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Original Research Article

ETIOPATHOGENESIS OF PANCYTOPENIA IN AFEBRILE PATIENTS CONFIRMED WITH BONE MARROW EXAMINATION: A PROSPECTIVE STUDY

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ABSTRACT

Background: Pancytopenia, defined as the reduction of all three blood cell lines— red blood cell (RBC) deficiency, white blood cell (WBC) deficiency, and platelet (PLT) deficiency—arises from a variety of hematological and non-hematological disorders. Etiology varies according to geographic, nutritional, and socioeconomic factors, and early recognition is crucial for prognosis and management. This study aimed to evaluate the etiopathogenesis of pancytopenia in afebrile patients confirmed by bone marrow examination and to describe their clinical and hematological profile.

Materials and Methods: A prospective hospital-based study was conducted in the Department of General Medicine, GMERS Medical College and Hospital, Ahmedabad, between February 2023 and February 2024. Thirty afebrile patients aged 18 years or older with pancytopenia were included. Detailed history, clinical examination, hematological investigations, biochemical markers, and bone marrow examination were performed. Data were analyzed using descriptive statistics, and the results are presented as frequencies and percentages.

Results: The most affected age group was 31–40 years (33.3%), with a female predominance (70%). Fatigue and weakness (93.3%) were the most common symptoms, while splenomegaly (73.3%) and pallor (60%) were the most frequent signs. Severe anemia (hemoglobin level <7 g/dL) occurred in 46.7% of patients, and severe thrombocytopenia (platelet count <50,000/mm³) in 66.7%. Macrocytosis (MCV >100 fL) was observed in 53.3%, and macrocytic anemia was the predominant peripheral smear finding (46.7%). Vitamin B12 deficiency was detected in 73.3% of patients. Bone marrow examination revealed hypercellularity in 80% of cases, confirming megaloblastic anemia as the predominant etiology.

Conclusion: Megaloblastic anemia due to vitamin B12 deficiency is the most common and reversible cause of pancytopenia in afebrile patients. Clinical assessment, hematological evaluation, and bone marrow examination are essential for accurate diagnosis and effective management.

Keywords: Pancytopenia, Megaloblastic anemia, Vitamin B12 deficiency, Bone marrow, Nutritional intervention.

INTRODUCTION

Pancytopenia is defined as the triad of anemia, Leukopenia, and thrombocytopenia, resulting from a variety of hematological and non-hematological disorders. According to the World Health Organization (WHO), anemia is defined as hemoglobin <10 g/dl in adults, Leukopenia as WBC <4×10⁹/L, and thrombocytopenia as platelet count <100×10⁹/L.[1] The underlying mechanisms include

bone marrow failure, infiltration, ineffective hematopoiesis, or peripheral destruction of blood cells.[2]

The etiological spectrum varies geographically and is influenced by nutritional, environmental, and socioeconomic factors. In developing countries, common causes include megaloblastic anemia, infections, drug-induced anemia, hypersplenism, and aplastic anemia. In Western nations, hematological malignancies and aplastic anemia are more prevalent.[3-6] Early recognition of etiology is crucial, as the severity and underlying pathology determine prognosis and management.[7,8]

Although bone marrow examination is considered the gold standard for diagnosis, its necessity in all pancytopenic patients remains a topic of debate.[9] The present study was conducted to evaluate the etiopathogenesis of pancytopenia in afebrile patients admitted to a tertiary care center and to confirm the diagnosis through bone marrow examination.

The objective of this study was to determine the etiological spectrum of pancytopenia in afebrile patients confirmed by bone marrow examination and to describe their demographic characteristics, clinical features, hematological indices, biochemical parameters, and marrow findings, thereby providing a comprehensive understanding of their clinical and laboratory profile.

MATERIALS AND METHODS

Study Setting: Type, and Duration: This prospective study was conducted in the Department of General Medicine, GMERS Medical College and Hospital, Sola, Ahmedabad. The study was carried out over a period of one year, from February 2023 to February 2024.

