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Original Research Article

Evaluation of Bone Marrow Aspirations and Biopsy Finding in Patients with Pancytopenia

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Abstract:

Background/Introduction: Nutritional deficiencies, bone marrow failure, and malignancies are just a few of the many causes of pancytopenia, a common hematological condition marked by a decrease in all three blood cell lineages. Appropriate management requires an accurate diagnosis. Trephine biopsy (BMB) and bone marrow aspiration (BMA) are essential tools for assessing these patients. The purpose of this study is to evaluate the results of bone marrow aspiration and biopsy in patients who present with pancytopenia and to determine the diagnostic utility of both procedures.

Methods: This prospective observational study was carried out at the Department of Pathology, Government Medical College, Bettiah, Bihar, over the course of a year (25 January 2025– 25 January 2026). There were 200 patients in all who met the requirements for pancytopenia. Comprehensive laboratory, hematological, and clinical data were documented. In every case, a trephine biopsy and bone marrow aspiration were carried out, followed by morphological evaluation and any necessary ancillary tests. Descriptive statistics were used to analyze the data.

Results: Of the patients, 40% were between the ages of 21 and 40, and 59% were male. Fever (55%), pallor (81%), and generalized weakness (85%) were common clinical features. In 52% of cases, a bone marrow examination showed hypercellular marrow. Megaloblastic anemia accounted for 40% of the cases, with aplastic anemia coming in second at 18%, acute leukemias at 15%, and myelodysplastic syndrome at 7%. In 77% of cases, bone marrow aspiration alone was diagnostic; in 23% of cases, biopsy yielded additional or confirmatory information, especially in cases involving hypocellular marrow, fibrosis, focal infiltration, and dry tap. In 82% of cases, aspiration and biopsy results were in agreement.

Conclusion: The most common cause of pancytopenia in this group is still megaloblastic anemia. Although bone marrow aspiration is a useful first diagnostic method, trephine biopsy greatly improves diagnostic precision, particularly in certain situations. For the best assessment of pancytopenia, both methods must be used in conjunction with clinical correlation.

Keywords: Hematological Disorders, Megaloblastic Anemia, Aplastic Anemia, Bone Marrow Biopsy, and Pancytopenia.

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Introduction

A common and clinically significant hematological issue that arises in both outpatient and inpatient practice is Pancytopenia, which is defined as a decrease in all three major blood cell lines (erythrocytes, leukocytes, and platelets). Nutritional deficiencies like megaloblastic anaemia, primary bone marrow failure syndromes like aplastic anaemia and myelodysplastic syndromes, hematological malignancies (acute leukemias, plasma cell myeloma, lymphomas, myeloproliferative neoplasms), infections, autoimmune diseases, and metastatic infiltration of the marrow are all part of its wide etiological spectrum [1,2,3]. Because the prognosis and therapy approach for various disorders vary significantly, a precise etiological diagnosis is crucial. Trephine biopsy (BMB) and bone marrow aspiration (BMA) are still essential tests in the diagnosis of pancytopenia. The biopsy offers vital information on general cellularity, marrow

architecture, fibrosis, granulomas, necrosis, and focal infiltrative lesions, whereas aspiration enables a thorough cytological assessment of specific cell lineages [1,4,2]. Megaloblastic anaemia, aplastic marrow, and haematological malignancies are among the most common diagnoses in cytopenic patients, according to a comprehensive descriptive series of 176 consecutive bone marrow procedures from a South Indian tertiary centre [1]. Careful evaluation of aspirate quality, gross trephine appearance, and core length significantly correlates with diagnostic yield. Malignancies and bone marrow failure are reported as the predominant causes in other large cohorts of pancytopenia or bicytopenia, with a significant portion exhibiting only reactive or non-specific alterations [2]

Characterising local patterns of bone marrow findings in pancytopenia is crucial to improving diagnostic techniques because of regional variations in illness prevalence, nutritional condition, and referral patterns. In this study, 200 patients with pancytopenia at Government Medical College, Bettiah, West Champaran, Bihar, India, have their bone marrow aspiration and biopsy results evaluated. The relative contributions of BMA and BMB in making a final diagnosis are also evaluated.

Materials and Methods

Study and Setting: This prospective observational study was carried out over the course of a year (25 January 2025 to 25 January 2026) at the Department of Pathology, Government Medical College, Bettiah, West Champaran, and Bihar, India. The study included 200 consecutive patients who were referred for a bone marrow examination after exhibiting pancytopenia in pediatric and medical wards or outpatient clinics.

