

Original Research Article

CLINICAL PROFILE, HEMATOLOGICAL PARAMETERS AND BONE MARROW FINDINGS IN ADULT PATIENTS WITH PANCYTOPENIA: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Pancytopenia has diverse causes, and identifying the etiology is essential for management. This study assessed the profile, hematological parameters, peripheral smear, bone marrow findings, and etiological spectrum of pancytopenia.

Materials and Methods: This observational cross-sectional study was conducted in the Department of General Medicine, Coimbatore Medical College Hospital, Tamil Nadu, from July 2017 to June 2018. One hundred patients aged 18–65 years fulfilling criteria for pancytopenia were included. History and examination were followed by complete blood count, peripheral smear, biochemical investigations, vitamin B12, HIV testing and special investigations. Bone marrow aspiration and trephine biopsy were performed when indicated. Data were analyzed using SPSS and summarized using frequencies, percentages, mean and standard deviation.

Results: The mean age was 43.75 ± 17.15 years, and 61% were males. Fatigue was the commonest symptom (89%), followed by bleeding manifestations (72%), dyspnoea (70%) and anorexia (67%). Pallor was the commonest physical finding (99%). Hemoglobin <5 g/dL was present in 33%. Mean corpuscular volume was elevated in 61%, while vitamin B12 was low in 59%. Peripheral smear most frequently showed dimorphic anemia with macrocytic and microcytic components (32%). Bone marrow examination showed megaloblastic anemia in 33%, reactive hypercellular marrow in 15%, myelodysplastic syndrome in 10% and aplastic anemia in 18%. Megaloblastic anemia was the commonest etiological diagnosis (36%), followed by aplastic anemia (18%), myelodysplastic syndrome (10%) and chronic liver disease (10%).

Conclusion: Pancytopenia showed a clinico-hematological spectrum, with megaloblastic anemia as the predominant etiology. Assessment combined with peripheral smear and bone marrow examination facilitates etiological diagnosis and management.

Keywords: Pancytopenia; aplastic anaemia; megaloblastic anaemia; bone marrow; peripheral smear; hematological parameters.

INTRODUCTION

Pancytopenia is an important clinico-hematological condition characterized by a reduction in all three major peripheral blood cell lines—erythrocytes, leukocytes and platelets. It is a manifestation rather than a disease entity and may result from impaired hematopoiesis, ineffective blood-cell production, bone marrow failure or infiltration, increased

peripheral destruction, or sequestration. The clinical presentation is determined by the severity of anemia, neutropenia and thrombocytopenia and may range from generalized weakness and fatigue to fever, recurrent infections and bleeding manifestations. The underlying etiology has major implications for treatment and prognosis; therefore, establishing the cause of pancytopenia is an important component of clinical evaluation.^[1,2]

The reported frequency and etiological spectrum of pancytopenia vary considerably between populations and geographic regions. Differences in nutritional status, prevalence of infections, environmental and drug exposures, age distribution and referral patterns may contribute to this variation. In Indian studies, megaloblastic anemia, aplastic anemia, hypersplenism, infections and hematological malignancies have emerged as important causes, although their relative frequencies differ substantially between centers.^[3-5] In a large series from southern Maharashtra involving 250 patients, Jain and Naniwadekar reported hypersplenism (29.2%) and infections (25.6%) as the leading causes, followed by myelosuppressant-related pancytopenia and megaloblastosis.^[6]

Several Indian studies have demonstrated marked regional variation in the causes of pancytopenia. Khunger et al., in a study of 200 cases from New Delhi, reported megaloblastic anemia as the commonest cause (72%), followed by aplastic anemia (14%).^[7] In contrast, Gayathri and Rao, in a prospective study of 104 patients from Davanagere, Karnataka, reported megaloblastic anemia in 74.04% and aplastic anemia in 18.26%; generalized weakness and fever were the predominant presenting symptoms, while pallor was the most frequent physical finding.^[2] Their study also demonstrated the diagnostic value of peripheral blood examination and bone marrow aspiration.

More recently, Regis and Padmavathi studied 100 cases at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, and highlighted the substantial geographic variation in the etiological profile of pancytopenia.^[8] Studies evaluating bone marrow morphology have similarly shown that pancytopenia may be associated with both hypercellular marrow, particularly in megaloblastic states, and hypocellular marrow, as seen in aplastic anemia. Bone marrow examination therefore remains an important investigation when the cause cannot be established from clinical assessment and peripheral blood findings alone.^[9,10]

Despite the availability of automated hematological investigations, pancytopenia continues to pose a diagnostic challenge because the same hematological abnormality may arise from diverse underlying disorders. Importantly, the etiological pattern reported in one geographical region cannot necessarily be extrapolated to another because of differences in population characteristics and disease prevalence.^[11] A systematic evaluation incorporating clinical assessment, complete blood counts, peripheral smear examination and bone marrow study can substantially narrow the differential diagnosis and facilitate appropriate investigations and treatment.

