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Original Research Article

Retrospective Evaluation of the Etiological Spectrum and Bone Marrow Findings in Patients with Pancytopenia

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Abstract:

Background: Pancytopenia is a clinically important hematological abnormality resulting from diverse underlying conditions ranging from nutritional deficiencies to bone marrow failure and hematological malignancies. Bone marrow examination plays an important role in establishing the underlying cause.

Aim: To retrospectively evaluate the etiological spectrum and bone marrow findings among patients presenting with pancytopenia.

Methodology: A retrospective observational study was conducted in the Department of Pathology, RDJM Medical College and Hospital, Turki, Muzaffarpur, Bihar, India, from March 2025 to February 2026. A total of 85 patients with documented pancytopenia who underwent hematological and bone marrow evaluation were included. Clinical records, complete blood counts, peripheral blood smear findings, and bone marrow morphology were reviewed and analyzed descriptively.

Result: Females constituted 62.35% of cases, with the 31–40-year age group being most frequent (23.53%). Macrocytic/megaloblastic morphology was predominant on peripheral smear (47.06%). Bone marrow was hypercellular in 56.47% of cases. Megaloblastic anemia was the leading etiology (52.94%), followed by aplastic anemia (12.94%) and acute leukemia (8.24%).

Conclusion: Pancytopenia has a heterogeneous etiological spectrum, and combined peripheral smear and bone marrow evaluation is valuable for establishing the underlying diagnosis.

Keywords: Pancytopenia, Bone marrow, Megaloblastic anemia, Aplastic anemia, Peripheral smear, Hematological disorders.

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Introduction

Pancytopenia is an important hematological disorder that is defined by the simultaneous decrease of the three main blood cell types, namely erythrocytes, leukocytes, and platelets, leading to anemia, leukopenia, and thrombocytopenia, respectively. It is not a disease in its own right but a symptom of a number of pathological conditions that affect the production, maturation or survival of the different types of hematopoietic cells. Pancytopenia may be a manifestation of a number of different pathological processes, such as nutritional deficiencies, bone marrow failure, hematological malignancies, myelodysplastic syndromes, infections, hypersplenism, liver disease and other systemic disorders [1]. The importance of pancytopenia is that when you have one, the cause can be something as simple as a nutritional deficiency that can be easily corrected, or it can be one of the serious, potentially life-threatening bone marrow disorders.

Accordingly, it is important to determine the underlying cause for proper treatment and prognosis. The symptoms of pancytopenia vary greatly according to the duration and severity of the individual cytopenia. A patient with leukemia may develop anemia which can lead to generalized weakness, fatigue, pallor, dizziness and exertional dyspnea, while leukopenia can make the patient sensitive to recurrent infection and fever. Petechiae, purpura, and mucosal bleeding, as well as other hemorrhagic features, are possible manifestations of thrombocytopenia [2]. Besides these symptoms, hepatomegaly and splenomegaly can also occur in patients with underlying hematological malignancies, infections, liver diseases or hypersplenism. Laboratory investigation is a key tool in determining the cause of pancytopenia, as clinical presentation may be rather nonspecific.

The etiologies of pancytopenia are different from population to population and region to region. In developing countries, vitamin B12 deficiency and folate deficiency are major causes, with dietary deficiencies and malabsorption adding to the ineffective hematopoiesis [3]. Megaloblastic anemia is hence one of the most common causes of pancytopenia reported in a few Indian studies. The ineffective hematopoiesis is caused by impaired DNA synthesis in vitamin B12 or folate deficiency and is characterized by peripheral blood and bone marrow morphological abnormalities. The appearance of peripheral blood may include macro cytosis, macro-ovalocytes, anisopoikilocytosis, and the presence of hyper segmented neutrophils; bone marrow analysis usually will show erythroid hyperplasia with megaloblastic maturation [4]. In contrast, aplastic anemia is a hypocellular bone marrow (with fat replacing the hematopoietic tissue) due to the failure of function of the hematopoietic stem-cell. It is an important differential diagnosis in those patients with pancytopenia and should be distinguished from other causes of marrow hypoplasia.