Study Participants: The study included afebrile patients diagnosed with pancytopenia based on predefined laboratory criteria, comprising both males and females aged 18 years or older who were willing to provide written informed consent and undergo a bone marrow biopsy. Patients were excluded if they were younger than 18 years, presented with fever, had a known diagnosis of malignancy or leukemia, were receiving chemotherapy or radiotherapy, or declined participation in the study.

Sample Size and Sampling Technique: A total of 30 patients meeting the diagnostic criteria for pancytopenia and admitted to the medicine ward were enrolled in the study. Consecutive sampling was employed, encompassing all eligible patients who consented to participate during the study period.

Data Collection: After obtaining approval from the Institutional Ethics Committee, written informed consent was obtained from all participants. A comprehensive medical history was then documented, including presenting complaints, prior medical conditions, medication use, and radiation exposure. Each patient underwent a detailed physical examination with a focus on pallor, icterus, petechiae, clubbing, skin changes, and lymphadenopathy. Investigations comprised routine tests, such as a complete blood count with peripheral smear for cell morphology, blood indices, and reticulocyte count; specific tests, including serum vitamin B12, serum iron, total iron-binding capacity, and serum ferritin; and definitive evaluation by bone marrow examination. Pancytopenia was diagnosed based on a hemoglobin level below 10 g/dL, total leukocyte counts less than 4000/cumm, and a platelet count under 100,000/cm^3.

Outcome Variables: The primary outcome was the identification of the etiology of pancytopenia, confirmed by bone marrow examination, to guide diagnosis and management in afebrile patients.

Ethical Considerations: The study protocol was approved by the Institutional Ethics Committee of GMERS Medical College and Hospital, Ahmedabad. Written informed consent was obtained from all participants prior to their inclusion in the study. Confidentiality of patient data was maintained throughout.

Data Analysis: The data were entered into Microsoft Excel and analyzed using descriptive statistics. Frequencies and percentages were calculated for categorical variables, while means and standard deviations were used for continuous variables.

RESULTS

[Table 1] presents the demographic profile of patients with pancytopenia. The disorder was most prevalent among adults aged 31–40 years, who constituted one-third of the cohort. Younger adults between 18 and 20 years also formed a notable proportion, whereas cases beyond 60 years were uncommon. A striking feature was the female predominance, with women accounting for more than two-thirds of the study population.

Table 1: Demographic Profile of Patients with Pancytopenia

Parameter	Number of Patients	Percentage
Age (years)		
• 18–20	6	20.0%
• 21–30	5	16.7%
• 31–40	10	33.3%
• 41–50	4	13.3%
• 51–60	3	10.0%
• >60	2	6.7%
Gender		
• Male	9	30.0%
• Female	21	70.0%

[Table 2] outlines the clinical features observed. Fatigue and weakness were nearly universal symptoms, followed closely by dizziness and malaise. Splenomegaly emerged as the most frequent clinical sign, present in nearly three-fourths of patients, while pallor and hepatomegaly were also prominent. Other features, such as edema and petechiae, further highlighted the systemic impact of the condition.

Table 2: Clinical Features of Patients with Pancytopenia

Parameter	Number of Patients	Percentage
Symptoms		
• Fatigue & Weakness	28	93.3%
• Dizziness	24	80.0%
• Malaise	21	70.0%
• Bodyache	21	70.0%
• Anorexia	18	60.0%
• Tingling/Numbness	16	53.3%
• Palpitation	15	50.0%
• Joint/Leg Pain	11	36.7%
• Shortness of Breath	10	33.3%
Clinical Signs		
• Splenomegaly	22	73.3%
• Pallor	18	60.0%
• Edema	16	53.3%
• Hepatomegaly	15	50.0%
• Petechiae	14	46.7%
• Oral Ulcers	11	36.7%