Inclusion Criteria: Pancytopenia was defined as hemoglobin <10 g/dL, total leukocyte count <4 × 10^9/L and platelet count <100 × 10^9/L on at least one occasion. Patients of all ages and both sexes were included after informed consent. Patients with known hematological malignancy on treatment, recent chemotherapy or radiotherapy, or those who declined the procedure were excluded.

Bone Marrow Procedure: Bone marrow aspiration and trephine biopsy were performed sequentially from the posterior superior iliac spine under strict aseptic precautions, following standard protocols similar to those used in other large series [1]. Following local anesthetic, smears were produced right away, air-dried, and stained with Wright-Giemsa after BMA was collected using a Salah or Klima needle. According to ICSH-oriented practice, the aspirate was classified as easy or difficult on-site and further described as particle, richly particulate, scant particulate, hemodilute, greasy, clotted, or dry tap [1]. To maximize the diagnostic yield, a Jamshidi needle was used to obtain a trephine biopsy with a core length of at least 15 mm [1]. Sections of 3–5 μm were stained with hematoxylin and eosin after cores were fixed in 10% buffered formalin, decalcified as needed, and normally processed. When fibrosis was suspected, reticulin staining was carried out.

Morphological Assessment

Aspirate smears were assessed for:

- Total cellularity and the ratio of myeloid to erythroid
- Erythroid, myeloid, and megakaryocytic lineage morphology and maturation
- The presence of hemophagocytosis, blasts, dysplasia, parasites or storage material.
- Trephine biopsies were evaluated for: * Cellularity (hypo-, norm-, and hypercellular) in relation to age
- Bony trabeculae, fat gaps, and marrow architecture
- Necrosis, osteosclerosis, and fibrosis
- Granulomas or inflammation that is either caseating or non-caseating
- Hematological or metastatic non-hematological malignant infiltration [1,3,5].

To discriminate between reactive and neoplastic processes, detect infections, or describe undifferentiated infiltrates, specific stains (reticulin, Ziehl-Neelsen, PAS, Alcian blue) and immunohistochemistry were used as needed [1,6,3). When acute leukemia, myelodysplastic syndrome, or clonal plasma cell or myeloproliferative neoplasm were suspected, flow cytometry and cytogenetics were specifically requested [1,2,5].

Laboratory and Clinical Data: Age, sex, peripheral blood counts and indices, liver and renal function tests, viral markers when indicated, folate levels when clinically suspected, and presenting symptoms and signs were all included in the baseline data. Clinical, peripheral blood, and bone marrow results were integrated to provide the final etiological diagnosis.

Statistical Analysis: Standard statistical software was used to examine the data after it was entered into a spreadsheet. For the diagnostic and demographic data, descriptive statistics (mean, standard deviation, proportions) were employed. Similar to the method used in the South Indian series, the chi-square test was used to investigate the relationship between aspirate type, trephine core length, and diagnostic yield [1]. The percentage of aspirate and trephine diagnoses that were in agreement was computed. Statistical significance was defined as a p-value of less than 0.05.

Results

Demographic profile

Table 1: Age Distribution of Patients:

Age group	Number (n)	Percentage (%)
≤20	40	20
21-40	80	40
41-60	56	28
≥60	24	12
Total	200	100

Table 2: Sex Distribution of the Patients:

Sex	Number (n)	Percentage (%)
Male	118	59
Female	82	41
Total	200	100

Table 3: Clinical Presentation of the Patients:

Clinical features	Number (n)	Percentage (%)
Generalized weakness	170	85
Pallor	162	81
Fever	110	55
Bleeding manifestation	64	32
Weight loss	46	23
Splenomegaly	60	30
Hepatomegaly	42	21
Lymphadenopathy	26	13
Total	200	100

***Many patients had multiple symptoms.**

Table 4: Haematological presentation of the Patients:

Parameters	Mean±SD	Range
Hemoglobin (g/dl)	6.4±1.8	2.5-9.8
Total Leukocyte count (×10⁹/L)	2.6±0.9	—
PLATELET count (×10⁹/L)	58 ± 24	—
MCV (fL, adults)	98 ± 12	—

Table 5: Bone marrow cellularity of the Patients:

marrow cellularity	Number	Percentage (%)
Hypercellular	104	52
Normocellular	38	19
Hypocellular	58	29
Total	200	100

Table 6: Etiological Spectrum of Pancytopenia:

Etiology	Number	Percentage (%)
Megaloblastic Anemia	80	40
Aplastic Anemia	36	18
Acute Leukemias (Total)	30	15
Acute myeloid leukemia (Aml)	18	9
Acute lymphoblastic leukamia (all)	12	6
Myelodysplastic syndrom (mds)	14	7
Hypersplenism	12	6
infection (leishmaniasis, tuberculosis)	10	5
Marrow infilteration (metastasis)	8	4
Other causes	10	5
Total	200	100

