

Etiological Spectrum of Bone Marrow and Trephine Biopsy in Patients Presenting with Pancytopenia and Bicytopenia: A Retrospective Analysis (2016-2024)

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Abstract

Background: The etiological spectrum varies across different populations due to geographic, socioeconomic, and disease-related factors. However, data describing the underlying causes of cytopenias in the local Pakistani population remain limited, making it difficult to establish region-specific diagnostic priorities.

Objective: To determine the etiological spectrum of pancytopenia and bicytopenia in patients undergoing bone marrow biopsy at a tertiary care hospital.

Methods: This retrospective study was conducted at the Civil Hospital, Karachi, Pakistan. We reviewed the bone marrow biopsy records of patients presenting with bicytopenia and pancytopenia between January 2016 and June 2024. A total of 200 cases were included in this study. Cytopenias were defined as hemoglobin <10 g/dL, a total leukocyte count <4,000/mm³ and a platelet count <150 × 10⁹/L. Data were analyzed using SPSS version 24.0 and summarized using descriptive statistics.

Results: Out of 200 patients, 172 (86%) had bicytopenia and 28 (14%) had pancytopenia, with a male predominance. The mean age was 24.8 years. Males were more frequently affected, and the male-to-female ratio was 1.04. Fever, 131 (65.5%), Pallor, 35 (17.5%), bleeding, 33 (16.5%), and splenomegaly, 31 (15.5%) were the most frequent presentations of bicytopenia and pancytopenia. The etiological spectrum showed that aplastic anemia was present in 43 (21.5%) of the cases, followed by acute leukemia in 26 (13.0%) and megaloblastic anemia in 21 (10.5%).

Conclusion: The most common cause of cytopenia was found to be aplastic anemia, followed by acute leukemia and megaloblastic anemia.

Key words: Bone marrow biopsy, bicytopenia, pancytopenia.

Introduction

In the peripheral blood, cytopenias reflect a reduction in any of the cellular components, namely white blood cells, red blood cells, or

platelets. Peripheral blood cytopenias were defined as hemoglobin <10 g/dL, TLC <4,000/mm³, or platelets <150 × 10⁹/L. In many cases, more than one cell line is reduced, which is termed bicytopenia, while a reduction in all three cell lines is called pancytopenia.^{1,2}

The etiology of cytopenias is variable; bicytopenia and pancytopenia can be caused by viral infections, nutritional deficiencies, and marrow infiltration.³ To determine the etiology behind bicytopenia and pancytopenia, a bone marrow examination is a necessary investigation alongside the clinical history and physical examination. Nutritional causes of pancytopenia are relatively more common in developing countries than in Western countries. The most common causes reported in children are aplastic anemia, megaloblastic anemia, infections (such as malaria,

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Received: 23 October 2025, Accepted: 16 September 2026

Published: 27 October 2026

Authors Contribution

SHA & NF conceptualized the project. SHK & KIF did the data collection. NF & SHK performed the statistical analysis. MN & KB did the literature search. Drafting, revision & writing of manuscript were done by SHA, NF & SHK.

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enteric fever, and leishmaniasis), Fanconi anemia, and malignancies like acute leukemia and myelodysplasia.⁴

Pancytopenia and bicytopenia can be presenting features of many severe diseases. The clinical presentation of bicytopenia and pancytopenia varies widely, ranging from fever and mild pallor to severe anemia and bleeding tendencies including petechiae, bruising, and life-threatening hemorrhage in vital organs.⁵ Peripheral bicytopenia and pancytopenia are primarily caused by peripheral cell destruction and inadequate hematopoiesis. On bone marrow biopsy, these findings are typically associated with a normocellular marrow.^{6,7}

Careful examination of a peripheral blood film followed by a bone marrow aspiration or biopsy may be required to establish a definitive diagnosis and guide the management of these patients. Most cases of cytopenias, including bicytopenia and pancytopenia, present with symptoms of weight loss, pallor, fatigue, bleeding, and visceromegaly. Isolated leukopenia is mostly due to drug-induced or congenital neutropenia disorders. An integrated approach to diagnosis should combine clinical findings and peripheral smear morphology with a bone marrow biopsy to establish a definitive diagnosis and plan effective treatment.⁸

On bone marrow biopsy, histological patterns vary depending on the underlying etiology; findings range from nonspecific changes with a normocellular marrow to hypercellularity associated with metastasis or malignant infiltration. Etiological factors behind the suppression of hematopoietic component, may be secondary to drugs, infection or marrow infiltration. In the cases of peripheral destruction of blood cells and hypersplenism, marrow will be hypercellular with normal trilineage hematopoiesis.⁹ The main goal of this study was to determine the etiological spectrum of bone marrow biopsy findings in patients presenting with pancytopenia and bicytopenia to our hospital.

