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*Original Research Article*

# Clinico-Hematological Evaluation in Pancytopenia


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***Abstract***: ***Background***: Pancytopenia is a significant clinical syndrome characterized by reduction in all three major formed elements of blood (hemoglobin <9g/dl, white blood cells <4000/µl with absolute neutrophil count <1,800/µl, and platelets <1,00,000/µl). The causes vary considerably across different populations due to variations in nutritional status, genetic factors, and exposure to myelotoxic agents. In India, the etiology of pancytopenia remains poorly defined, necessitating comprehensive evaluation to establish appropriate diagnostic and therapeutic approaches. ***Objective***: To evaluate the various causes of pancytopenia and correlate peripheral blood findings with bone marrow aspiration findings in patients presenting to a tertiary care center. ***Methods***: A prospective study was conducted on 40 patients with pancytopenia from August 2022 to January 2024. Detailed clinical examination, complete blood count, peripheral smear evaluation, bone marrow aspiration, and Perl's stain for iron assessment were performed in all cases. ***Results***: The study population showed a bimodal age distribution with peaks at 18-30 years and 61-75 years (35% each), with male predominance (55%). Fatigue (90%) and dyspnea (62.5%) were the most common symptoms, while pallor (97.5%) was the predominant sign. Megaloblastic anemia was the leading cause (45%), followed by aplastic anemia (22.5%). Hypercellular bone marrow was observed in 77.5% of cases. The majority of patients (67.5%) had severe thrombocytopenia (<40,000/µl). ***Conclusion***: This study demonstrates that megaloblastic anemia and aplastic anemia are the primary causes of pancytopenia in our population. Detailed clinical evaluation combined with bone marrow examination is essential for accurate diagnosis and appropriate management of pancytopenia patients.



**Keywords**: Pancytopenia, Bone Marrow Aspiration, Megaloblastic anemia, Aplastic anemia, Hematological disorders.


## INTRODUCTION

Pancytopenia represents a complex hematological syndrome characterized by simultaneous reduction in all three major cellular components of blood. The condition is defined by specific laboratory criteria: hemoglobin <9g/dl, total leucocyte count <4,000/µl (or absolute neutrophil count <1,500/µl), and platelet count <1,00,000/µl.[1] The global incidence varies significantly, with 2-5 cases per million annually worldwide, but 5-12 cases per million in industrialized nations like the United States. Asian countries demonstrate approximately twice the incidence, with peak occurrence between ages 15-25 and 65-69 years[1].

The underlying pathophysiology of pancytopenia encompasses diverse mechanisms including decreased hematopoietic cell production due to bone marrow destruction, replacement by neoplastic cells, or suppression of normal growth and differentiation. Additionally, conditions associated with normocellular or hypercellular bone marrow may result from ineffective haematopoiesis, removal of defective cells from circulation or antibody-mediated sequestration and destruction.[2] The clinical manifestations depend on the severity of individual cytopenias and the underlying causative disorder, with patients typically presenting with symptoms related to anemia, increased infection risk, and bleeding tendencies.

In India, the causes of pancytopenia remain poorly characterized, with limited studies reporting varying frequencies of diagnostic entities. This variation has been attributed to differences in methodology, diagnostic criteria, geographic factors, genetic differences, and exposure to myelotoxic agents[3]. The

delineation of etiologies and assessment of severity determines patient management and prognosis, making early diagnosis crucial since many causes are potentially curable with appropriate intervention.[2] This study was undertaken to evaluate the various causes of pancytopenia and establish correlations between peripheral blood findings and bone marrow aspiration results in our population.

## METHODOLOGY

A hospital-based prospective case series study was conducted at the Department of Pathology, S. Nijalingappa Medical College and HSK Hospital and Research Centre, Bagalkot, over 18 months from August 2022 to May 2024. The study included 40 consecutive patients diagnosed with pancytopenia, aged 18-75 years, meeting the inclusion criteria of hemoglobin <9gm/dl, total leucocyte count <4,000/µL (absolute neutrophil count <1,500/µL), and platelet count <1,00,000/µL. Patients receiving radiotherapy or chemotherapy, those with coagulation disorders, bone deformities, or non-cooperative patients were excluded.

After obtaining written informed consent, detailed clinical examination was performed for all patients. 2ml of venous blood was collected in EDTA vacutainer tubes for hematological analysis using Mindray BC-6800 analyzer. Peripheral blood smears were prepared simultaneously and stained with Leishman stain for morphological examination. ESR was estimated using Westergren's method in all cases.

