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Research Article

# ETIOLOGICAL PROFILE OF PANCYTOPENIA

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**ABSTRACT**

**Objective:** The objective of the study was to describe the etiological profile of pancytopenia.

**Methods:** This was an observational study done in 85 patients who presented with pancytopenia to the Department of General Medicine, Government Medical College, Kottayam. The study was carried out over a period of 1 year. The data were collected in a structured pro forma and analyzed using SPSS version 24.

**Results:** The most common age group was 21–30 years, 29 (34.1%) of the 85 patients. 48 (56.5%) were males and 37 (43.5%) were females. Megaloblastic anemia was the most common etiology constituting 60 (70.6%). The most common presenting complaint was generalized weakness in 74 (87.1%). The most common clinical finding was pallor 77 (90.6%). The mean hemoglobin level was 6.81±1.51 g/dl, the mean total WBC count was 2768.39±791.2, and the mean platelet count was 0.87±0.43. Macrocytic anemia was the predominant blood picture in cytopenic patients. Hypercellular marrow was the most common marrow finding in 78.1%.

**Conclusion:** Megaloblastic anemia was the most common cause of pancytopenia followed by aplastic anemia in the present study. Clinical alertness and suspicion can assure early diagnosis and treatment.

**Keywords:** Pancytopenia, Anemia, Bone marrow, Megaloblastic anemia.

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## INTRODUCTION

Pancytopenia is characterized by a decrease in all the three cellular elements of the peripheral blood, red blood cells, white blood cells, and platelets [1]. Usually caused by bone marrow failure pancytopenia is not a disease entity, but rather a triad of anemia with hemoglobin <13.5 g/dl in males and <11.5g/dl in females, leukopenia with total leukocyte counts <4000/mm$^3$, and thrombocytopenia with platelet count <1.5 lakh/mm [2-4]. Pancytopenia may be associated with a hypocellular bone marrow, hypercellular marrow, or bone marrow infiltration. Pancytopenia with a hypocellular bone marrow may be caused by aplastic anemia, drugs, viruses, radiation, toxins, autoimmune disease, malignancy, and paroxysmal nocturnal hemoglobinuria (PNH). In cases of pancytopenia with hypercellular bone marrow, the causative factor maybe hypersplenism, megaloblastic anemia, myelodysplastic syndrome, infections such as human immunodeficiency virus (HIV), and tuberculosis. Malignancies, granulomas, and fibrosis are causes of pancytopenia with bone marrow infiltration. The etiology of pancytopenia differs from one geographical area to another and varies in different population groups with their differences in nutritional status and prevalence of ineffective disorders. In India, cause of pancytopenia is not well defined which is a major cause for diagnostic dilemma. The present study was undertaken to evaluate the various causes of pancytopenia.

## METHODS

This was a descriptive cross-sectional study done in the Department of General Medicine, Government Medical College, Kottayam, for a period of 12 months from the Institutional Review Board approval. Ethics committee clearance was obtained vide IRB No.28/2020 dated September 29, 2021. Patients with pancytopenia presenting to the Department of General Medicine, Government Medical College Kottayam, satisfying the inclusion criteria of hemoglobin level <13.5 g/dl in males or <11.5 g/dl in females, leukocyte count <4000 cells/cu mm, and platelet count <1.5 lakhs/cu mm were recruited after obtaining their informed consent. Those with age <12 years and those on cancer chemotherapy or radiation therapy were excluded from the study. A sample size of 85 was calculated based on the prevalence of megaloblastic anemia 54% in a study by Yadav *et al.* [3]. Consecutive sampling was done.

Data were collected using a structured pro forma which included hemoglobin, red blood cell (RBC) count, white blood cell count (WBC), platelet count, red cell indices, RDW (Red Cell Distribution Width), retic count, peripheral smear, and erythrocyte sedimentation rate (ESR). Bone marrow study was done in those cases,where the cause of pancytopenia was elusive after initial investigations. The data were entered in Microsoft Excel and analyzed using SPSS software version 24. For qualitative variables, frequencies were calculated, and for quantitative variables, mean and standard deviation were calculated.

## RESULTS

This was a descriptive cross-sectional study done in 85 patients diagnosed with pancytopenia. The age of the patients ranged from 13 to 60 years with a mean age of 34.78±10.95 years. As shown in Table 1, the most common age group was 21–30 followed by 31–40 years. As shown in Fig. 1, 48 (56.5%) cases were males and 37 (43.5%) were females. There was a male preponderance with a male: female ratio of 1.3:1.