Pancytopenia may also be caused by replacement or suppression of normal hematopoiesis and ineffective blood cell production in other marrow disorders, such as acute leukemia and myelodysplastic syndromes. Other diseases of marrow, such as infiltrative disorders, can also lead to a decrease in blood cells [5]. Therefore, assessment of the bone marrow is especially crucial where the peripheral blood findings do not provide a definite diagnosis. A complete blood count and peripheral blood smear examination are performed in the initial laboratory evaluation of pancytopenia. These investigations will help to establish the presence of cytopenia and may be helpful to determine important clues about the cause. Peripheral smear findings, however, cannot always distinguish nutritional deficiency, marrow failure, leukemia, myelodysplasia, and other hematologic disorders. Thus, the aspiration and biopsy of bone marrow have an important role in diagnosis of patients with unexplained pancytopenia where it allows to directly inspect marrow cellularity, erythroid and myeloid maturation, megakaryopoiesis, abnormal cell populations, dysplastic changes and marrow infiltration [6].

Peripheral blood morphology can then give a conclusive or very suggestive diagnosis if the peripheral blood is inconclusive, and bone marrow morphology can give a definitive diagnosis in cases where the peripheral blood is not conclusive. Bone marrow cellularity is particularly useful in differentiating various causes of pancytopenia. Increased numbers of cells are present in the marrow of megaloblastic anemia and other disorders of ineffective hematopoiesis, while decreased numbers of cells are present in the marrow of aplastic anemia. In systemic and hematological diseases, normocellular marrow can be found. Hypercellular marrow was found in 60%, normocellular in 28%, and hypocellular in 12% of patients with pancytopenia in a study of 100 patients. In the same study, the most common causes were megaloblastic anemia (58%) followed by aplastic anemia (12%), cirrhosis of liver (8%), leukemia (6%) and dengue, myelodysplastic syndrome and malaria (4% each) [7]. These results show that there is a large variability between the different disorders that can be associated with pancytopenia. In previous studies, significant differences in the relative frequencies of individual etiologies have also been reported.

Some studies have concluded that megaloblastic anemia is the main cause, while others suggest that hematological malignancies, hypo splenism, infections or aplastic anemia were the main factors [8]. These disparities could be associated with geographical variation, nutritional status, environmental exposures, the prevalence of infectious diseases, and/or the types of study populations. Therefore, it is necessary to assess the local etiological spectrum associated with the pattern of pancytopenia in the specific health care environment. The bone marrow is an additional tissue that can be useful for diagnosing serious underlying hematological disorders. In acute leukemia, abnormal blast populations, in myelodysplastic syndromes, dysplastic changes, in nutritional anemia, megaloblastic changes, and in aplastic anemia, marked hypocellularity can be demonstrated using morphological assessment. Thus, the systematic evaluation of these bone marrow features could help to increase diagnostic accuracy and help to plan the appropriate management [9]. It is important to locate the potentially reversible causes early, especially nutritional deficits and some infections, for early treatment can lead to a hematological recovery.

The present study was conducted with the above purpose in mind and in view of the various etiological spectrum and importance of bone marrow examination in diagnosis therefore the study was undertaken to evaluate etiological spectrum and bone marrow findings of patients with Pancytopenia retrospective evaluation of the same in RDJM Medical College and Hospital, Turki, Muzaffarpur, Bihar, India. The study will focus on the major underlying causes to be identified and the corresponding patterns of hematological and bone marrow morphologies to be recorded. This regional evaluation could be helpful for understanding the major etiologies of pancytopenia in the study population and highlight the role of bone marrow examination in evaluating the patient with this important hematological abnormality.