Bone marrow aspiration was performed in all 40 patients under aseptic conditions from the right posterior superior iliac spine using Salah's needle. Bone marrow smears were prepared immediately and stained with Leishman stain for morphological evaluation. Perl's Prussian blue stain was performed on bone marrow aspirates to assess iron storage status according to Gale et al. grading system. Data was analyzed using SPSS version 19, with chi-square analysis for categorical variables and t-test for continuous variables, with significance set at $p<0.05$.

## RESULTS

Statistical analysis was performed on all 40 patients to evaluate demographic characteristics, clinical presentations, hematological parameters, and bone marrow findings. Descriptive statistics were calculated for quantitative variables, while categorical variables were analyzed using frequency distributions and percentages. Associations between bone marrow findings and various clinical parameters were assessed using chi-square test and ANOVA where appropriate.

**Table 1: Demographics and Clinical Characteristics**

| Parameter | Frequency | Percentage |
|---|---|---|
| **Age Distribution** | | |
| 18-30 years | 14 | 35% |
| 31-40 years | 6 | 15% |
| 41-50 years | 4 | 10% |
| 51-60 years | 2 | 5% |
| 61-75 years | 14 | 35% |
| **Gender** | | |
| Male | 22 | 55% |
| Female | 18 | 45% |
| **Major Symptoms** | | |
| Fatigue | 36 | 90% |
| Dyspnea | 25 | 62.5% |
| Anorexia | 24 | 60% |
| Bleeding manifestations | 23 | 57.5% |
| **Clinical Signs** | | |
| Pallor | 39 | 97.5% |
| Hepatomegaly | 11 | 27.5% |
| Splenomegaly | 8 | 20% |
| Jaundice | 5 | 12.5% |

**Table 2: Hematological Parameters**

| Parameter | Distribution | Frequency | Percentage | Mean±SD |
|---|---|---|---|---|
| **Hemoglobin (g/dl)** | | | | 5.4±1.8 |
| <5 g/dl | | 15 | 37.5% | |
| >5 g/dl | | 25 | 62.5% | |
| **Total Leucocyte Count (/µl)** | | | | 2554±893.1 |
| <1000 | | 3 | 7.5% | |
| 1000-2000 | | 6 | 15% | |
| 2000-3000 | | 20 | 50% | |
| 3000-4000 | | 11 | 27.5% | |
| **Platelet Count (/µl)** | | | | 31060±24991.1 |
| <40,000 | | 27 | 67.5% | |
| 40,000-80,000 | | 9 | 22.5% | |
| 80,000-100,000 | | 4 | 10% | |
| **Reticulocyte Count (%)** | | | | 1.56±0.54 |
| 0.6-1% | | 9 | 22.5% | |
| 1.1-2% | | 31 | 77.5% | |

**Table 3: (A) Peripheral Blood Findings in Pancytopenia Patient**

| Peripheral smear findings | (n=) | Anisocytosis | Circulating erythroblasts | Hypersegmented polymorphs | Circulating immature cells | Relative lymphocytosis | Reticulocytosis |
|---|---|---|---|---|---|---|---|
| Megaloblastic anemia | 18 | 15 | 13 | 18 | - | 7 | 1 |
| Aplastic anemia | 9 | 4 | - | - | - | 5 | - |
| Acute Promyelocytic Leukemia-M3 | 1 | 1 | 1 | - | 1 | - | - |
| Hairy cell leukemia | 1 | 1 | - | - | - | - | - |
| Multiple myeloma | 1 | 1 | - | - | - | - | - |
| Myelodysplastic syndrome - Multilineage | 1 | 1 | - | - | - | - | - |
| ALL-L2 | 2 | - | - | - | 2 | 2 | - |
| Reactive Hypercellular Marrow | 6 | 2 | 1 | - | - | - | - |
| Micro-erythroblastic Maturation | 1 | 1 | - | - | - | - | 1 |

**Table 3: (B) Bone marrow findings (M:E ratio- Myeloid:Erythroid ratio;I- Increased; N-Normal ; D-Decreased ; L-Lymphocyte ; P-Plasma cell ; MM – Metamyelocytes ; Normo – Normoblastic ; Megalo – Megaloblastic ; )**