Table 7: Diagnostic Yield of Bone Marrow Aspiration vs Biopsy:

Parameter	Number (n)	Percentage (%)
Aspiration alone diagnostic	154	77
Biopsy added/confirmatory	46	23
Total cases	200	100

Table 8: Situation where Biopsy Provided Additional information (N=46):

Finding	Number (n)
Hypocellular marrow better characterized	20
Myelofibrosis detected only on biopsy	8
Focal infilteration	12
Dry tap	6
Total	46

Table 9: Concordance between Aspiration and Biopsy:

Parameter	Percentage (%)
Concordant finding	82
Discordant finding	18

Discussion

Nutritional, marrow failure, clonal, viral, and reactive/systemic causes are all covered in this 200-patient series of pancytopenia, highlighting a common yet clinically significant etiological pattern. The predominance of marrow-intrinsic disorders in cytopenic cohorts is in line with recent research that, when carefully assessed by bone marrow and molecular testing, unexplained cytopenia often reflects clonal myeloid disease or clonal cytopenia of unknown significance [7,8,9]. On the other hand, the marrow is frequently normal or only slightly dysplastic in situations where cytopenias are obviously secondary, such as advanced liver disease or HIV, and seldom indicates a primary hematopoietic malignancy [10,11].

The high percentage of clonal myeloid conditions in cytopenic patients is consistent with a large prospective cohort in Leeds, where 400 out of 1,485 non-diagnostic marrows were ultimately classified as clonal cytopenia of undetermined significance (CCUS) based on somatic mutations, and 28.7% of referred cytopenic adults had a diagnostic marrow lesion [7]. Similarly, 131 (65.5%) of the 200 cytopenic patients examined using paired bone marrow (BM) and peripheral blood (PB) next-generation sequencing had at least one myeloid mutation, with a median of two mutations per patient [8,9]. These findings highlight the fact that, even in cases with modest morphology, a significant portion of an adult cytopenic population such as the current 200-case series would have myeloid mutations and/or myelodysplastic neoplasms.

However, only reactive or secondary cytopenias were probably present in a non-trivial fraction of the 200 individuals. Bone marrow was normocellular on average, dysplasia was often low-grade, and primary myeloid malignancy was discovered in only 5% of the 147 patients with liver failure and cytopenia in a 10-year transplant center evaluation [11]. Only one patient's transplant choices were affected by the marrow findings. In HIV-positive individuals receiving antiretroviral medication, a similar trend was observed: 40% had at least one cytopenia, although genuine pancytopenia was uncommon (1%), and cytopenias were more linked with CD4 count and treatment (such as zidovudine) than with primary marrow illness [10]. These results lend credence to a more nuanced interpretation of the present cohort's bone marrow results: individuals with advanced systemic illness who have normal or slightly dysplastic marrows shouldn't be mistakenly classified as having primary clonal pathology. In the age of genomics, the findings further support the changing diagnostic function of bone marrow biopsy. An algorithmic strategy to pancytopenia was described in a recent comprehensive review [12]. It involves front-loading peripheral genomic testing and non-invasive examinations, with marrow reserved for those with high pre-test likelihood of clonal illness or unexplained chronic cytopenias. PB-based NGS can function as an initial screen, with marrow targeted to mutation-positive or clinically high-risk patients, according to the high concordance of mutation profiles between BM and PB in cytopenic adults (95% of individual mutations; 99.5% of patients with any mutation detected in at least one compartment) [8,9]. Such a technique might capture the majority of clonal and myelodysplastic patients while reducing the number of invasive operations for the current 200-patient series.

However, the current data and comparison studies also caution against fully abandoning marrow examination. For evaluating cellularity, fibrosis, architectural alterations, and localized infiltrates—features that PB sequencing cannot capture on its

own—BM is still crucial [8,12]. Marrow biopsies still result in a new diagnosis for around 40% of patients in cohorts with unexplained cytopenias, and they alter treatment for about 30% of patients, particularly when blasts, severe dysplasia, or a history of chemotherapy are present [13]. Similarly, marrow hypercellularity with hemophagocytosis or granulomas is often diagnostic in infectious contexts such brucellosis with pancytopenia; however, in a small percentage, concomitant leukemic infiltration is only detected by biopsy [14]. These findings support the benefit of biopsy over aspiration alone in the 200-patient series, especially in dry-tap operations and hypocellular, fibrotic, or infiltrated marrows.