Methodology

Study Design: The present study was designed as a retrospective observational study to evaluate the

etiological spectrum and bone marrow findings among patients presenting with pancytopenia. The study involved retrospective analysis of available clinical, hematological, peripheral blood smear, and bone marrow examination records of eligible patients diagnosed with pancytopenia during the defined study period.

Study Area: The study was conducted in the Department of Pathology, RDJM Medical College and Hospital, Turki, Muzaffarpur, Bihar, India.

Study Duration: The study covered a period of one year, from March 2025 to February 2026.

Sample Size: A total of 85 patients (N = 85) diagnosed with pancytopenia and fulfilling the predefined inclusion criteria were included in the study.

Sample Population: The study population comprised patients presenting with pancytopenia who underwent hematological evaluation and bone marrow examination during the study period. Patients of both sexes and different age groups were included. The study population consisted of cases in which relevant clinical, hematological, peripheral blood smear, and bone marrow findings were available for evaluation.

Data Collection: Data were collected retrospectively from patient records, complete blood count reports, peripheral blood smear reports, bone marrow aspiration/biopsy records, and pathology registers maintained during the study period. Relevant demographic and clinical information, including age, sex, presenting complaints, and relevant examination findings, was recorded. Hematological parameters including hemoglobin level, total leukocyte count, platelet count, and peripheral smear findings were documented where available. Bone marrow findings such as cellularity, erythroid and myeloid series, megakaryocytes, abnormal cell populations, maturation patterns, and other relevant morphological features were recorded. The final etiological diagnosis of pancytopenia was documented based on the available clinical, hematological, peripheral smear, and bone marrow findings.

Inclusion Criteria

- Patients diagnosed with pancytopenia involving all three peripheral blood cell lines.

Patients evaluated during the study period March 2025 to February 2026.

- Patients of either sex or all eligible age groups.
- Patients with available complete blood count and peripheral blood smear findings.
- Patients who underwent bone marrow aspiration and/or biopsy examination.
- Patients with adequate clinical and hematopathological records for assessment of the underlying etiology.

Exclusion Criteria

- Patients with incomplete or insufficient clinical and laboratory records.
- Cases in which essential bone marrow examination findings were unavailable or non-interpretable.
- Duplicate records of the same patient.
- Cases outside the defined study period.
- Patients in whom pancytopenia could not be confirmed from the available hematological records.
- Cases with inadequate clinical or morphological information for determining the underlying etiology.

Procedure: All records of patients diagnosed with pancytopenia between March 2025 to February 2026. were identified from the pathology and hematology records and screened according to the predefined eligibility criteria. Available complete blood count and peripheral blood smear findings were reviewed to confirm the presence of pancytopenia and to identify preliminary morphological clues regarding its etiology. Bone marrow aspiration and, where available, biopsy findings were subsequently reviewed with emphasis on marrow cellularity, erythropoiesis, granulopoiesis, megakaryopoiesis, maturation abnormalities, blast population, dysplastic changes, abnormal infiltrates, and other relevant morphological features. Based on the combined clinical, hematological, peripheral smear, and bone marrow findings, cases were classified into appropriate etiological categories such as megaloblastic anemia, aplastic anemia, leukemia, myelodysplastic syndrome, infections, hypersplenism, and other identified causes. The overall distribution of etiologies and associated bone marrow patterns was then evaluated.

Statistical Analysis: The collected data were entered into a structured database and analyzed using descriptive statistical methods. Continuous variables such as age, hemoglobin, total leukocyte count, and platelet count were summarized using mean ± standard deviation or median with range, as appropriate. Categorical variables such as sex, clinical presentation, peripheral smear findings, bone marrow cellularity, morphological diagnosis, and etiological category were expressed as frequencies and percentages. The distribution of different causes of pancytopenia and their corresponding bone marrow findings was calculated and presented using tables and figures. Where appropriate, associations between categorical variables were assessed using the chi-square test or Fisher's exact test. A p-value <0.05 was considered statistically significant".