| Sl. no | Cellularity | M:E ratio | Erythrocyte | Myelocyte | Megakaryocyte | Blast | | | | L and P cells | Final diagnosis |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | N:C ratio | Cytoplasm | Nucleoli | Chromatin | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Hypercellular | 2:5 | Megalo | Gaint MM | D | - | - | - | - | N | Megaloblastic anemia |
| 2 | Hypercellular | 1:2 | Normo | N | N | - | - | - | - | N | Reactive Hypercellular marrow |
| 3 | Hypercellular | 1:3 | Megalo | Gaint MM | D | - | - | - | - | N | Megaloblastic anemia |
| 4 | Hypercellular | 1:2 | Normo | N | N | - | - | - | - | N | Reactive Hypercellular marrow |
| 5 | Hypocellular | 1:3 | Normo | D | D | - | - | - | - | I | Aplastic anemia |
| 6 | Hypercellular | - | - | - | I | I | scant | conspicuous | clumped | I | Multiple myeloma |
| 7 | Hypocellular | 1:1 | Normo | D | D | - | - | - | - | I | Aplastic anemia |
| 8 | Hypercellular | 1:3 | Megalo | Gaint MM | N | - | - | - | - | N | Megaloblastic anemia |
| 9 | Hypercellular | 2:5 | Megalo | Giant MM | N | - | - | - | - | N | Megaloblastic anemia |
| 10 | Hypercellular | 1:3 | Megalo | Giant MM | N | - | - | - | - | N | Megaloblastic anemia |
| 11 | Hypercellular | 1:3 | Dyserythropoiesis | Dysgranulopoiesis | dysmegakayopoieosis | - | - | - | - | N | Myelodysplastic Syndrome-Multilineage |
| 12 | Hypocellular | - | - | - | - | - | - | - | - | - | Hairy cell leukemia |
| 13 | Hypercellular | - | Normo | - | D | I | Moderate | Conspicuous | Fine | N | ALL-L2 |
| 14 | Hypercellular | 1:2.5 | Megalo | Giant MM | N | - | - | - | - | N | Megaloblastic anemia |
| 15 | Hypercellular | - | Normo | - | D | I | - | - | - | N | Acute Promyelocytic Leukemia – M3 |
| 16 | Hypocellular | 1:1 | Normo | D | D | - | - | - | - | I | Aplastic anemia |
| 17 | Hypocellular | 1:3 | Normo | D | D | - | - | - | | I | Aplastic anemia |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 18 | Hypercellular | 1.5:1 | Mixed | N | N | - | - | - | - | N | Reactive Hypercellular marrow |
| 19 | Hypercellular | 1:2.5 | Megalo | Giant MM | D | - | - | - | - | N | Megaloblastic anemia |
| 20 | Hypercellular | 1:1.5 | Megalo | Giant MM | D | - | - | - | - | N | Megaloblastic anemia |
| 21 | Hypercellular | 1:3 | Megalo | Giant MM | D | - | - | - | - | N | Megaloblastic anemia |
| 22 | Hypercellular | 1:1.5 | Mixed | N | N | - | - | - | - | N | Reactive Hypercellular marrow |
| 23 | Hypocellular | 1:1 | Normo | D | D | - | - | - | - | I | Aplastic anemia |
| 24 | Hypercellular | 1:3 | Megalo | Giant MM | N | - | - | - | - | N | Megaloblastic anemia |
| 25 | Hypercellular | 1:1.4 | Megalo | Giant MM | N | - | - | - | - | N | Megaloblastic anemia |
| 26 | Hypercellular | 1:2.5 | Megalo | Giant MM | N | - | - | - | - | N | Megaloblastic anemia |
| 27 | Hypocellular | 1:2 | Mixed | D | D | - | - | - | - | I | Aplastic anemia |
| 28 | Hypercellular | 1.5:1 | Mixed | N | N | - | - | - | - | N | Microerythroblastic maturation |
| 29 | Hypercellular | 1:2.4 | Megalo | Giant MM | D | - | - | - | - | N | Megaloblastic anemia |
| 30 | Hypocellular | 1:1 | Normo | D | D | - | - | - | - | I | Aplastic anemia |
| 31 | Hypercellular | - | Normo | - | D | I | Moderate | Conspicuous | Fine | N | ALL-L2 |
| 32 | Hypercellular | 1:3 | Megalo | Giant MM | N | - | - | - | - | N | Megaloblastic anemia |
| 33 | Hypercellular | 1:2.5 | Megalo | Giant MM | N | - | - | - | - | N | Megaloblastic anemia |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 34 | Hypercellular | 1:3 | Megalo | Giant MM | N | - | - | - | - | N | Megaloblastic anemia |
| 35 | Hypocellular | 1:1 | Normo | D | D | - | - | - | - | I | Aplastic anemia |
| 36 | Hypercellular | 1:4 | Megalo | Giant MM | D | - | - | - | - | N | Megaloblastic anemia |
| 37 | Hypercellular | 1.5:1 | Mixed | N | N | - | - | - | - | N | Reactive Hypercellular marrow |
| 38 | Hypercellular | 1:3 | Megalo | Giant MM | N | - | - | - | - | N | Megaloblastic anemia |
| 39 | Hypercellular | 2:3 | Normo | N | N | - | - | - | - | N | Reactive Hypercellular marrow |
| 40 | Hypocellular | 1:1 | Normo | D | D | - | - | - | - | I | Aplastic anemia |