The most common presenting complaint was generalized weakness in 74 patients (87.1%). Fever was present in 20 (23.5%), dyspnea in 22 (25.9%), bleeding manifestations in 28 (32.9%), pallor in

**Table 1: Age distribution**

| Age in years | Frequency | Percent |
|---|---|---|
| ≤20 | 6 | 7.1 |
| 21–30 | 29 | 34.1 |
| 31–40 | 24 | 28.2 |
| 41–50 | 16 | 18.8 |
| >50 | 10 | 11.8 |
| Total | 85 | 100 |

77 (90.6%), splenomegaly in 28 (32.9%), hepatomegaly in 21 (24.7%), jaundice in 13 (15.3%), lymphadenopathy in 9 (10.6%), Purpura in 11 (12.9%), and edema in 10 (11.8%) in this study, as shown in Table 2.

As shown in Fig. 2, the peripheral blood picture showed that macrocytosis was present in majority 69 (81.2%) of patients with pancytopenia. Microcytic anemia was the least common type and was present in 2 (2.4%). Bone marrow study was performed in 73 patients.

As shown in Fig. 3, the majority of them had a hypercellular marrow picture 57 (78.1%). Among them, most common cause was megaloblastic anemia.

As shown in Table 2, the mean hemoglobin level was 6.81±1.51 g/dl, mean WBC count was 2768±791.2, and the mean count of platelet was 0.87±0.43 lakhs.

Out of the 85 patients with 29 (34.1%) in the age group of 21–30 years had pancytopenia, of which 17 were males and 12 females. The number of patients above the age of 50 was 10 (11.8%) and those less than 20 were 6 (7.1%) (Table 3).

Megaloblastic anemia was the most common etiology, constituting 60 cases (70.6%). Aplastic anemia was present in 7 cases (8.2%), cirrhosis of liver in 4 cases (4.7%), leukemia in 4 cases (4.7%), dengue in 3 cases (3.5%), sepsis in 3 cases (3.5%), myelodysplastic syndrome in 2 cases (2.4%), AIDS was present in a single case (1.2%), and one case (1.2%) was post-COVID (Table 4).

## DISCUSSION

The present study was conducted in patients with pancytopenia who presented to the Department of General Medicine, Government Medical College, Kottayam. A total of 85 patients were included in this study. The mean age in the present study was 34.78 ± 10.95 years with the age range of 13–60 years. In the study by Khunger *et al*., in 200 cases of pancytopenia, the age group ranged from 2 to 70 years [5]. In a study by Kumar *et al*., the age group was 12–73 years, while in Khokde *et al*., it was 3–69 years, and in Tilak, it was 5–70 years V *et al.* [6-8].

In this study, 48 (56.6%) were males and 37 (43.5 %) were females. The male-to-female ratio was 1.3:1. The male: female ratio was comparable to that of Khunger *et al*. and Khokde Tilak *et al*., while Kumar *et al*. showed a further higher ratio of 2.1:1 [5-8]. There was a male preponderance in the present study as seen with the other studies.

The most common presenting complaint in the present study was generalized weakness (87.1%), followed by bleeding (32.9%), dyspnea (25.9%), and fever (23.5%). In the study by Gayathri *et al*., generalized weakness was present in all cases and dyspnea in 48.25% cases [9]. Physical findings such as pallor, icterus, hepatomegaly, splenomegaly, and lymphadenopathy were comparable with the study by Gayathri *et al*. [9]. Similarly, Pallor and splenomegaly were also the most common signs observed by Niazi *et al*.; however, generalized weakness was the most common symptom (68.2%) followed by fever (47.7%) and bleeding manifestations(33.33%) [10].

The most common physical finding in the present study was pallor (90.6%), followed by splenomegaly (32.9%) and hepatomegaly (24.7%). Physical findings were comparable with other studies, though lymphadenopathy (10.6%) was found in more cases in the present study. This was corroborated by Yadav *et al*., who reported 60% of the patients to be presenting with pallor, followed by 41.5% with fever [11]. In a study by Agarwal *et al*., the most common presenting symptom was fever with 64.28%, followed by pain in legs in 34.28% [12]. Similar results were found by Khokde *et al*., who also found fever to be the most common symptom [7]. In the present study, fever was present in 23.5% of the cases.