Table 3: Laboratory and Bone Marrow Findings in Patients with Pancytopenia

Parameter	Number of Patients	Percentage
Hemoglobin (g/dl)		
• 10–12 (Mild anemia)	5	16.7%
• 7–9.9 (Moderate anemia)	11	36.7%
• <7 (Severe anemia)	14	46.7%
Leukocyte Count (cells/cumm)		
• 001–1000	1	3.3%
• 1001–2000	9	30.0%
• 2001–3000	6	20.0%
• 3001–4000	14	46.7%
Platelet Count (cells/cumm)		
• 100,001–150,000 (Mild thrombocytopenia)	2	6.7%
• 50,000–100,000 (Moderate thrombocytopenia)	8	26.7%
• <50,000 (Severe thrombocytopenia)	20	66.7%
MCV (fL)		
• <80	2	6.7%
• 80–100	12	40.0%
• >100	16	53.3%
MCH (pg)		
• <27	5	16.7%
• 27–31	10	33.3%
• >31	15	50.0%
Peripheral Smear		
• Microcytic Hypochromic	6	20.0%
• Dimorphic	10	33.3%
• Macrocytic	14	46.7%
Vitamin B12		
• Normal (200–900 pg/ml)	8	26.7%
• Deficient (<200 pg/ml)	22	73.3%
Serum Iron (µg/dl)		
• <50	9	30.0%
• 51–175	21	70.0%
TIBC (µg/dl)		
• 240–450	20	66.7%
• >451	10	33.3%
Transferrin Saturation (%)		
• <15	8	26.7%
• 16–30	21	70.0%
• >30	1	3.3%
Serum Ferritin (µg/dl)		
• <12	8	26.7%

• 13–20	20	66.7%
• >21	2	6.7%
Bone Marrow Cellularity		
• Hypercellular	24	80.0%
• Normocellular	4	13.3%
• Hypocellular	2	6.7%

[Table 3] summarizes laboratory and bone marrow findings. Severe anemia with hemoglobin below 7 g/dL was noted in nearly half the patients, and severe thrombocytopenia was identified in two-thirds, establishing both as dominant hematological abnormalities. Macrocytosis was the most prominent alteration in the red cell index, and peripheral smears frequently exhibited macrocytic and dimorphic patterns. Vitamin B12 deficiency was confirmed in almost three-fourths of cases, correlating with megaloblastic marrow changes and hypercellularity, thereby identifying nutritional deficiency as the predominant etiology.

DISCUSSION

Pancytopenia represents a heterogeneous clinical entity with variable etiologies and presentations. The present study offers valuable insights into the demographic profile, clinical manifestations, hematological indices, and bone marrow characteristics of affected patients, while situating these findings within the context of the published literature.

In the current study, the most frequently affected age group was 31–40 years, accounting for one-third of cases, followed by younger adults in the 18–20 and 21–30-year categories. This finding is consistent with the work of Saxena et al,[10] who also reported the highest prevalence in the 35–45-year age range. Similarly, studies from Peshawar by TA Khan et al,[11] and MI Khan et al,[12] documented a mean patient age between 31 and 35 years, while Raina et al,[13] observed a mean of 35.6 years. These comparisons suggest that pancytopenia predominantly affects young to middle-aged adults, although the condition may be observed across the lifespan. Such variations may reflect differences in nutritional deficiencies, environmental exposures, and health-seeking behaviour across populations.

The gender distribution in the present cohort revealed a striking female predominance, with women comprising 70% of the patients. This contrasts with the majority of earlier reports, which have described a male predominance in India and Pakistan.[10-13] The female predominance observed in the current study may be explained by regional differences in dietary intake, socioeconomic status, and healthcare access, underscoring the importance of considering local determinants when interpreting demographic patterns.