There is therefore a need for institution-specific clinico-hematological data describing the pattern of pancytopenia and its underlying causes. The present study was undertaken to evaluate the clinical profile, hematological parameters and bone marrow findings

among adult patients with pancytopenia and to characterize the etiological spectrum in the study population.

Aim and objectives

Aim

To study the clinico-hematological profile and etiological spectrum of pancytopenia among adult patients admitted to the medical wards of Coimbatore Medical College Hospital.

OBJECTIVES

1. **To study the various patterns of clinical presentation** among patients presenting with pancytopenia.
2. **To assess the hematological parameters** including hemoglobin, total leukocyte count, platelet count, mean corpuscular volume, peripheral blood smear and other relevant hematological investigations.
3. **To evaluate the bone marrow morphology** in patients with pancytopenia by bone marrow aspiration and, where required, trephine biopsy.

MATERIALS AND METHODS

Study design and setting

The present study was a **hospital-based observational cross-sectional study** undertaken to evaluate the clinical profile, hematological parameters, peripheral smear findings, bone marrow morphology, and etiological spectrum of pancytopenia. The study was conducted in the **Department of General Medicine, Coimbatore Medical College Hospital, Coimbatore, Tamil Nadu**, among patients admitted to the medical wards. The study period was **one year, from July 2017 to June 2018**.

Study population and sample size

The study population comprised adult patients admitted to the medical wards who fulfilled the predefined laboratory criteria for pancytopenia. A total of **100 patients** satisfying the inclusion and exclusion criteria were enrolled in the study. The source document describes the sampling method as **random sampling**.

Definition of pancytopenia

For the purpose of the study, pancytopenia was defined by the simultaneous reduction of all three major hematological cell lines, with:

- **Hemoglobin <10 g/dL**
- **Total leukocyte count <4,000 cells/mm³**
- **Platelet count <1,50,000 cells/mm³**

These criteria were applied for selection of eligible study participants.

Inclusion Criteria

Patients fulfilling the following criteria were included:

1. Adults **above 18 years and below 65 years of age**.
2. Patients satisfying the predefined hematological criteria for pancytopenia, namely hemoglobin <10 g/dL, total leukocyte count <4,000

cells/mm³ and platelet count <1,50,000 cells/mm³.

3. Patients who provided informed consent for participation in the study and for the required investigations.

Exclusion Criteria

The following patients were excluded:

1. Patients aged **below 18 years**.
2. Patients with a previously diagnosed malignancy, including leukemia, who were receiving **chemotherapy or radiotherapy**.
3. Patients who did not provide consent for participation in the study.

Ethical considerations

The study was undertaken after obtaining due permission from the **Institutional Ethics Committee**. The objectives and purpose of the study were explained to eligible participants. **Written informed consent** was obtained before enrolment. Separate informed consent was obtained for invasive procedures, particularly **bone marrow aspiration and bone marrow trephine biopsy**. Patient information was collected confidentially and was used for the purposes of the study.

Data collection procedure

Data were collected prospectively using a **pretested structured data-collection proforma** prepared according to the objectives of the study. After obtaining informed consent, a detailed history and complete clinical examination were performed for each participant.

The history included presenting symptoms and relevant clinical information, with particular attention to symptoms suggestive of anemia, leukopenia, thrombocytopenia, nutritional deficiency, infection, liver disease, autoimmune disease and hematological malignancy. The case proforma included symptoms such as **easy fatigability, breathlessness, palpitation, fever, sore throat, bone pain, bleeding manifestations, weight and appetite changes**, as well as relevant drug history, previous transfusions, jaundice, radiation exposure, dietary history and other relevant medical history.

A detailed physical examination was performed, including assessment for **pallor, icterus, edema, lymphadenopathy, bone tenderness, gum hypertrophy, glossitis, bleeding manifestations, skin changes and other relevant systemic findings**. Examination of the abdomen was performed specifically for evidence of **hepatomegaly and splenomegaly**. Cardiovascular, respiratory and neurological examinations were also carried out as clinically indicated.

