



Research Article

Clinico-Hematological Spectrum of Pancytopenia: A Study of Peripheral Smear and Bone Marrow Findings in a Tertiary Care Center in India

Aditi N Patel¹, Abhilasha P Zala², Naushin A Ghori³

¹ Assistant Professor, Department of Pathology, Gujarat Medical Education & Research Society, Dharpur, Patan, Gujarat, India

² Affiliation: Assistant Professor, Department of Pathology, Parul Institute of Medical Sciences and Research, Gujarat, India

³ Tutor, Department of Pathology, Narendra Modi Medical college, Ahmedabad, Ahmedabad, Gujarat, India



Corresponding Author:

Aditi N Patel

Assistant Professor, Department of Pathology, Gujarat Medical Education & Research Society, Dharpur, Patan, Gujarat, India.

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ABSTRACT

Introduction: Pancytopenia, defined as a reduction of erythrocytes, leukocytes, and platelets, is a manifestation of diverse underlying disorders. Early diagnosis is essential since many causes are reversible. This study evaluated the clinico-hematological spectrum of pancytopenia and correlated peripheral smear with bone marrow findings in a tertiary care center in India.

Materials and Methods: A descriptive observational study was conducted on 190 patients (13–65 years) with pancytopenia. Clinical details, complete blood counts, and peripheral smears were obtained. Bone marrow aspiration and trephine biopsy were performed in 58 patients. Data were analyzed for demographic, clinical, and etiological patterns.

Results: Of 190 patients, 52% were males. The most affected age group was 27–36 years. Generalized weakness and pallor were the most common symptom and sign, respectively. Severe anemia (Hb 5.1–7.0 g/dL), leukopenia (1,001–2,500/mm³), and thrombocytopenia (<50,000/mm³) predominated. Peripheral smears most often showed microcytic hypochromic morphology. Bone marrow examination revealed normal trilineage maturation (25.9%), megaloblastic anemia (19%), aplastic anemia (17.2%), dimorphic anemia (12.1%), and acute leukemia (8.6%) as leading etiologies.

Conclusion: Pancytopenia has a heterogeneous etiology, with nutritional deficiencies and marrow failure syndromes being major causes. Peripheral smear gives preliminary clues, but bone marrow examination is vital for accurate diagnosis. Early evaluation allows identification of reversible conditions and timely management.

Keywords: Pancytopenia, Bone marrow, Peripheral smear.

INTRODUCTION

Pancytopenia is an important clinico-hematological condition frequently encountered in medical practice, characterized by the simultaneous reduction of all three major blood cell lines i.e. erythrocytes, leukocytes, and platelets.^(1,2) It is defined by hemoglobin levels of less than 13.5 g/dL in males and 11.5 g/dL in females, a total leukocyte counts below $4 \times 10^3/\mu\text{L}$, and platelet counts less than $150 \times 10^3/\mu\text{L}$.⁽³⁾ Patients often present with fatigue and weakness due to anemia, increased susceptibility to infections because of leukopenia, and bleeding tendencies resulting from thrombocytopenia.⁽¹⁾ Common clinical signs include fever, pallor, dizziness, weight loss, anorexia, night sweats, splenomegaly, hepatomegaly, lymphadenopathy, and bleeding manifestations.^(4,5) The etiologies of pancytopenia are diverse and may involve decreased hematopoietic cell production from the bone marrow due to infections, toxins, malignant infiltration, chemotherapeutic agents, radiation, or parasitic infestations.⁽¹⁾ Because pancytopenia is a manifestation of multiple underlying disease processes rather than a disease entity itself,⁽⁵⁾ prompt and accurate etiological diagnosis is essential for appropriate management. Peripheral blood smear evaluation and bone marrow examination are the cornerstone diagnostic tools, providing valuable morphological details and guiding clinical decision-making. While aspiration smears offer better

cytological resolution, trephine biopsies provide a more reliable assessment of marrow cellularity. Performing both procedures concurrently is recommended in the diagnostic workup of pancytopenia. ⁽¹⁾ The incidence and spectrum of underlying causes vary geographically due to differences in genetic, nutritional, infectious, and environmental factors. ⁽¹⁾ Since many causes are reversible, early detection and intervention can significantly improve patient outcomes.