Methods

This was a retrospective study conducted at the Department of Hematology, Civil Hospital Karachi, Pakistan. As this was a retrospective study involving the review and collection of data from existing bone marrow biopsy records, the requirement for informed consent was waived by the Institutional Ethics Committee.

The bone marrow biopsy records maintained in the Central Laboratory of the Civil Hospital were sorted for patients presenting with bicytopenia and pancytopenia between January

2016 and June 2024. All consecutive patient records presenting with cytopenias (bicytopenia or pancytopenia; hemoglobin <10 g/dL, total leukocyte count <4,000/mm³, and platelet count <150 × 10⁹/L) during the study period were included. Patients receiving chemotherapeutic drugs or undergoing radiation therapy were excluded.

Clinical presentation, along with bone marrow aspirate and trephine biopsy findings, were collected from the bone marrow report registers maintained at the Hematology Department of the Civil Hospital Karachi (CHK) Central Laboratory.

Bone marrow aspiration and trephine biopsy were performed according to the department's standard operating procedures. Aspirate smears were stained with Leishman stain, while trephine biopsy sections were stained with hematoxylin and eosin (H&E). Hematological neoplasms were classified according to the 2022 WHO Classification of Hematolymphoid Tumors. Leishman-stained peripheral blood and bone marrow smears were studied. Leishman-stained peripheral blood and bone marrow smears were evaluated. The 2022 WHO classification of hematolymphoid tumors was applied to diagnose various hematological neoplasms. Cytopenias were defined as: hemoglobin <10g/dl, white cell count < 4000/mm³ and, platelet count < 150 × 10⁹/L

The patient identification number, clinical findings peripheral blood findings and blood counts were collected. Patient confidentiality was maintained throughout the study by anonymizing all extracted data, and no personally identifiable information was recorded.

The data were analyzed using IBM SPSS Statistics version 24.0. Continuous variables were summarized as mean±standard deviation (SD), while categorical variables were expressed as frequencies and percentages. As this study was descriptive in nature, no inferential statistical tests were performed.

Results

A total of 200 patients with cytopenias underwent bone marrow examination between January 2016 and June 2024. The mean age was 26.4±18.9 years (range: 1-75 years). Of the study population, 102 (51.0%) were males and 98 (49.0%) were females (Figure).

Bicytopenia was observed in 172 (86.0%) patients, while pancytopenia was present in 28 (14.0%) patients. Bone marrow examination revealed normal bone marrow in 53 (26.5%) patients, followed by aplastic anemia in 43 (21.5%), acute leukemia in 26 (13.0%), and megaloblastic

anemia in 21 (10.5%) patients. Less frequent diagnoses included myelodysplastic syndrome (3.0%), lymphoproliferative disorders (3.5%), miscellaneous conditions (14.5%), and inconclusive findings (7.5%) (Table-1). The miscellaneous category comprised less common bone marrow disorders that individually occurred infrequently and therefore were grouped together for analysis.

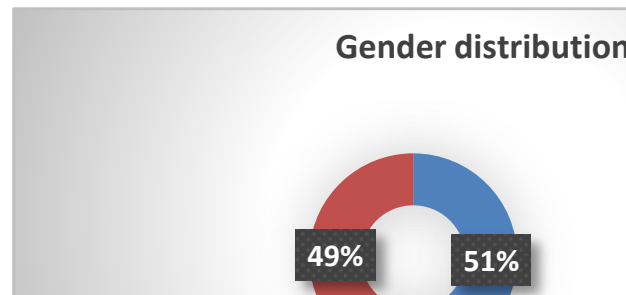


Figure: Gender distribution.

Table 1: Frequency and percentage bone marrow examination findings among study patients. (N = 200)

Bone Marrow Examination	N	%
Normal bone marrow	53	26.5
Aplastic anemia	43	21.5
Acute leukemia	26	13.0
Megaloblastic anemia	21	10.5
Myelodysplastic syndrome	06	3.0
Lymphoproliferative disorder	07	3.5
Miscellaneous	29	14.5
Inconclusive	15	7.5

The most common clinical presentation was fever, occurring in 131 (65.5%) patients, followed by pallor in 35 (17.5%), bleeding in 33 (16.5%), splenomegaly in 31 (15.5%), shortness of breath in 18 (9.0%), hepatomegaly in 12 (6.0%), and jaundice in 7 (3.5%) (Table-2).