Result

Table 1 shows the age- and sex-wise distribution of the 85 patients with pancytopenia. Females

constituted the majority of the study population, with 53 (62.35%) cases, while males accounted for 32 (37.65%) cases. The highest number of patients belonged to the 31–40 years age group, comprising 20 (23.53%) cases, followed by the 21–30 years group with 17 (20.00%) cases and the 41–50 years group with 15 (17.65%) cases. Patients aged ≤20 years accounted for 12 (14.12%) cases, while 11 (12.94%) and 10 (11.76%) cases were observed in the 51–60 years and >60 years groups, respectively. Overall, pancytopenia was more frequently observed among females, with the greatest proportion of patients occurring in the 31–40 years age group

Table 1: Age- and Sex-wise Distribution of Patients with Pancytopenia (N=85)

Age Group (years)	Male, n (%)	Female, n (%)	Total, n (%)
≤20	5 (5.88)	7 (8.24)	12 (14.12)
21–30	6 (7.06)	11 (12.94)	17 (20.00)
31–40	7 (8.24)	13 (15.29)	20 (23.53)
41–50	6 (7.06)	9 (10.59)	15 (17.65)
51–60	5 (5.88)	6 (7.06)	11 (12.94)
>60	3 (3.53)	7 (8.24)	10 (11.76)
Total	**32 (37.65)**	**53 (62.35)**	**85 (100)**

Table 2 presents the distribution of patients according to their hematological parameters. Regarding hemoglobin levels, the largest proportion of patients, 38 (44.71%), had hemoglobin levels between 5–7 g/dL, followed by 27 (31.76%) patients with levels above 7 g/dL and 20 (23.53%) with severe anemia having hemoglobin below 5 g/dL. For total leukocyte count, 42 (49.41%) patients had counts between 2,000–3,000/µL, while 19 (22.35%) had counts below 2,000/µL and 24 (28.24%) had counts above 3,000/µL. Regarding platelet counts, the majority, 46 (54.12%) patients, had platelet counts between 20,000–50,000/µL, followed by 21 (24.71%) with counts above 50,000/µL and 18 (21.18%) with counts below 20,000/µL. Thus, moderate-to-severe reductions in all three hematological parameters were commonly observed among the study participants.

Table 2: Distribution of Patients According to Hematological Parameters (N=85)

Hematological Parameter	Category	No. of Cases	Percentage (%)
Hemoglobin	<5 g/dL	20	23.53
	5–7 g/dL	38	44.71
	>7 g/dL	27	31.76
Total Leukocyte Count	<2,000/µL	19	22.35
	2,000–3,000/µL	42	49.41
	>3,000/µL	24	28.24
Platelet Count	<20,000/µL	18	21.18
	20,000–50,000/µL	46	54.12
	>50,000/µL	21	24.71

Table 3 demonstrates the peripheral blood smear findings among the 85 patients with pancytopenia. A macrocytic/megaloblastic blood picture was the most common finding, observed in 40 (47.06%) cases. This was followed by a normocytic normochromic picture in 18 (21.18%) cases and a dimorphic anemia pattern in 10 (11.76%) cases. A microcytic hypochromic picture was observed in 7 (8.24%) patients. Abnormal or blast cells were identified in 6 (7.06%) cases, while a leukoerythroblastic picture was observed in 4 (4.71%) cases. The predominance of macrocytic/megaloblastic morphology suggests that nutritional or megaloblastic processes constituted an important component of the pancytopenia spectrum in the present study.

Table 3: Peripheral Blood Smear Findings in Patients with Pancytopenia (N=85)

Peripheral Smear Finding	No. of Cases	Percentage (%)
Macrocytic/Megaloblastic picture	40	47.06
Normocytic normochromic picture	18	21.18
Dimorphic anemia	10	11.76
Hypocytic hypochromic picture	7	8.24
Abnormal/blast cells	6	7.06
Leukoerythroblastic picture	4	4.71
Total	**85**	**100**

Table 4 presents the distribution of patients according to bone marrow cellularity. Hypercellular marrow was the most frequent finding, observed in 48 (56.47%) cases, followed by normocellular marrow in 25 (29.41%) cases. Hypocellular marrow was identified in 12 (14.12%) patients. The predominance of hypercellular marrow indicates that ineffective or abnormal hematopoiesis was more frequently encountered than marrow aplasia in the present study. The relatively smaller proportion of hypocellular marrow findings may correspond to the lower frequency of aplastic marrow disorders among the evaluated cases.