The present study was undertaken to comprehensively evaluate the clinico-hematological spectrum of pancytopenia in patients attending a tertiary care center in India. The study aimed to assess the hematological parameters of these patients, classify cases according to their underlying etiology, and document the range of clinical presentations. Furthermore, it sought to correlate peripheral smear findings with bone marrow aspiration and/or biopsy results, thereby providing an integrated clinicopathological perspective on the condition. ^(1–3,6)

MATERIALS AND METHODS

This descriptive observational study was conducted in the Department of Pathology, Medical College Baroda, after approval from the Institutional Ethics Committee (IEC). [IECBHR/04-2020]

Study Population

Patients admitted under General Medicine, S.S.G. Hospital, Baroda, with peripheral blood pancytopenia were prospectively enrolled. Inclusion criteria were: haemoglobin <9 g/dL, total leukocyte count <4,000/mm³, platelet count <1,50,000/mm³, age 13–65 years, and consent for bone marrow examination. Exclusion criteria included: age <13 or >65 years, decompensated chronic liver disease, pregnancy, recent significant bleeding, and known genetic causes. Consecutive sampling was used.

Clinical and Laboratory Evaluation

Demographic data, clinical history, and examination findings were recorded. Laboratory investigations included complete blood count (CBC) by automated 3-part haematology analyser, peripheral smear examination, reticulocyte count, malarial parasite screening, erythrocyte sedimentation rate, and coagulation profile. EDTA vacutainers were used for CBC, and trisodium citrate vacutainers for coagulation studies. Peripheral smears were assessed for red cell morphology, anisocytosis, poikilocytosis, chromia, polychromasia, nucleated red cells, inclusions, and rouleaux formation.

Bone Marrow Examination

Bone marrow aspiration was performed using Salah's needle from the posterior superior iliac spine. Smears were air-dried and stained with Giemsa. Trephine biopsy was done using a Jamshidi needle (core length 1–3 cm), touch imprints were prepared, and cores were fixed in 10% buffered formalin, decalcified, processed, paraffin-embedded, sectioned, and stained with haematoxylin–eosin. Perl's iron stain was performed on all aspirate smears.

Data Analysis

Data were analysed for demographic variables, clinical features, peripheral smear findings, and bone marrow aspiration/biopsy results.

RESULTS

A total of 190 patients with pancytopenia were studied, comprising 99 males (52.10%) and 91 females (47.89%) (male-to-female ratio: 1.08:1). The age range was 17–76 years, with the highest incidence in the 27–36-year group (28.94%), followed by 17–26 years (26.31%). [Table 1]

Table 1: Age and Sex Distribution of Study Subjects (n=190)

Age group (years)	Male [n (%)]	Female [n (%)]	Total [n (%)]
17–26	23 (12.10)	27 (14.21)	50 (26.31)
27–36	29 (15.26)	26 (13.68)	55 (28.94)
37–46	19 (10.00)	16 (8.42)	35 (18.42)
47–56	17 (8.94)	15 (7.89)	32 (16.84)
57–66	10 (5.26)	6 (3.15)	16 (8.42)
67–76	1 (0.52)	1 (0.52)	2 (1.05)
Total	99 (52.10)	91 (47.89)	190 (100)

Clinical Presentation

Generalized weakness was the most frequent presenting symptom (28.94%), followed by fever (16.31%). Pallor was the most common sign, observed in 108 patients (56.84%), followed by splenomegaly (11.57%), hepatomegaly (9.47%), jaundice (4.73%), bleeding manifestations (4.21%), and pedal edema (2.10%). [Table 2]

Table 2: Presenting Symptoms and Signs (n=190)

Presentation	n (%)
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Symptoms	
Generalized weakness	55 (28.94)
Fever	31 (16.31)
Respiratory symptoms	19 (10.00)
Abdominal pain	14 (7.36)
Signs	
Pallor	108 (56.84)
Splenomegaly	22 (11.57)
Hepatomegaly	18 (9.47)
Jaundice	9 (4.73)
Bleeding manifestations	8 (4.21)
Pedal edema	4 (2.10)

Hematological Parameters

Haemoglobin levels ranged from 1.5–7.0 g/dL, with more than half of the patients (51.05%) in the 5.1–7.0 g/dL range. Total leukocyte count (TLC) varied from 100–4,000/cu mm, with the majority (51.05%) between 1,001–2,500/cu mm. Platelet counts ranged from 1,000–1,50,000/cu mm, with severe thrombocytopenia (<50,000/cu mm) seen in 73.15% of patients. [Table 3]

