

## Original Research Article

# Clinical profile of patients with pancytopenia in a tertiary care centre

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**Received:** 08 March 2018

**Accepted:** 12 March 2018

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### ABSTRACT

**Background:** Pancytopenia is a condition in which all three cell lines i.e. erythroid, myeloid and megakaryocytic are affected resulting in anaemia, leukopenia and thrombocytopenia. It can be a manifestation of a wide variety of disorders which primarily or secondarily affect the bone marrow. Early diagnosis of these conditions will help in implementing the appropriate treatment. The objective of the study was to know the clinical presentation and etiology of patients presenting with pancytopenia.

**Methods:** A one year study from April 2016 to March 2017 was conducted in the department of medicine at a tertiary care centre. Total 32 patients with pancytopenia were studied to determine their clinical features and etiology through relevant investigations.

**Results:** Our study revealed megaloblastic anaemia (46.87%) as the most common cause of pancytopenia, followed by malaria (12.5%). Other causes included hypothyroidism (6.2%), hypersplenism (6.2%), drugs (12.5%) and miscellaneous (9.43%).

**Conclusions:** Megaloblastic anaemia was found to be the major cause of pancytopenia in patients. Other causes of pancytopenia were malaria, drugs, hypersplenism and hypothyroidism. These should be kept in mind while evaluating patients with pancytopenia.

**Keywords:** Anaemia, Malaria, Megaloblastic anaemia, Pancytopenia

### INTRODUCTION

Although pancytopenia is a relatively common hematological entity and a serious clinical problem with exhaustive differential diagnoses, there is relatively little discussion on this abnormality in major textbooks of hematology and internal medicine.<sup>1</sup> It is a disorder in which all three major formed elements of blood (red blood cells, white blood cells and platelets) are decreased in number. It is not a disease entity by itself, but rather a triad of findings.<sup>2</sup> Anaemia can present with fatigue, breathlessness and cardiac symptoms. Thrombocytopenia leads to bruising and mucosal bleeding and neutropenia increases susceptibility to infection. Pancytopenia is a

striking feature of many serious and life-threatening illnesses, ranging from simple drug-induced bone marrow hypoplasia, megaloblastic anemia to fatal bone marrow aplasias and leukemias. The incidence of megaloblastic anaemia varies from 0.8% to 32.26% of all pancytopenia patients.<sup>3,4</sup>

The severity of pancytopenia and the underlying pathology determine the management and prognosis. Thus, identification of the correct cause will help in implementing appropriate therapy. The present study was conducted to ascertain the causes of pancytopenia, based on clinical and haematological parameters including bone marrow examination.

**METHODS**

The present study was conducted in the department of medicine at a tertiary care hospital in South Delhi over a period of one year from April 2016 to March 2017. A total of 32 patients were selected based on the criteria defined by de Gruchy, i.e. hemoglobin (Hb.) level - below 13.5g/L for males and below 11.5g/L for females, total leucocyte count (TLC) - below  $4 \times 10^9/L$  and platelet count - below  $150 \times 10^9/L$ .<sup>5</sup>

A detailed history and relevant clinical examination, various hematologic parameters including iron studies, serum vitamin B12 levels, serum thyroid stimulating hormone (TSH), antinuclear antibody (ANA), viral markers (HBsAg, HIV, Anti HCV), liver function test (LFT), kidney function test (KFT) along with electrocardiogram (ECG), chest X-ray (CXR) and ultrasound (USG) abdomen were done in all cases. Peripheral smear examination was also performed in all cases. Bone marrow aspiration was done in 9 out of 32 cases. The data was compiled and analysed for various parameters like presenting symptoms, clinical features, peripheral blood smear, and bone marrow morphology. Ethics committee clearance for this study was obtained.

**RESULTS**

A total of 32 patients were studied with 15 males and 17 females. The male to female ratio was 0.88. The age range was between 16 to 66 years. Maximum patients were in the 2<sup>nd</sup> (34.3%) or 3<sup>rd</sup> decade (25%) of life (total 59.3%).