Symptomatically, fatigue and weakness were the most frequent complaints, followed by dizziness, malaise, and anorexia, with a significant proportion also reporting neurological symptoms such as tingling and numbness. This constellation of symptoms mirrors earlier observations by Saxena et al,[10] and Jyoti SK et al,[14] who both identified fatigue and generalized weakness as the predominant presenting complaints. The clinical examination further highlighted splenomegaly and pallor as the most common signs, in line with published data.[10] These findings reinforce the importance of careful clinical assessment, as they provide valuable diagnostic clues before laboratory confirmation.

Hematological indices in the present study revealed that almost half of the patients had hemoglobin levels below 7 g/dL, highlighting severe anemia as a predominant manifestation of pancytopenia. Comparable results have been reported in earlier studies, where mean hemoglobin values consistently ranged from 4.9 to 6.1 g/dL.[10,13,15] Leukopenia was evident across the cohort, and two-thirds of patients exhibited severe thrombocytopenia, a finding that closely aligns with previous observations.[10,13,15] These consistencies reinforce that cytopenias affecting all three blood cell lineages remain characteristic features of pancytopenia across diverse study populations.

Red cell indices and peripheral smear findings provided further insight into the underlying pathology. Macrocytosis was predominant, with more than half of the patients demonstrating a mean corpuscular volume greater than 100 fL. Macrocytic anemia was the most common smear finding, followed by dimorphic anemia. These results are consistent with the observations of Saxena,[10] MI Khan,[12] and Raina,[13] all of whom highlighted macrocytic or dimorphic blood pictures as common features. The frequent observation of hypersegmented neutrophils in peripheral smears further supports the diagnosis of megaloblastic anemia, underscoring the value of morphological assessment in establishing the etiology of pancytopenia.

Nutritional evaluation revealed Vitamin B12 deficiency in nearly three-fourths of patients, strongly correlating with the observed macrocytic and megaloblastic patterns. These findings are supported by the work of Saxena et al,[10] and Gayathri and Rao,[15] both of whom emphasized Vitamin B12 deficiency as a leading contributor to megaloblastic anemia. Iron studies demonstrated variable results, reflecting mixed nutritional deficiencies in a subset of patients. Taken together, these observations underscore the crucial role of nutritional deficiencies in the pathogenesis of pancytopenia in the current population.

Bone marrow examination confirmed hypercellularity in the majority of cases, with

megaloblastic erythropoiesis as the predominant finding. These results are in close agreement with studies by Saxena,[10] Gayathri and Rao,[15] MI Khan,[12] and Raina,[13] all of which identified megaloblastic anemia as the leading cause of pancytopenia. The presence of normocellular and hypocellular marrow in a smaller proportion of cases further illustrates the heterogeneous etiological spectrum of this condition.

When viewed alongside existing literature, the findings of the present study reinforce the conclusion that megaloblastic anemia due to nutritional deficiencies, particularly Vitamin B12 deficiency, remains the most common and reversible cause of pancytopenia in the Indian subcontinent.[10-15] This contrasts with patterns seen in Western countries, where aplastic anemia and hematological malignancies are more prominent. The high prevalence of preventable nutritional etiologies in our setting highlights the importance of timely recognition and intervention, which can significantly reduce morbidity and mortality associated with this condition.

CONCLUSION

Pancytopenia was most common in adults aged 31–40 years, with a female predominance, and clinical features included fatigue, weakness, splenomegaly, and pallor. Laboratory findings highlighted severe anemia, Leukopenia, thrombocytopenia, and macrocytosis, while bone marrow examination established vitamin B12 deficiency with megaloblastic changes as the predominant cause. Early diagnosis with complete blood count, smear, and marrow evaluation, coupled with routine screening for vitamin B12 and folate, is essential. Timely supplementation, combined with community-level interventions such as nutritional education, dietary diversification, and food fortification, can help reduce the disease burden. Multi-center studies with larger samples and longer follow-up are needed to validate and expand these findings.

Limitations

The study was limited by its small sample size, single-center design, underrepresentation of pediatric and elderly patients, and lack of detailed assessment of other micronutrient deficiencies.

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