**Table 4: Etiology and Iron Status**

| Parameter | Frequency | Percentage |
|---|---|---|
| **Causes of Pancytopenia** | | |
| Megaloblastic anemia | 18 | 45% |
| Aplastic anemia | 9 | 22.5% |
| Solid malignancy | 7 | 17.5% |
| Fever | 3 | 7.5% |
| Chronic hepatitis | 2 | 5% |
| Systemic lupus erythematosus | 1 | 2.5% |
| **Perl's Stain Iron Grading** | | |
| Grade 0 (decreased) | 17 | 42.5% |
| Grade 1-3 (normal) | 13 | 32.5% |
| Grade 4-6 (increased) | 10 | 25% |
| **Age-specific Patterns** | | |
| Megaloblastic anemia (18-30 years) | 9 | 50% of MA cases |
| Aplastic anemia (61-75 years) | 9 | 100% of AA cases |

The study demonstrated that megaloblastic anemia predominantly affected younger patients (18-30 years), while aplastic anemia exclusively occurred in elderly patients (61-75 years). Severe thrombocytopenia (<40,000/µl) was observed in 67.5% of patients, with aplastic anemia showing the highest frequency (88.9%). Iron stores were decreased in 42.5% of cases, with significant association between iron status and bone marrow diagnosis ($p<0.05$).

## DISCUSSION

The present study of 40 pancytopenia patients revealed a bimodal age distribution with peaks at 18-30 years and 61-75 years, each comprising 35% of cases, which differs from other studies showing varying peak incidences in different age groups.[3] The male to female ratio of 1.2:1 demonstrated slight male predominance, consistent with findings from Gayathri et al.[1], Khan SP et al.[3], and Jain A et al.[4], though some studies report female predominance.[5,6] The clinical presentation was dominated by fatigue (90%) and dyspnea (62.5%), with pallor being

 

universal (97.5%), consistent with previous studies.[1,7,8] However, bleeding manifestations were more frequent in our study (57.5%) compared to other reports ranging from 3.84% to 28.6%[1,7,9], possibly reflecting more severe disease at presentation in our population.

Megaloblastic anemia emerged as the leading cause of pancytopenia (45%), followed by aplastic anemia (22.5%), which aligns with multiple previous studies.[1,4,7,10,11] The high prevalence of megaloblastic anemia likely reflects nutritional deficiencies of vitamin B12 and folate, common in the Indian subcontinent due to dietary habits and malabsorption syndromes. Notably, all aplastic anemia cases occurred in the elderly (61-75 years), suggesting age-related factors in pathogenesis. The bone marrow examination was diagnostic in all cases, with 77.5% showing hypercellularity, emphasizing the importance of bone marrow aspiration in pancytopenia evaluation. The identification of hematological malignancies including acute lymphoblastic leukemia-L2 (5%), acute promyelocytic leukemia-M3 (2.5%), and rare entities like hairy cell leukemia and myelodysplastic syndrome highlights the diverse etiology requiring systematic evaluation.[12-14]

The iron status assessment using Perl's stain revealed decreased iron stores in 42.5% of patients, with significant association between iron status and underlying diagnosis ($p<0.05$). Severe thrombocytopenia (<40,000/µl) was observed in 67.5% of cases, particularly in aplastic anemia (88.9%) and megaloblastic anemia (66.7%), correlating with bleeding manifestations. The study limitations include relatively small sample size and lack of advanced investigations like cytogenetics and immunophenotyping, which would have enhanced diagnostic accuracy. Future studies incorporating molecular techniques and larger patient cohorts would provide better understanding of pancytopenia etiology in our population and guide targeted therapeutic interventions.

## CONCLUSION

This study demonstrated that pancytopenia can be the initial symptom of a wide range of illnesses; with the three most common categories in the cases examined being megaloblastic anemia, dimorphic anemia, and aplastic anemia.

Our research suggests that megaloblastic anemia is the most common cause of pancytopenia, despite the fact that there are many other etiologies for the condition and its different presentations.

Furthermore, a shortage in vitamin B12 is the most frequent cause of megaloblastic anemia. Therefore, regardless of the patient's diet, it is recommended that the first screening test for megaloblastic anemia evaluation be a B12 deficient screening because this condition is not only the most prevalent cause of megaloblastic anemia but also occurs in patients who follow a varied diet. If necessary, additional investigations, such as a upper GI endoscopy, can be conducted in light of the clinical situation. While ordering additional studies, other illnesses such as hypersplenism, cancer, and aplastic anemia—the next most common cause in our study—should also be taken into consideration.

The results of the aforementioned study also suggest that pancytopenia and its many complications can be prevented by promptly identifying patients with megaloblastic anemia and treating the underlying cause in the early stages of the condition.

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