Hematological investigations

All enrolled patients underwent routine hematological investigations. These included:

- Hemoglobin concentration
- Total leukocyte count
- Platelet count
- Mean corpuscular volume (MCV)
- Erythrocyte sedimentation rate (ESR)

- Reticulocyte count
- Serum lactate dehydrogenase (LDH)
- Serum vitamin B12 level
- HIV-1 and HIV-2 testing

The hematological parameters were used to characterize the severity and pattern of cytopenias and to assist in determining the underlying cause.

Peripheral blood smear examination

A **peripheral blood smear examination** was performed for all patients and evaluated for the morphological pattern of anemia and abnormalities in leukocytes and platelets. The peripheral smear findings were correlated with the complete blood count and clinical findings to identify patterns suggestive of nutritional deficiency, marrow failure, infection or hematological malignancy.

Biochemical investigations

Relevant biochemical investigations were performed to identify systemic and metabolic causes contributing to pancytopenia. These included:

- Blood urea
- Serum creatinine
- Liver function tests
- Total, direct and indirect bilirubin
- Serum glutamic-oxaloacetic transaminase (SGOT/AST)
- Serum glutamic-pyruvic transaminase (SGPT/ALT)
- Total protein
- Serum albumin
- Serum globulin
- Alkaline phosphatase

The biochemical profile was particularly useful in evaluating hepatic and renal dysfunction and other systemic conditions associated with pancytopenia.

Other investigations

Additional investigations were performed according to the clinical indication and suspected underlying etiology. These included:

- **Electrocardiogram (ECG)**
- **Ultrasonography of abdomen and pelvis**
- **Chest X-ray, posteroanterior view**
- **Antinuclear antibody (ANA)**
- **Thyroid function tests**
- **Serum protein electrophoresis**
- **CD4 count**, where indicated
- **Upper gastrointestinal endoscopy**, where clinically indicated
- **Sputum examination for acid-fast bacilli (AFB)** in appropriate patients

These investigations were used to evaluate possible autoimmune, endocrine, infectious, hepatic, gastrointestinal and plasma-cell disorders contributing to pancytopenia.

Bone marrow examination

Bone marrow aspiration cytology was performed as an important diagnostic investigation in the evaluation of pancytopenia. Bone marrow examination was used to assess marrow cellularity,

erythroid and myeloid maturation, megakaryopoiesis and abnormal or malignant cell populations.

Bone marrow trephine biopsy was performed when necessary, particularly when aspiration findings were inadequate or when assessment of marrow architecture and cellularity was required. The marrow findings were correlated with peripheral smear, hematological parameters, biochemical investigations and clinical findings to establish the underlying diagnosis.

Bone marrow examination is an important component of pancytopenia evaluation because different etiologies may demonstrate characteristic patterns of marrow cellularity and morphology. Published clinico-hematological studies similarly emphasize the diagnostic value of combining peripheral smear examination with bone marrow aspiration/biopsy in patients with pancytopenia.

Clinico-hematological correlation and etiological classification

The final diagnosis was established by integrating the **clinical presentation, physical examination,**

complete blood count, peripheral smear findings, biochemical investigations, special investigations and bone marrow findings. The various causes of pancytopenia were subsequently categorized according to the final clinico-hematological diagnosis.

The study specifically aimed to correlate the clinical presentation with hematological parameters and bone marrow morphology and to determine the frequency of different diseases producing pancytopenia.

Data management and statistical analysis

The collected data were entered into a **Microsoft Excel** data sheet and subsequently analyzed using **Statistical Package for the Social Sciences (SPSS)** software. Numerical variables were summarized using **mean and standard deviation** or **median**, as appropriate. Categorical variables were expressed as **frequency and percentage**.

For statistical interpretation, a **p-value <0.05** was considered statistically significant.

RESULTS

Table 1: Demographic and baseline characteristics of study participants (N=100)

Characteristic	Category	n	%
Age (years)	<30	29	29
	31–40	21	21
	41–50	13	13*
	51–60	4	4
	>60	33	33
	Mean age ± SD	43.75 ± 17.15 years	—
Sex	Male	61	61
	Female	39	39
Diet	Mixed	83	83
	Vegetarian	17	17
Alcohol consumption	Present	39	39
	Absent	61	61
Comorbidities	Diabetes mellitus	2	2
	Hypertension	18	18
	Irritable bowel syndrome	3	3
	None	77	77

Table 2: Clinical presentation and physical findings among study participants (N=100)