Table 3: Hematological Parameters in Pancytopenia (n=190)

Parameter	Range	n (%)
Hb (g/dL)	1.5–3.0	40 (21.05)
	3.1–5.0	53 (27.89)
	5.1–7.0	97 (51.05)
TLC (/mm ³)	100–1000	39 (20.52)
	1001–2500	97 (51.05)
	2501–4000	54 (28.42)
Platelets (/mm ³)	<50,000	139 (73.15)
	51,000–1,00,000	41 (21.57)
	1,00,000–1,50,000	10 (5.26)

Peripheral Smear Findings

The predominant peripheral smear pattern was microcytic hypochromic (43.68%), followed by macrocytic (21.05%), dimorphic (18.94%), normocytic normochromic (14.73%), and normocytic hypochromic (1.57%). [Table 4]

Table 4: Peripheral Smear Findings (n=190)

Morphology	n (%)
Microcytic hypochromic	83 (43.68)
Macrocytic	40 (21.05)
Dimorphic	36 (18.94)
Normocytic normochromic	28 (14.73)
Normocytic hypochromic	3 (1.57)

Bone Marrow Findings

Bone marrow examination was performed in 58 patients. Hypercellular marrow was observed in 50.00% of cases, hypocellular in 27.58%, and normocellular in 22.41%. [Table 5]

Table 5: Bone Marrow Cellularity (n=58)

Cellularity	n (%)
Hypercellular	29 (50.00)
Hypocellular	16 (27.58)
Normocellular	13 (22.41)

The most common diagnosis was normal trilineage maturation (25.86%), followed by megaloblastic anaemia (18.96%), aplastic anaemia (17.24%), dimorphic anaemia (12.06%), and acute leukaemia (8.62%). Other causes included iron deficiency anaemia, metastatic malignancy, anaemia of pregnancy, haemophagocytic lymphocytosis, parvovirus B19 infection, haematolymphoid neoplasm, myelodysplastic syndrome (MDS), and ineffective haematopoiesis. [Figure 1 and Table 6]

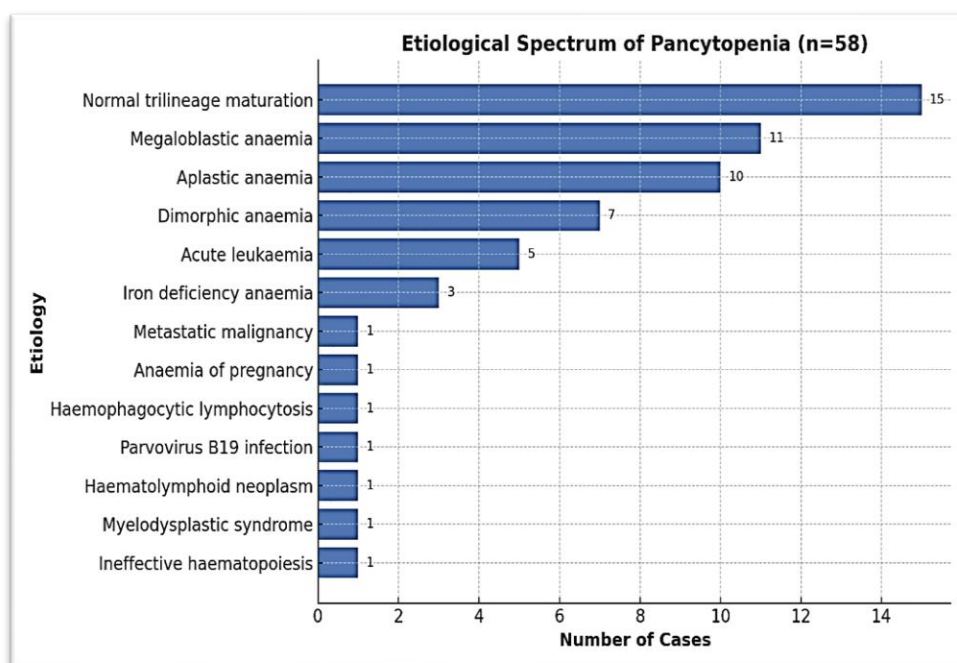


Figure 1: Etiological Spectrum of Pancytopenia (n=58)