Table 4: Bone Marrow Findings According to Cellular Pattern (N=85)

Bone Marrow Finding	No. of Cases	Percentage (%)
Hypercellular marrow	48	56.47
Normocellular marrow	25	29.41
Hypocellular marrow	12	14.12
Total	**85**	**100**

Table 5 shows the etiological spectrum of pancytopenia based on hematological and bone marrow findings. Megaloblastic anemia was the most common etiology, accounting for 45 (52.94%) of the 85 cases, followed by aplastic anemia in 11 (12.94%) cases. Acute leukemia was identified in 7 (8.24%) cases, while hypersplenism accounted for 6 (7.06%) cases. Myelodysplastic syndrome was diagnosed in 5 (5.88%) patients, whereas infectious causes and nutritional/other anemias each accounted for 4 (4.71%) cases. Other marrow disorders were identified in 3 (3.53%) cases. Thus, the etiological distribution indicates that megaloblastic anemia was the predominant cause of pancytopenia, while aplastic anemia and hematological malignancies constituted other important diagnostic.

Table 5: Etiological Spectrum of Pancytopenia Based on Bone Marrow and Hematological Findings (N=85)

Etiological Diagnosis	No. of Cases	Percentage (%)
Megaloblastic anemia	45	52.94
Aplastic anemia	11	12.94
Acute leukemia	7	8.24
Hypersplenism	6	7.06
Myelodysplastic syndrome	5	5.88
Infectious causes	4	4.71
Nutritional/other anemia	4	4.71
Other marrow disorders	3	3.53
Total	**85**	**100**

Discussion

In the present retrospective study, 85 patients with pancytopenia were studied and it was observed that there was a predominance of females (62.35%) and that the 31–40-year age group had the highest incidence (23.53%). The demographic distribution of this population suggests that pancytopenia was more commonly seen in the younger and middle-aged adult population in the current study. Chandan and Giriyan (2018) reported a similar age-group distribution of young adults with 40% of pancytopenic patients being in the age range of 21-30 years [10]. In contrast, Yokuş and Gedik (2016) reported that pancytopenia occurred more commonly in older individuals with a greater proportion of individuals ≥65 years old (67%) [11]. This difference could be explained by differences in the referral rates, population characteristics, nutritional status and the underlying etiological profile of pancytopenia".

Based on the hematological profile, in the present study, 44.71% of the patients presented with hemoglobin levels of 5-7 g/dL and 23.53% of the patients had severe anemia with hemoglobin being less than 5 g/dL. Likewise, total leukocyte counts of 2,000-3,000/µL were seen in 49.41% of patients and platelets count of 20,000-50,000/µL were seen in 54.12% of the patients. These results show that there is a significant decrease in all three blood cell lines. Sharma et al. stressed the varying grade of cytopenia in the pancytopenic patients and found that 96.9% had pallor which indicated the clinical significance of severe anemia [12]. The relatively high percentage of patients with moderate to severe anaemia in the present study may relate to delayed presentation or referral of patients with known hematological abnormalities. Peripheral blood smear examination showed macrocytic/megaloblastic picture in 47.06% of cases, and it was the most common morphological pattern. 21.18% showed normocytic normochromic morphology, 11.76% showed dimorphic anemia and 8.24% showed microcytic hypochromic morphology. In this predominance of macrocytic

morphology, nutritional and megaloblastic disorders are important causes of pancytopenia.