Table 1: Distribution of clinical features among patients with cytopenias. (N = 200)

Clinical Features	N	%
Fever	131	65.5
Pallor	35	17.5
Bleeding	33	16.5
Splenomegaly	31	15.5
Shortness of breath	18	9.0
Hepatomegaly	12	6.0
Jaundice	7	3.5

Discussion

Cytopenias, particularly bicytopenia and pancytopenia, have diverse causes, including

impaired marrow production, ineffective haematopoiesis, peripheral destruction, sequestration, infection, nutritional deficiency and malignancy. The present study demonstrated considerable clinical and aetiological heterogeneity, highlighting the value of systematic haematological assessment and bone marrow examination in selected patients. A male predominance was observed in the present study.¹⁰ A recent study from Lady Reading Hospital, Peshawar, involving 120 patients with pancytopenia, reported that 61.7% of patients were male.¹¹ These findings are broadly comparable with present study findings. However, this pattern is not universal. A 2024 study from Islamabad comprising 98 adults with pancytopenia reported a slight female predominance (54 females versus 44 males).¹²

According to the present study, most of the patients present with fever, followed by pallor. Around 63.6% of individuals presented with fever, which was similar to the findings of Kumar et al.¹³ However, another study by Porwal et al. revealed that the most common symptom was generalized weakness.¹⁴ According to present study data, the third most common symptom was bleeding in 15.2% of patients. Anaemia was also very common in all of the patients, with 59.1% having severe anaemia. The most frequent haematological abnormality after anaemia was thrombocytopenia, with nearly all of the patients having it, 68.2% severe thrombocytopenia. Leukopenia was present in a few patients, with 10.6% having severe leukopenia and the remainder exhibiting mild to moderate leukopenia. These haematological results are consistent with those of Singh et al., who noted anaemia and thrombocytopenia as the most frequent abnormalities, seen in 61% of cases.¹⁵ In this research, normal bone marrow features were the most common finding, observed in 28.8% of cases. This is significant because other research did not mention this.¹⁶ In the present study, the second most common diagnosis was aplastic anemia in around 18.2% of cases, followed by acute leukemia (13.6%). Various regional studies have also depicted the same pattern where aplastic anaemia is a common non-malignant cause. For example, according to a study conducted by Sweta et al, 20 % of cytopenias cases were found to be aplastic anaemia.¹⁷ whereas Neha et al. cited it in 23%, pinpointing its high prevalence among South Asian populations.¹⁸ Acute leukaemia, being the third most common cause, is also in agreement with studies conducted by Muneer et al., where it was found that it was responsible for about 12–15% cases of pancytopenia.¹⁹ Most of the cases of acute leukemia presents with pancytopenia; thus, pancytopenia can

be a presenting clinical feature. The Leukemic blasts also gradually destroy the architecture of normal marrow, occupying the space and supportive stromal microenvironment necessary for normal haematopoiesis. Leukemic cells also release inhibitory cytokines (e.g., TNF- α , TGF- β) to suppress normal marrow cell proliferation, differentiation and apoptosis of normal progenitor cells by cell-to-cell contact or soluble factors, contributing to cytopenias. Such fluctuations in findings and frequencies of different etiologies of cytopenias are potentially attributable to geographic, environmental, and referral biases as well as variability in diagnostic facilities and inclusion criteria among studies. Notably, in this study, megaloblastic anaemia (MA) was responsible for 10.5% of the cases. This is contrary to Rasool et al.²⁰ and Rathod et al.²¹ findings, where megaloblastic anaemia was shown to be the most common cause of pancytopenia, noted in 18.1%, and the most frequent aetiology, respectively.

Furthermore, Tang et al. also emphasized the correlation of megaloblastic anaemia with profound pancytopenia and complications such as infections and extended hospital stays.²² The present study also identified infectious aetiologies, such as malaria and dengue, as underlying factors for pancytopenia, though they were not predominant in the study population.^{21,22} The variation between these types underscores the necessity of localized diagnostic approaches and highlights the differential aetiology of pancytopenia in different contexts. In a study from India, it was revealed that acute leukaemia was the most frequent aetiology. The high rates of this aetiology could be driven by environmental exposures and genetic susceptibility, whereas the unavailability of diagnostic facilities often hinders timely diagnosis and treatment. This information contrasts with a number of other studies, which found the most frequent aetiology to be megaloblastic anaemia, led mainly by nutritional deficiencies among the population.

Conclusion

The present research emphasizes the wide range of etiology of bicytopenia and pancytopenia. Most patients were young, with a slight predominance of males. The most common clinical presentation was fever, followed by pallor and bleeding. Interestingly, many patients had normal bone marrow findings, suggesting that peripheral causes were the cause of cytopenias in a substantial proportion of the cohort. In the bone marrow pathologies that can be diagnosed, aplastic anaemia and acute leukaemia were the

most common. These results highlight the necessity of proper diagnostic workups in cytopenic patients, since peripheral explanations might simulate marrow pathology. The etiological spectrum of bicytopenia/pancytopenia ranges from nutritional deficiency to neoplasm. The identification of the definitive aetiology will assist in efficient clinical management of such patients.

Funding: None.

Availability of Data: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval: The Institutional Bioethical Committee/Review Board of Dow University of Health Sciences, Karachi approved the study via letter no. 3827/2025/41 dated 10/02/2025.

Conflict of Interest: None declared.

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