Table 6: RBC Morphology by Final Diagnosis

Diagnosis	Dimorphic [n (%)]	Microcytic Hypochromic [n (%)]	Normocytic Normochromic [n (%)]	Normocytic Hypochromic [n (%)]	Macrocytic [n (%)]
Normal trilineage maturation (n=15)	2 (13.33)	5 (33.33)	5 (33.33)	1 (6.66)	2 (13.33)
Megaloblastic anaemia (n=11)	6 (54.54)	1 (9.09)	—	—	4 (36.36)
Aplastic anaemia (n=10)	1 (10.00)	—	9 (90.00)	—	—
Dimorphic anaemia (n=7)	3 (42.85)	4 (57.14)	—	—	—
Acute leukaemia (n=5)	—	2 (40.00)	2 (40.00)	—	1 (20.00)
Iron deficiency anaemia (n=3)	1 (33.33)	2 (66.66)	—	—	—

Etiology by Age and Sex

Megaloblastic anaemia, dimorphic anaemia, and aplastic anaemia predominated in the 27–36-year age group. MDS was more frequent in older patients (47–56 years), while metastatic malignancy occurred in the 57–66-year group. Slight male predominance was noted in megaloblastic anaemia, gender parity in aplastic anaemia, and female predominance in dimorphic anaemia, IDA, and acute leukaemia.

Clinical Features by Etiology

Pallor was the most common feature across all etiologies. In megaloblastic anaemia, pallor (90.90%) was followed by generalized weakness (63.63%) and fever (18.18%). Acute leukaemia presented with pallor and generalized weakness in all patients (100%), followed by bleeding manifestations (60%) and fever (40%). Splenomegaly was seen in all IDA cases.

RBC Morphology by Etiology

Dimorphic picture was seen in 54.54% of megaloblastic anaemia cases, 42.85% of dimorphic anaemia, and 13.33% of normal trilineage maturation. Macrocytosis was predominantly associated with megaloblastic anaemia (36.36%) and acute

leukaemia (20%). Normocytic normochromic morphology was seen in 90% of aplastic anaemia cases, while microcytic hypochromic picture predominated in IDA (66.66%) and dimorphic anaemia (57.14%).

Peripheral Smear Details in Megaloblastic Anaemia

Macroovalocytes were seen in all megaloblastic anaemia cases (100%), followed by teardrop cells (90.90%), hypersegmented neutrophils (63.63%), elliptocytes (45.45%), polychromasia (36.36%), and nucleated RBCs and Cabot rings (9.09% each).

Additional Peripheral Smear Findings

Across all etiologies, aniso-poikilocytosis and hypersegmented neutrophils were observed in 15.51% each, immature WBCs (including blasts) in 10.34%, sickle cells in 3.44%, and malignant cells, pro-erythroblasts, and reactive lymphocytes in 1.72% each.

DISCUSSION

Pancytopenia is a common yet clinically significant haematological condition encountered in tertiary care settings. It is not a diagnosis in itself but a haematological manifestation of a wide range of underlying pathologies. The current study comprehensively evaluated the clinical profile, peripheral smear, and bone marrow findings of adults presenting with pancytopenia, aiming to delineate its aetiological spectrum and to compare the results with previous studies conducted in India and other regions.

Clinical Presentation

In our study, the most frequent presenting symptoms were generalised weakness and fatigue, followed by fever and bleeding tendencies. These findings are consistent with the pathophysiological basis of pancytopenia: anaemia causing fatigue and pallor, leukopenia predisposing to recurrent or persistent infections, and thrombocytopenia leading to mucocutaneous bleeding. Similar symptom patterns have been reported by Santra & Das ⁽⁴⁾, Makheja et al. ⁽³⁾, and Agarwal et al. ⁽¹⁾, suggesting that this clinical triad remains a reliable indicator for suspecting pancytopenia in adults.

On physical examination, pallor was almost universally observed, followed by splenomegaly and hepatomegaly. Splenomegaly has been particularly associated with hypersplenism and chronic infections, whereas hepatomegaly may indicate underlying infiltrative or storage disorders. These organomegaly findings are in agreement with the work of Mansuri & Thekdi ⁽²⁾, who reported similar frequencies in a Western Indian population.