Out of 32 patients, 23 were vegetarian (71.9%) and rest 9 were non- vegetarian (28.1%). Macrocytic anaemia (n=15) was predominantly observed in vegetarian patients (86.67%). Only 2 patients with macrocytic anaemia were non-vegetarians (13.33%). There were 5 patients with history of alcohol consumption and one was a smoker. Rest 26 patients had no addictions.

**Table 1: Presenting symptoms of pancytopenia.**

Symptom	No. of cases
Fatigue	29 (90.6%)
Fever	12 (37.5%)
Breathlessness	6 (18.75%)
Oedema	3 (9.3%)
Tingling sensation	2 (6.2%)

Fatigue was the most common presenting symptom present in 90.6% patients. Dyspnoea was seen in 18% patients (Table 1). Most common sign present was pallor (93.75%). Splenomegaly (56.3%) was observed in 13 out of 32 patients (Table 2).

There were two patients who diagnosed to have chronic liver disease had dimorphic anaemia with low values of

serum iron and serum ferritin. One of them had low serum vitamin B12 level and the other had normal vitamin B12 level as he was receiving vitamin B12 supplementation. Another possible reason for pancytopenia in these patients could be hypersplenism.<sup>4</sup>

**Table 2: Clinical signs of pancytopenia.**

Sign	No. of cases
Pallor	30 (93.75%)
Splenomegaly	18 (56.3%)
Pigmentation over knuckles	7 (21.9%)
Hepatomegaly	8 (25%)
Lymphadenopathy (cervical)	1 (3.13%)

The haematological parameters obtained were analysed. Haemoglobin values varied from 2.1 to 10gm%. Lowest haemoglobin level was 2.1gm% with dimorphic anaemia. Twenty three patients had total leucocyte count in the range of 2000-4000cells/mm<sup>3</sup> and rest nine patients had values <2000 cells/mm<sup>3</sup>. Lowest value of TLC was 1200 cells/mm<sup>3</sup>. Twenty two patients had platelet count of <50000 cells /mm<sup>3</sup> and three patients had platelet count <20000 cells/mm<sup>3</sup>. One patient with platelet count 2000 cells/mm<sup>3</sup> presented without any bleeding manifestations. Twenty five (78.12%) patients had a mean corpuscular volume (MCV) >90 fl out of which 14 patients had MCV >110 fl. One patient with MCV >110 fl and normal serum vitamin B12 level (319 pg/ml), had high TSH value (25.9mIU/L). All other patients with high MCV had low vitamin B12 levels.

On peripheral smear examination, 46.87% patients had macrocytic anaemia. 25 out of 32 patients i.e. 78.12% patients had low vitamin B12 levels (<200pg/ml) (Table 3).

**Table 3: Peripheral blood smear in pancytopenia.**

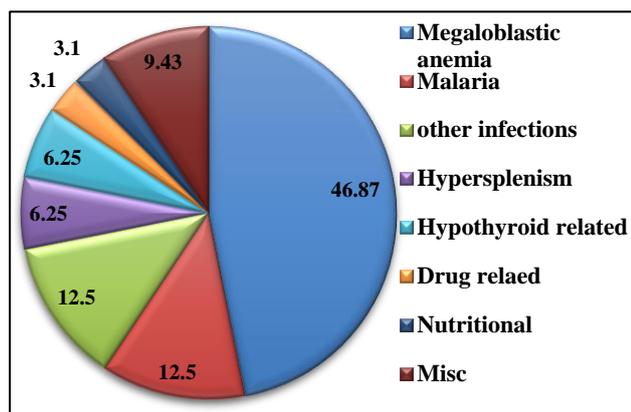
Peripheral blood picture	No. of patients
Macrocytic anaemia	15(46.87%)
Dimorphic anaemia	10(31.3%)
Normocytic anaemia	6(18.75%)
Microcytic anaemia	1(3.13%)

Increased value of TSH (>5.5mIU/L) was found in 5 out of 32 patients i.e. 15.62%. Out of these five, two had normal B12 levels and 3 of them had peripheral smear suggestive of macrocytic anaemia, 1 had dimorphic anaemia and one had normocytic normochromic anaemia.

Association of pancytopenia with malaria (Plasmodium vivax) was found in 6 (18.75%) patients. Out of six, two of them had low vitamin B12 levels and rest four had normal values and all of them responded to treatment.

