancytopenia through various hematological parameters, peripheral blood film and bone marrow examinations.

### Materials and Methods

The present study was conducted in the hematology section of department of Pathology Government Medical College Srinagar. Study Participants were selected from among the patients referred to department of pathology for CBC. All the patients having pancytopenia on CBC were included in the study the over a period of 1 year from 1 Jan 2018 to 31 Dec were included. Case selection was based on clinical features and supported by laboratory evidence, which included peripheral blood counts for hemoglobin, leukocytes and platelets. Inclusion criteria were presence of all 3 of the following: hemoglobin,  $<10 \text{ g/dL}$ ; total leukocyte count (TLC),  $<4,000 / \mu\text{L}$ ; platelet count,  $<100,000/ \mu\text{L}$ . Patients on chemotherapy, those who didn't give consent and in whom bone marrow procedure was contraindicated were excluded from the study. Two milliliters of EDTA (ethylene diamine tetra-acetic acid) anti-coagulated blood was collected and processed through a hematology analyzer. The various hematological parameters

i.e.hemoglobin, total leukocyte count, differential leukocyte count, platelet count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) were noted down. Peripheral blood film was made and stained by Leishman's stain for all the cases and examined in detail.

Bone marrow procedure was carried out under aseptic conditions after obtaining written consent from the patient or guardian. This include bone marrow aspirate in all the cases and bone marrow trephine biopsy wherever required. Relevant clinical history and physical examination were noted down. The standard technique for bone marrow aspiration and trephine biopsy was followed. The site of procedure was posterior iliac crest. Bone marrow aspirate smears were prepared directly on the slides at the time of procedure, air dried and stained with MGG. Touch imprints of trephine biopsy were made as an adjunct to biopsy. The biopsy was preserved in 10% buffered neutral formalin and sent for processing. Thin sections were cut and stained with Hematoxylin & Eosin. Special stains like pearls and reticulin were done wherever required.

### Results

A total of 143 patients presenting with pancytopenia were included in this study. 80 (55.94%) were males and 63 (44.06%) females with a male: female ratio of 1.27:1 depicting male preponderance. The age of presentation varied considerably. The youngest patient was 18 months old and the oldest one was 94 years of age. The most common age group involved was 16-30 years of age. Another peak was observed at 45-60 years of age. (Table 1)

The most common presenting feature was easy fatigability followed by fever. Bleeding manifestation was the presenting feature in some of the cases. The most common physical sign observed was pallor followed by splenomegaly. Lymphadenopathy was a less common feature of pancytopenia, however, a significant one. The

hemoglobin varied from 2.1 gm% to 9.8 gm%. Most of the patients presented with hemoglobin ranging from 4-7 gm%. A significant number of cases presented with Hemoglobin < 4gm%. The total leukocyte count of cases ranged from 500u/dl to 4000 u/dl with most of the cases presenting with 1000 u/dl to 2500 u/dl. A few cases presented with a very low total leukocyte count < 1000. The platelet count varied from 10,000 u/dl to 1, 50,000 u/dl. Most of the cases presented with platelet count <50,000 u/dl. Macrocytosis was seen in majority of the cases followed by normocytosis. Microcytosis was the least common finding. The most common finding on peripheral blood film was anisocytosis followed by macrocytosis. Hyper segmented neutrophils were observed in many cases mostly categorized as megaloblastic anemia on bone marrow evaluation. Circulating blasts were seen in acute leukemias both myeloid and lymphoid. Immature cells were seen in a few cases of megaloblastic anemia.

On bone marrow evaluation the distribution of cases on the etiology underlying the pancytopenia is shown table 2. Megaloblastic anemia was found to be the most common cause followed by dual deficiency anemia. Thus nutritional cause was the most significant one. Almost all age groups were involved by megaloblastic anemia; however the most common age group involved was 45-60 years of age. Acute myeloid leukemia was found to be the most common hematological malignancy associated with pancytopenia. Overall it was the third most common cause. The other hematological malignancies seen were acute lymphoblastic leukemia and multiple myeloma. Aplastic anemia was the other significant cause comprising the fourth most common cause. Most cases of aplastic anemia presenting in the age group of adolescents and young adults. There were 4 cases of myelodysplastic syndrome and all of them presented after 45 years of age. The other causes seen in lesser frequency were anemia of chronic disease, Non-hodgkin lymphoma. One case each of malaria and drug induced presented

with pancytopenia. Two cases depicted normocellular marrow.