Aetiological Spectrum

The present study reaffirms the heterogeneity of pancytopenia causes in the Indian subcontinent. Megaloblastic anaemia emerged as the leading cause, followed by aplastic anaemia, haematological malignancies (including acute leukaemia and myelodysplastic syndromes), and hypersplenism. This distribution closely parallels that observed by Varma et al. ⁽⁶⁾ in Central India and by Agarwal et al. ⁽¹⁾ in North India, underlining that nutritional deficiencies, primarily folate and vitamin B₁₂ remain a major contributor despite improvements in dietary availability.

The ongoing prevalence of megaloblastic anaemia in our setting is likely due to dietary patterns that are low in animal proteins, insufficient folate supplementation, and unrecognized malabsorption syndromes. In contrast, studies from developed nations typically identify aplastic anaemia, myelodysplastic syndromes, or marrow infiltration by malignancies as the leading causes, emphasizing how nutritional, socio-economic, and environmental factors shape the pancytopenia profile.

Aplastic anaemia, the second most frequent cause in our series, represents a severe bone marrow failure syndrome with significant morbidity and mortality if untreated. The prevalence in our cohort is comparable to that reported by Makheja et al. ⁽³⁾, and its detection underscores the necessity of early bone marrow examination in cases with hypocellular marrow on aspiration.

Haematological malignancies were less frequent but remain clinically critical due to their aggressive course. Acute leukaemia was the most common malignant cause in our series, consistent with the literature. ⁽¹⁾

Peripheral Smear and Bone Marrow Correlation

Peripheral smear examination provided valuable preliminary diagnostic clues, such as macrocytosis in megaloblastic anaemia, circulating blasts in leukaemia, and pancytopenia with normocytic normochromic morphology in aplastic anaemia. However, bone marrow aspiration and trephine biopsy were indispensable for definitive diagnosis, as also emphasised by Agarwal et al. ⁽¹⁾ and Mansuri & Thekdi. ⁽²⁾

In our study, bone marrow aspiration provided better morphological detail, while trephine biopsy offered a more reliable assessment of cellularity and architecture, especially in cases of aplastic anaemia and myelofibrosis. The combined use of

both techniques enhanced the diagnostic yield, reinforcing the recommendation to perform both procedures in all cases of pancytopenia. ⁽²⁾

Demographic Distribution

We observed a male predominance and a peak incidence in the third and fourth decades of life, which is comparable to the findings of Santra & Das ⁽⁴⁾ and Varma et al. ⁽⁶⁾ Possible explanations for male predominance include gender-related healthcare-seeking behaviour, occupational exposure to environmental toxins, and referral bias. The exclusion of paediatric (<13 years) and elderly (>65 years) patients in our study may also have influenced age distribution.

Clinical Implications

The high proportion of reversible causes—particularly nutritional deficiencies—emphasises the importance of early detection and intervention. Pancytopenia due to megaloblastic anaemia often responds dramatically to vitamin supplementation, preventing long-term morbidity. On the other hand, early diagnosis of aplastic anaemia and haematological malignancies allows timely initiation of specific therapies such as immunosuppressive treatment or chemotherapy.

Comparison with Global Data

While the Indian data, including ours, highlight megaloblastic anaemia as the dominant cause, Western literature reports a higher incidence of bone marrow failure syndromes and haematological malignancies as aetiologies of pancytopenia. ^(7,8) This difference is attributable to socio-economic conditions, dietary habits, and healthcare accessibility, illustrating the importance of region-specific epidemiological studies in guiding diagnostic protocols.

CONCLUSION

This study highlights that pancytopenia in adults is caused by a wide range of factors. The most common diagnoses were normal trilineage maturation, megaloblastic anaemia, and aplastic anaemia. Among these, nutritional deficiency-related anaemias, especially megaloblastic and dimorphic types, were significant contributors, pointing to the need for preventive measures and early treatment. By comparing peripheral smear morphology with bone marrow aspiration and trephine biopsy results, the study emphasized the importance of accurate diagnosis, which allows for better-targeted treatment. Overall, the findings stress the value of a comprehensive clinicopathological approach to pancytopenia, ensuring timely identification of reversible causes and the start of effective treatment.

Conflict of Interest: The authors declare that there is no conflict of interest regarding the publication of this study.

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