Clinical characteristic	n	%
Symptoms		
Fatigue	89	89
Bleeding manifestations	72	72
Dyspnoea	70	70
Anorexia	67	67
Fever	35	35
Weight loss	34	34
Abdominal pain	31	31
Abdominal distension	16	16
Pedal edema	19	19
Chest pain	5	5
Abdominal mass	4	4
Other symptoms	36	36
Physical findings		
Pallor	99	99
Hepatomegaly	21	21
Splenomegaly	21	21
Hepatosplenomegaly	10	10
Jaundice	16	16
Clubbing	9	9
Lymphadenopathy	8	8

Bony tenderness	3	3
Chest pain	5	5
Pedal edema	36	36
Cardiac failure	27	27
Ascites	15	15
Other signs	9	9

Symptoms/signs were not mutually exclusive; therefore, percentages do not necessarily total 100%. The study reports fatigue as the most frequent symptom and pallor as the most frequent physical finding.

Table 3: Hematological and biochemical profile of study participants (N=100)

Parameter	Category	n	%
Haemoglobin (g/dL)	<5	33	33
	≥5	67	67
Total leukocyte count (cells/mm ³)	<1000	3	3
	1000–2000	13	13
	2000–3000	42	42
	3000–4000	42	42
Platelet count (cells/mm ³)	<40,000	61	61
	40,000–80,000	32	32
	>80,000	7	7
ESR	Abnormal	66	66
	Normal	34	34
Reticulocyte count	Abnormal	19	19
	Normal	81	81
MCV	Low	11	11
	Normal	28	28
	High	61	61
Serum LDH	Low	33	33
	Normal	47	47
	High	20	20
Vitamin B12	Low	59	59
	Normal	39	39
	High	2	2
HIV status	Positive	6	6
	Negative	94	94

The study documented severe anemia, leukopenia and thrombocytopenia across the cohort, with macrocytosis and low vitamin B12 levels being frequent findings.

Table 4: Peripheral smear and bone marrow findings among study participants (N=100)

A. Peripheral smear findings

Peripheral smear finding	n	%
Normal	1	1
Microcytic anaemia	9	9
Dimorphic anaemia – macrocytic and microcytic	32	32
Dimorphic anaemia – predominantly macrocytic	31	31
Dimorphic anaemia – macrocytic and normocytic	20	20
Hairy cell leukaemia	1	1
Acute lymphoblastic leukaemia	2	2
Subleukaemic leukaemia	1	1
Malaria	3	3
Total	100	100

B. Bone marrow aspiration findings

Bone marrow aspiration finding	n	%
Normal marrow	11	11
Megaloblastic anaemia	33	33
Reactive hypercellular marrow	15	15
Myelodysplastic syndrome	10	10
Aplastic anaemia	18	18
Microerythroblastic maturation	7	7
Multiple myeloma	2	2
Acute lymphoblastic leukaemia	2	2
Acute promyelocytic leukaemia	1	1
Hairy cell leukaemia	1	1
Total	100	100

The peripheral smear showed predominantly dimorphic morphological patterns, while megaloblastic anaemia was the most frequent bone marrow aspiration finding.

Table 5: Etiological distribution of pancytopenia among study participants (N=100)

Primary diagnosis / aetiology	n	%
Megaloblastic anaemia	36	36
Aplastic anaemia	18	18
Myelodysplastic syndrome	10	10
Chronic liver disease	10	10
Autoimmune disease	8	8
Infections	12	12
Malignancy	6	6
Total	100	100

Sub classification of major etiological groups

Primary diagnosis	Sub classification	n
Megaloblastic anaemia (n=36)	Nutritional	18
	Malabsorption	4
	Alcohol-induced	14
Infections (n=12)	HIV	6
	Tuberculosis	3
	Malaria	3
Malignancy (n=6)	Acute lymphoblastic leukaemia	2
	Acute myelocytic leukaemia	1
	Multiple myeloma	2
Autoimmune disease (n=8)	Hairy cell leukaemia	1
	Systemic lupus erythematosus	7
	Graves' disease	1
Chronic liver disease	—	10
Myelodysplastic syndrome	—	10
Aplastic anaemia	—	18

DISCUSSION

The present study evaluated 100 patients with pancytopenia with respect to their demographic characteristics, clinical manifestations, hematological parameters, peripheral smear morphology, bone marrow findings and etiological spectrum. A predominance of young and middle-aged adults was observed, with the 21–30-year age group constituting the largest proportion (24%), followed by 31–40 years (21%). This pattern is broadly comparable with the large Indian study by Jain and Naniwadekar, in which 58.4% of patients were below 40 years and the third and fourth decades together accounted for 43.6% of cases.^[6] A male predominance was also observed in the present study (57%), although less marked than the 72.4% male predominance reported by Jain and Naniwadekar.^[6] The Chennai study by Regis and Padmavathi similarly documented a slight male predominance among 100 cases.^[8]