Lastly, it is important to evaluate the range of immunological cytopenic syndromes and marrow failure seen in pancytopenic cohorts in the context of developing disease-specific recommendations. Bone marrow tests are seldom necessary in normal ITP, according to updated consensus guidelines for immune thrombocytopenia [15,16], with biopsy reserved for unusual presentations or suspected marrow failure. Similarly, current recommendations for aplastic anemia emphasize the need for thorough morphologic and molecular differentiation between hypoplastic myelodysplastic neoplasms, hereditary marrow failure syndromes, and acquired aplastic anemia, and they increasingly use cytogenetics and targeted NGS to direct treatment [17,18]. This paradigm, in which marrow morphology is essential but insufficient and has to be combined with genetic, clinical, and exposure data, is well aligned with the 200-patient series.

Comparison with key Cytopenic studies: There are a number of significant similarities and differences between the current 200-case series and major cytopenia investigations. 28.7% of 2,083 patients in a large prospective cohort study from Leeds Teaching Hospitals NHS Trust had a diagnostic bone marrow lesion, and 400 cases were classified as clonal cytopenia of undetermined significance (CCUS); notably, mutation burden was found to predict disease progression [7]. A high concordance rate of 95% was found in a study of 200 patients assessing paired bone marrow and peripheral blood next-generation sequencing, supporting the use of peripheral blood NGS as a first-line clonality screening method [8,9]. Bone marrow examination changed the diagnosis in 42% of instances and affected treatment choices in 30.4% of cases, according to another research of 170 patients with unexplained cytopenias [13].

This suggests that clinical predictors might assist determine if a biopsy is necessary. On the other hand, only 5% of 147 patients with liver failure and cytopenias had underlying myeloid cancer, and bone marrow testing had little bearing on the choice to get a transplant [11]. While pancytopenia was rare (1%), 40% of 499 persons using HAART for HIV infection had at least one cytopenia; the majority of these instances were linked to peripheral or systemic reasons rather than marrow pathology [10]. Furthermore, a research of 30 Brucellosis patients who presented with pancytopenia showed mostly hypercellular bone marrow with characteristics including granuloma development and hemophagocytosis, and it notably found five instances of concomitant hematological malignancies [14].

Limitations

Several important limitations apply to the 200-patient study:

- Single center, observational design: Similar to the majority of cytopenia studies, the data are from a single institution and may be impacted by practice style, illness frequency, and local referral patterns, which limits generalizability [7,12,11].
- Selection bias toward unexplained cases: Compared to unselected primary care populations, only patients sent for bone marrow assessment were included, which probably enriched for more severe or diagnostically complicated pancytopenias [7,8,13.
- Limited molecular work-up: As shown in prospective CCUS cohorts [1,17], early or low burden clonal entities like CCUS or low grade MDS may have gone unnoticed if NGS panels and thorough cytogenetics were not consistently carried out.
- Limited longitudinal follow-up: The research cannot accurately quantify the progression from seemingly reactive or idiopathic cytopenias to overt myeloid neoplasms in the absence of comprehensive long-term follow-up. This risk has been amply documented in cohorts with CCUS and non-severe aplastic anaemia [7,18].
- Heterogeneity of underlying conditions: Differences in drug exposures, autoimmune diseases, HIV status, and concomitant liver illness make it more difficult to attribute cytopenia to intrinsic versus peripheral processes in the bone marrow and may skew etiology percentages [12,10,11].
- No formal evaluation of biopsy complications or patient-reported outcomes: Bone marrow biopsy in cytopenic patients carries a risk of bleeding and is frequently perceived as painful and inconvenient; these issues are highlighted in the literature on cytopenia and MDS but are not quantified here [8,12].

Serious adverse events are rare. When extrapolating results or comparing etiologic proportions across cohorts, it is important to

recognize these limitations, which are similar to those of other cytopenia and marrow failure datasets.

Conclusion

Bone marrow examination, ideally combining aspiration, trephine biopsy, and targeted molecular testing, showed a diagnostic profile in a 200-patient cohort of pancytopenia that was generally similar to that reported in large cytopenia studies. Similar to prospective CCUS and myelodysplastic cohorts, a significant portion of patients had clonal or primary marrow disorders, while many others displayed reactive or secondary changes akin to those observed in HIV-associated cytopenias or liver failure (7)(8)(10(11). High-quality PB NGS can safely function as a first-line screen for clonality in unexplained cytopenia, according to comparison with recent work on PB–BM genomic concordance (8)(12)(9)(13). Invasive marrow procedures should be reserved for cases that are mutation-positive or clinically high-risk, as well as for circumstances where evaluation of cellularity, fibrosis, or focal infiltration is crucial. The study supports an integrated, risk-adapted diagnostic strategy that combines clinical assessment, non-invasive investigations, peripheral genomic data, and selectively deployed bone marrow biopsy to optimize care for adults with pancytopenia, despite methodological and single-center limitations.

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