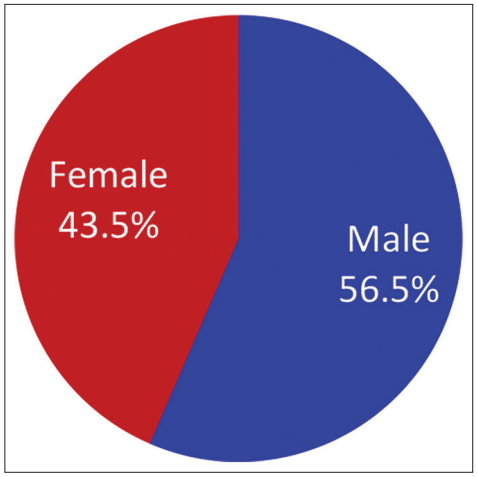


**Fig. 1: Gender distribution**

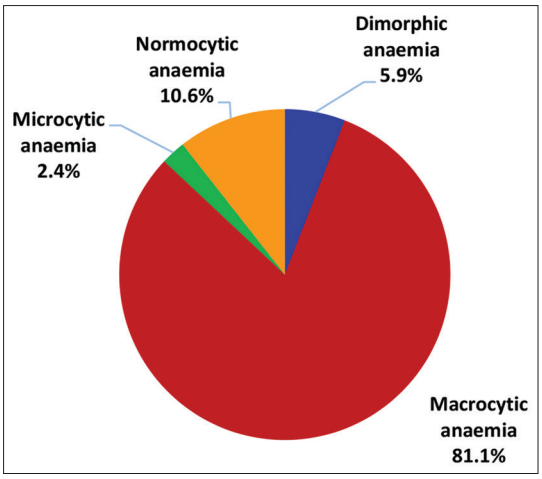


**Fig. 2: Peripheral blood picture**

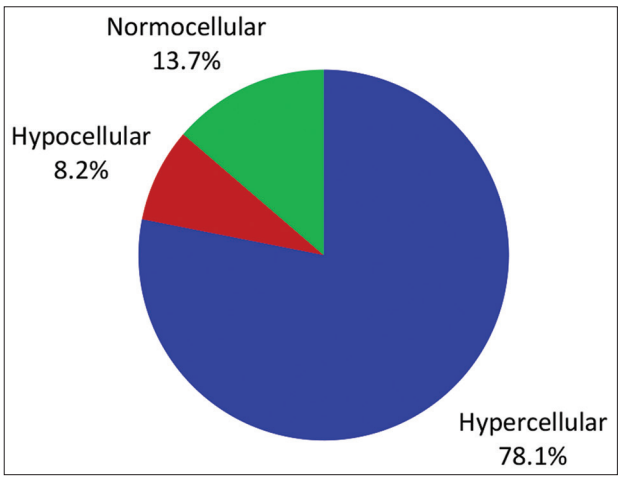


**Fig. 3: Cellularity of bone marrow**

**Table 2: Vital hematological parameters**

| | N | Minimum | Maximum | Mean | SD |
|---|---|---|---|---|---|
| Hb (g/dl) | 85 | 1.7 | 9.2 | 6.81 | 1.51 |
| Total count (/mm$^3$) | 85 | 1100 | 3960 | 2768.39 | 791.20 |
| Platelet/lakh | 85 | 0.04 | 1.46 | 0.87 | 0.43 |

**Table 3: Age-wise and sex-wise distribution of pancytopenia in the present study**

| Age in years | Sex | | | | Total | |
|---|---|---|---|---|---|---|
| | Male | | Female | | | |
| | n | % | n | % | n | % |
| ≤20 | 4 | 8.3 | 2 | 5.4 | 6 | 7.1 |
| 21–30 | 17 | 35.4 | 12 | 32.4 | 29 | 34.1 |
| 31–40 | 13 | 27.1 | 11 | 29.7 | 24 | 28.2 |
| 41–50 | 5 | 10.4 | 11 | 29.7 | 16 | 18.8 |
| >50 | 9 | 18.8 | 1 | 2.7 | 10 | 11.8 |
| Total | 48 | 100 | 37 | 100 | 85 | 100 |