A total of 9 bone marrow aspirations were performed out of which 6 had changes suggestive of megaloblastic

anaemia (66.6%), two had normoblastic reaction and one had nutritional anaemia.



**Figure 1: Etiology of pancytopenia.**

From among 32 patients, 21 patients reported for follow up and were monitored for response to treatment. Response to vitamin B12 therapy was seen in 18 patients, 2 of them responded to antimalarials and one responded to folic acid supplementation alone.

## DISCUSSION

Most common symptom observed in this study was fatigue (90.6%), Pallor (93.75%), and splenomegaly (56.3%) were the most common signs, which was similar to that found in study by Khodke et al.<sup>6</sup>

In this study, incidence of megaloblastic anaemia based on peripheral smear findings (macrocytic anaemia and hyper segmented neutrophils) was found to be 46.87%. However, on bone marrow examination, 6 out of 9 had megaloblastic changes (66.67%). These results are comparable to studies of Tilak et al, and Khunger et al, where incidence of megaloblastic anemia was 68% and 72% respectively.<sup>3,4</sup>

There were six (18.75%) patients who had Plasmodium vivax infection, of which 4 had normal vitamin B12 and folate assays and no other cause could be determined, i.e. 6.25% incidence was attributed to malaria, making it the second most common cause. This is contrary to the results of other studies in which aplastic anaemia was the second most common cause.<sup>3,4</sup> Incidence of malaria in these studies was 1-4%.<sup>3,4</sup> However, malaria was attributed to be the second most common cause by Hossain et al.<sup>7</sup>

From among 5 patients who had raised TSH (>5.5mIU/L), in 2 patients (6.25%) no other cause of pancytopenia could be found. Hypothyroidism can lead to pancytopenia due to bone marrow hypoplasia and secondary to panhypopituitarism.<sup>8,9</sup>

In some patients, there was history of prolonged fever (>2 weeks) and pancytopenia with no other inciting factor. Such patients were included under infectious causes of pancytopenia (12.5%). Infections can cause pancytopenia by involvement of the bone marrow with infectious organisms.

In this study we had five patients with history of alcohol consumption. Of these, 3 patients had low vitamin B12 values and 2 of them had high TSH levels. One patient had both low B12 and high TSH levels. In one patient no cause other than alcohol consumption could be established for pancytopenia.<sup>10</sup>

There were four patients who gave history of drug intake of whom one consumed methotrexate for psoriasis. Other drugs consumed were oral anti diabetic agents. Methotrexate was discontinued in that patient and significant improvement in lab parameters was observed on follow up after few months.<sup>11</sup>

A single case of nutritional deficiency associated pancytopenia was also reported. Patient had microcytic anaemia with decreased serum iron, serum ferritin and normal serum vitamin B12 and folate levels.

There was only one patient in whom etiology couldn't be established. The peripheral smear showed normocytic normochromic anaemia with normal vitamin B12 and TSH values. Even his BMA was suggestive of normoblastic erythropoiesis. Explanation for pancytopenia could be hypersplenism but further work up for splenomegaly also didn't reveal anything.

The study was conducted with a cohort of 32 patients. Of these, only nine patients underwent bone marrow aspiration examination. Hence, cases of aplastic anaemia, myelofibrosis and myelodysplastic syndromes could have been underdiagnosed.

## CONCLUSION

Megaloblastic anaemia was found to be the major cause of pancytopenia in the present study. Other causes of pancytopenia were malaria, drugs, hypersplenism and hypothyroidism. These causes should be kept in mind while evaluating patients with pancytopenia.

## ACKNOWLEDGEMENTS

Authors would like to thank their colleagues from the Department of Pathology for assistance with reporting of peripheral smear and bone marrow studies. Also, authors extend their sincere gratitude to the Department of Biochemistry and Department of Microbiology respectively for their support with various laboratory investigations.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Jyotsana, Khan A, Sharma V, Kapur P, Manjavkar S, Jain V, et al. Clinical profile of patients with pancytopenia in a tertiary care centre. *Int J Res Med Sci* 2018;6:1187-90.