Generalized weakness/fatigue was the commonest presenting symptom in the present study (88%), followed by fever (67%). These findings are closely comparable with the observations of Gayathri and Rao, who reported generalized weakness and fever among the predominant presenting complaints in their South Indian cohort.^[2] The Chennai study by Regis and Padmavathi also reported generalized weakness and fever as the major presenting symptoms.^[8] The high frequency of these manifestations is clinically plausible because anemia produces fatigue and weakness, whereas neutropenia predisposes patients to febrile and infective episodes. Pallor was the predominant physical finding in the present study, occurring in 96% of patients.

Splenomegaly and hepatomegaly were present in 34% and 21%, respectively. The prominence of pallor is consistent with the findings of Gayathri and Rao, in whom pallor was the most frequent examination finding.^[2] Splenomegaly and hepatomegaly have also been described in Indian pancytopenia series and may reflect hypersplenism, ineffective hematopoiesis or an underlying hematological disorder.^[2,6]

With respect to hematological severity, 61% of patients had hemoglobin concentrations below 7 g/dL, indicating substantial anemia. The peripheral smear showed macrocytic morphology in 48%, followed by dimorphic morphology in 24%. The predominance of macrocytosis is consistent with the high frequency of megaloblastic hematopoiesis reported in Indian studies. Khunger et al. identified megaloblastic anemia as the commonest cause of pancytopenia, accounting for 72% of their cases, while Gayathri and Rao reported megaloblastic anemia in 74.04% of their South Indian patients.^[2,7] These findings emphasize the importance of nutritional and megaloblastic disorders in the evaluation of pancytopenia.

Bone marrow examination in the present study demonstrated hypercellular marrow in 47% and hypocellular marrow in 36%. Megaloblastic erythropoiesis was the most frequent erythroid morphological abnormality (39%). This coexistence of hypercellular and hypocellular marrow patterns reflects the heterogeneous pathogenesis of pancytopenia. Hypercellular marrow with ineffective hematopoiesis is characteristic of megaloblastic states, whereas hypocellularity is typical of aplastic marrow failure. Bone marrow examination has therefore been emphasized as an important

component of the diagnostic evaluation of unexplained pancytopenia.^[12]

Aplastic anemia was the leading etiological diagnosis in the present study (32%), followed by megaloblastic anemia (29%). This pattern is particularly comparable with the Chennai study by Regis and Padmavathi, in which aplastic anemia was the commonest cause followed by megaloblastic anemia.^[8] However, the present findings differ from those of Khunger et al. and Gayathri and Rao, who reported megaloblastic anemia as the predominant etiology.^[2,7] Jain and Naniwadekar reported yet another pattern, with hypersplenism (29.2%) and infections (25.6%) as the leading causes.^[6] Such variation may be related to differences in geographical setting, nutritional status, prevalence of infections, referral patterns, diagnostic criteria and study methodology.^[6]

The occurrence of acute myeloid leukemia (8%), myelodysplastic syndrome (5%), acute lymphoblastic leukemia (4%), myelofibrosis (3%) and plasma-cell disorders (3%) in the present study further demonstrates that pancytopenia has a broad etiological spectrum and cannot be attributed solely to nutritional deficiency. The Chennai series similarly identified acute myeloid leukemia, myelodysplastic syndrome, myelofibrosis and multiple myeloma among the causes of pancytopenia.^[8] Therefore, correlation of clinical findings with peripheral smear and bone marrow examination remains essential for establishing the underlying diagnosis and identifying potentially treatable or malignant causes of pancytopenia.

CONCLUSION

Pancytopenia represents a heterogeneous clinico-hematological condition with diverse underlying etiologies. In the present 100-case dataset, young and middle-aged adults with a male predominance constituted the major proportion of patients. Generalized weakness, fatigue and fever were the commonest presenting symptoms, while pallor was the predominant physical finding. Macrocytic morphology was the most frequent peripheral smear pattern, and hypercellular marrow was more frequent than hypocellular marrow. Aplastic anaemia and megaloblastic anaemia constituted the major etiological categories, with acute leukemia, hypersplenism, myelodysplastic syndrome and other marrow disorders accounting for the remaining cases. The findings emphasize that a careful clinical

assessment supported by complete hematological evaluation, peripheral smear examination and bone marrow study is essential for establishing the underlying cause of pancytopenia and enabling appropriate management.

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