**Table 4: Etiology of pancytopenia**

| Diagnosis | Frequency | Percent |
|---|---|---|
| Megaloblastic anemia | 60 | 70.6 |
| Aplastic anemia | 7 | 8.2 |
| Cirrhosis of liver | 4 | 4.7 |
| Leukemia | 4 | 4.7 |
| Dengue | 3 | 3.5 |
| Sepsis | 3 | 3.5 |
| Myelodysplastic syndrome | 2 | 2.4 |
| Post-COVID | 1 | 1.2 |
| AIDS | 1 | 1.2 |
| Total | 85 | 100 |

Megaloblastic anemia was the most common cause of pancytopenia in the study. The incidence of megaloblastic anemia is said to vary from 0.8 to 32.26%. However, in the present study, this incidence was higher with 70.6 %. Yadav *et al*. found an incidence of megaloblastic anemia to be 35.84% [11]. A very high incidence of 68% of megaloblastic anemia was reported by Tilak *et al*. in their study, while only 1.43 % was observed by Agarwal *et al.* [8,12].

In a study by Khunger *et al*. and Khokde *et al*., megaloblastic anemia was the most common cause for pancytopenia accounting for 72% and 44%, respectively [5,7]. In the study by Kumar *et al*., also megaloblastic anemia was the most common cause [6]. The second most common cause of pancytopenia in the present study was aplastic anemia, which accounted for 8.2% of the cases. The incidence of aplastic anemia worldwide is said to vary between 10% and 52.7%. In the study by Agarwal *et al*., Kumar *et al*., and Khodke et al., aplastic anemia was the second most common cause of pancytopenia accounting for 14.28%, 14%, and 29.5%, respectively [6,7,12]. It was much more comparable with Tilak *et al*. where its incidence was 7.8% [8]. Aplastic anemia was the most common cause of pancytopenia in several other studies [10,13,14]. Aplastic anemia is the most common cause of pancytopenia reported from various studies throughout the world and it shows a higher frequency in the developing world than in industrialized Western countries [15,16]. The more incidence of megaloblastic anemia as compared to aplastic anemia in this study in concurrence with other Indian studies reflects the higher prevalence of nutritional anemia in Indian subjects.

According to Prem Kumar *et al*. in developing countries, pancytopenia is mostly attributed to infectious diseases such as tuberculosis and HIV, which poorly correlates with the present study [17]. Cirrhosis of liver accounted for 4.7% of the cases which was not a notable cause in the other studies. Leukemia also accounted for 4.7% of cases. It was comparable to Khunger *et al*.'s study where leukemia was present in 5% of the cases [5]. A higher incidence of 12.1% was seen with Kumar *et al* [6]. In Khodke *et al*., 2% of cases were due to leukemia, and in Tilak *et al*., 1.3% cases were due to leukemia [7,8]. Niazi *et al*. have reported 13.6% cases of acute leukemia as a cause for pancytopenia [10]. Acute leukemia was found to be the major cause, especially in children by Naseem *et al*. in his study [18]. Dengue accounted for 3.5% of the cases in the present study, which was not a cause in the other studies mentioned so far. Myelodysplastic syndrome (MDS) was present in 2.4%. In Khunger *et al*., 4 cases (2%), Khodke *et al*., 1 case (2%), and Kumar *et al*., 6 cases (3.6%) were due to MDS [5,6].

The present study had a single case of each of AIDS and Post-COVID which accounted for only 1.2% of the cases. Khodke *et al*. have reported 1 case of AIDS (2%) [7].

The variation in the frequency of the causes of pancytopenia has been attributed to the differences in methodology and stringency of diagnostic criteria, period of observation, varying exposure to myelotoxic agents apart from the geographical area and genetic mutations [19,20]. Screening programs at community level will help in diagnosis and benefit avoiding further complications by offering adequate patient counseling, especially for anemia [21].

The limitations of this study are that it is a single-center study. A study with longer duration and better sample size might provide more insights into the etiology.

## CONCLUSION

The most common presenting complaint was generalized weakness and clinical finding was pallor. Megaloblastic anemia was the most common cause of cytopenia, followed by aplastic anemia. Macrocytic anemia was predominant blood picture in cytopenic patients. Hypercellular marrow was the most common marrow finding and the most common cause was megaloblastic anemia.

## AUTHORS' CONTRIBUTION

Athira Surendran: Project idea, protocol preparation, literature review, data collection, data analysis, manuscript preparation. Padmakumar NN: Project idea, protocol review, manuscript review. Anoop Kumar N: Project idea, protocol review, manuscript preparation, manuscript editing, corresponding author.

## CONFLICTS OF INTERESTS

None.

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