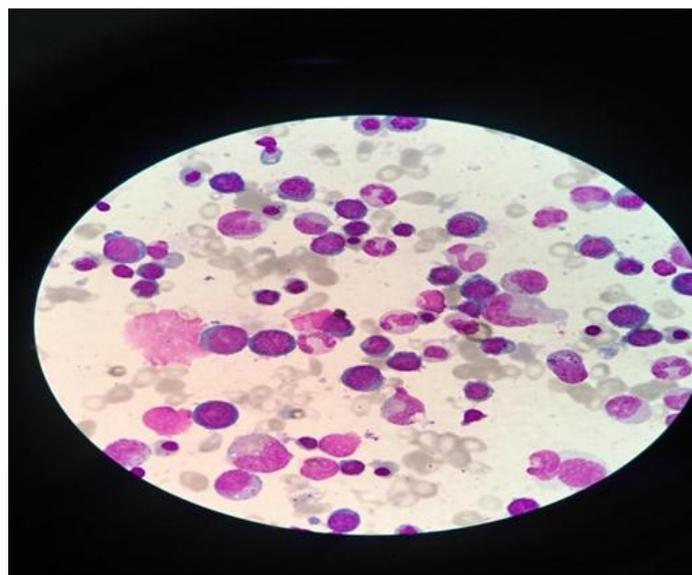
**Table 1:** Age distribution of study participants

Age group	Number (%)
≤15 years	4(2.79)
16-30 years	45(31.4)
31-45 years	32(22.3)
45-60 years	36(25.1)
>60	26(18.18)
<b>Total</b>	<b>143(100)</b>

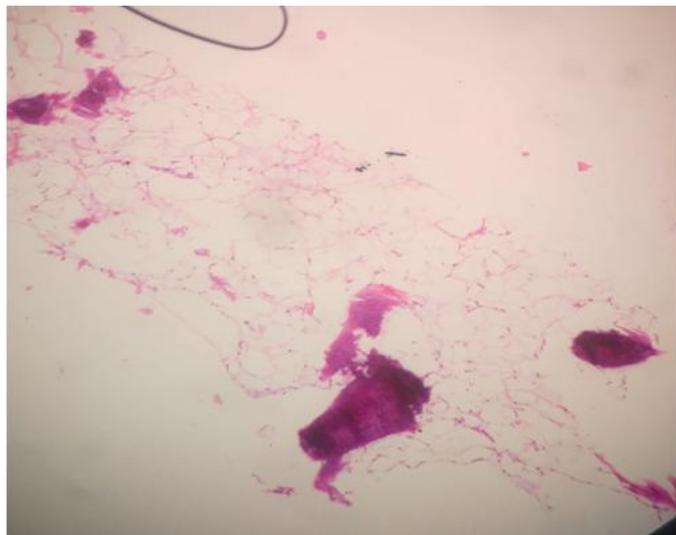
**Table 2:** Causes of pancytopenia found on bone marrow examination of the patients

Bone marrow finding	Number (%)
Megaloblastic anemia	63(44.05)
Dual deficiency anemia	36(25.1)
Aplastic anemia	9(6.2)
MDS	3(2.09)
Chronic Myeloid Leukemia	3(2.09)
Acute Myeloid leukemia	10(6.99)
Acute Lymphocytic Leukemia	3(2.09)
Anemia of chronic diseases	6(4.1)
Others *	10(6.99)
<b>Total</b>	<b>143(100)</b>

\*others include 3 normal, 3erythroid hyperplasia, 1 case of NHL and 3 cases of drug induced pancytopenia on bone marrow examination



**Fig 1:** Bone marrow biopsy of patient with pancytopenia showing megaloblastic anemia



**Fig 2:** Aplastic anemia seen in bone marrow biopsy of pancytopenia patient

### Discussion

In our study among the total of 143 patients with pancytopenia more than half were males and almost same finding was also seen in other similar studies.<sup>3</sup> Most common age group of presentation was the young adult age group, this finding is consistent with many other studies done on pancytopenia.<sup>3,4,5</sup> The commonest presentation of the patients was easy fatigability followed by fever and pallor was the clinical sign present in majority of the participants. Other studies also have found these symptoms and signs as the most common presentations in the patients with pancytopenia.<sup>3,5</sup> On CBC macrocytosis was seen in majority of cases and these results were consistent with other studies.<sup>4,5</sup> Megaloblastic anemia, dual deficiency anemia were the most common causes found on bone marrow examination. Acute myeloid leukemia was the third common diagnosis found on Bone marrow examination. Globally studies have found aplastic anemia to be the most common cause for pancytopenia but difference in the results could be because of the differences in geography, nutritional status of community and its genetic pool. However studies done on this topic in India have found similar results as our study regarding the findings on bone marrow examination for pancytopenia.<sup>3,4,6,7,8</sup> The major causes of pancytopenia in our study shows the probable

severe deficiency of micronutrients among the participants leading to this level of decrease in all the hematological cells.

### Conclusion

In our study majority of the participants had nutritional deficiency leading to pancytopenia which points towards the need for proper nutritional education to the people at community level to improve their nutritional status. Studies about the nutritional assessment at the community level can help to gain more insight for the reasons and ways to improve this nutritional deficiency. Further patients with symptoms which can point towards hematological involvement need to be referred at the earliest for proper and complete investigation and further management.

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