A significant association between cobalamin and folate deficiency with pancytopenia has been shown among adults from North India by Premkumar et al. (2012) [13]. They conclude that the findings agree with the observation that nutritional deficiency should be considered as an important underlying cause if macrocytosis and megaloblastic morphology are seen in the blood picture. In the present study, hypercellular marrow was observed in 56.47%, normocellular marrow in 29.41% and hypocellular marrow in 14.12% of the cases as observed by bone marrow examination. The hypercellular marrow predominance is typical of disorders of ineffective hematopoiesis, especially megaloblastic anemia. Shah et al. 2017 highlighted the significance of the bone marrow examination in pancytopenia and showed that the morphology of marrow may be useful to differentiate the nutritional, aplastic and malignant causes [14]. The incidence of hypocellular marrow, as was observed in the present study, is similar to the incidence of aplastic anemia (smaller than megaloblastic anemia).

Etiological analysis revealed the highest incidence was megaloblastic anemia (45/85, 52.94%). This result corroborates the findings from Gandhi et al. in their retrospective study of bone marrow examination and clinical records who identified megaloblastic anemia as one of the important causes of pancytopenia [15]. Another finding of a predominance of megaloblastic anemia in the present study is the high prevalence of macrocytic/megaloblastic peripheral smear and hypercellularity in bone marrow. The present population study indicates that the deficient nutritional status was a major factor in causing pancytopenia, due to ineffective hematopoiesis. Aplastic anemia was the second most common etiology in the present study (12.94%). This prevalence is similar to that observed by Porwal et al. in 100 pancytopenic patients (12%) [16]. But, in contrast, Dasgupta et al. (2015) have reported pancytopenia as most common cause of aplastic anemia followed by leishmaniasis, hypersplenism, tuberculosis, and connective tissue disorders [17]. The geographic and population-specific variation of the etiological spectrum of pancytopenia is emphasized by such differences. In the current study, the percentage of acute leukemia patients was 8.24% and the percentage of myelodysplastic syndrome patients was 5.88%.

These results suggest that malignant and clonal marrow diseases were major causes, but not common, of pancytopenia. Similarly, Chandra et al. (2019) highlighted the significance of bone marrow examination in the diagnosis of hematological disorders among pancytopenic patients [18]. The identification of abnormal blast populations and dysplastic changes by marrow examination is especially relevant as these conditions are likely to require early diagnosis and specific treatment. Hypersplenism (7.06%), infection (4.71%), nutritional/other anaemia (4.71%) and other marrow disorders (3.53%) were other etiologies seen in the present study. Makheja et al. (2013) also found pancytopenia can occur due to a variety of nutritional, hematological, hepatic, infectious and systemic conditions [19].

In conclusion, the present study shows that pancytopenia is a disease with a multitude of different underlying causes, but that the most common cause was megaloblastic anemia, and the most common marrow pattern was hypercellular marrow. The results highlight that all three tests (CBC, peripheral smear and BM evaluation) should be combined to determine the underlying pathogenesis and provide proper treatment for patients with pancytopenia.

Conclusion

The present retrospective study of 85 patients showed that the etiological spectrum of pancytopenia is very broad with female predominance (62.35%) and age group 31-40 years (23.53%). The most common etiology was megaloblastic anemia (52.94%), followed by aplastic anemia (12.94%), acute leukemia (8.24%), hypersplenism (7.06%) and myelodysplastic syndrome (5.88%). Macrocytic/megaloblastic was the most common peripheral smear pattern (47.06%) and hypercellular bone marrow was the most common marrow pattern (56.47%). The results highlight the need to systematically evaluate complete blood count, peripheral smear examination and bone marrow evaluation for proper diagnosis of the underlying cause of pancytopenia and timely management. Knowing that potentially reversible causes such as megaloblastic and nutritional disorders exist early in the course of the disease may help attain a better hematological recovery and patient outcomes. The study also stresses the importance of bone marrow examination in distinguishing between the various causes of pancytopenia, such as nutritional, marrow failure, infectious and malignant conditions.

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