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Original Research Article

Morphological Spectrum of Bone Marrow Findings and its role in the Evaluation of Haematological Disorders

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Abstract

Introduction: Bone marrow examination (BME) is a cornerstone diagnostic procedure for evaluating hematological disorders, providing critical insights into cellular morphology, architecture, and iron stores. This study aimed to describe the clinico-morphological spectrum of bone marrow findings and assess the diagnostic utility of bone marrow aspiration (BMA) and biopsy (BMB) in a tertiary care center in the Bundelkhand region of Madhya Pradesh, India.

Materials and Methods: A prospective, observational study was conducted over a specified period, including 90 patients who underwent BME for various hematological indications. Peripheral blood parameters, clinical features, and bone marrow morphology from both aspiration and trephine biopsy were analyzed. Special stains (Perls' Prussian blue, Reticulin) were employed as needed.

Results: The study population had a mean age skewing towards younger adults (20-29 years, 31.1%), with a slight male predominance (53.3%). The most common clinical features were weakness (90%) and pallor (88.9%). Megaloblastic anemia (MA) was the most frequent diagnosis (31.1%), followed by mixed deficiency anemia (MDA, 20.0%) and iron deficiency anemia (IDA, 11.1%). Non-neoplastic disorders constituted 85.5% of cases, while neoplastic conditions like acute leukemia, aplastic anemia, and myelofibrosis accounted for 14.4%. Bone marrow biopsy was pivotal in cases of dry tap or when architectural assessment was crucial, such as in myelofibrosis and aplastic anemia.

Conclusion: Nutritional deficiency anemias, particularly megaloblastic anemia, are the predominant hematological disorders in the Bundelkhand region. Bone marrow examination remains an indispensable, cost-effective tool for definitive diagnosis, especially in differentiating between nutritional deficiencies, marrow failure syndromes, and hematological malignancies.

Keywords: Bone Marrow Aspiration, Bone Marrow Biopsy, Megaloblastic Anemia, Pancytopenia, Hematological Disorders, Bundelkhand, Morphological Spectrum.

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Introduction

The bone marrow is the primary site of hematopoiesis in adults, responsible for the production of erythrocytes, leukocytes, and platelets. Evaluation of bone marrow is thus fundamental in diagnosing a wide array of hematological disorders, ranging from benign nutritional deficiencies to life-threatening malignancies. The procedure, pioneered in clinical practice by Giovanni Ghedini and later refined by Arinkin, involves two complementary techniques: bone marrow aspiration (BMA) and bone marrow trephine biopsy (BMB) [1, 2]. BMA provides excellent cytological detail, allowing for assessment of cell morphology, differential counts, and iron stores. In contrast, BMB offers a superior evaluation of marrow architecture, cellularity, and the detection of focal lesions, fibrosis, or infiltrative disorders that may be missed on aspiration [3, 4]. Together, they form a powerful diagnostic duo, particularly in evaluating cytopenias—anemia, leukopenia, and thrombocytopenia—which are common presenting features of both benign and malignant marrow pathologies [5]. In India, the spectrum of

hematological diseases varies significantly by region, influenced by genetic, nutritional, and socioeconomic factors. The Bundelkhand region of Madhya Pradesh is characterized by economic challenges and potential nutritional deficiencies, which may reflect in the local disease profile. While numerous studies from other parts of India have reported their findings, there is a paucity of data from this specific region [6].

This prospective study was undertaken to analyze the morphological spectrum of bone marrow findings, correlate them with clinical and peripheral blood parameters, and establish the diagnostic role of BMA and BMB in evaluating hematological disorders in patients attending a tertiary care hospital in Sagar, Madhya Pradesh.

Materials and Methods

Study Design and Setting: This was a prospective, observational study conducted in the Department of Pathology, Government Bundelkhand Medical College, Sagar, from March 2024 to October 2025.

Study Population: A total of 90 consecutive patients requiring bone marrow examination for various hematological indications were included.

Inclusion Criteria:

- All patients with unexplained cytopenias (anemia, leukopenia, thrombocytopenia, pancytopenia).
- Suspected hematological malignancies (e.g., acute leukemia, myelodysplastic syndrome).
- Suspected myeloproliferative neoplasms.
- Evaluation of nutritional deficiency anemias not responding to therapy.
- Unexplained organomegaly or fever.

Exclusion Criteria:

- Patients with severe coagulation disorders.
- Local infection at the biopsy site.
- Patients aged below 10 years and above 75 years.
- Uncooperative patients or those refusing consent.

Ethical Considerations: Informed written consent was obtained from all patients or their legal guardians. The study protocol was approved by the institutional ethics committee.

Procedure

Bone Marrow Aspiration (BMA): Performed from the posterior superior iliac spine or sternum under aseptic precautions and local anesthesia (2% lignocaine) using a Salah needle. Smears were prepared, air-dried, and stained with Leishman stain. Cellularity, myeloid-to-erythroid (M:E) ratio, and detailed morphology of all cell lines were assessed.

Bone Marrow Biopsy (BMB): Performed from the posterior iliac crest using a Jamshidi needle when aspiration yielded a dry tap, was hemodiluted, or when architectural assessment was deemed necessary. The biopsy core was fixed, decalcified, processed, and embedded in paraffin. Sections were stained with Hematoxylin and Eosin (H&E). Reticulin stain was used to grade fibrosis (WHO 2016 criteria: MF-0 to MF-3) [7].

Special Stains: Perls' Prussian blue stain was performed on aspirate smears to assess bone marrow iron stores, graded from 0 to 6 [8].

Data Collection and Analysis: A detailed proforma captured demographic data, clinical features, complete blood count (CBC), peripheral smear findings, and final bone marrow diagnosis. Data were entered into a master chart and analyzed using descriptive statistics (mean, frequency, percentage). Chi-square test was used to analyze the significance of age and diagnostic category distributions.

Results

Demographic Profile: The age of patients ranged from 10 to 75 years. The largest cohort was in the 20-29 years' age group (31.1%), followed by 10-19 years (17.8%). The distribution was statistically non-uniform (χ^2=24.81, $p<0.05$), indicating a significant representation of young adults. There were 48 males (53.3%) and 42 females (46.7%), with no statistically significant gender predilection ($p>0.05$) (Table 1).

Table 1: Demographic Distribution of cases (N=90)

Sub Group	Count (N)	Percentage (%)	Chi-Square (χ^2)	p-Value
Gender				
Male	48	53.3	0.4	0.527
Female	42	46.7		
Age Groups				
11-20	16	17.8	24.81	< 0.05
21-30	28	31.1		
31-40	10	11.1		
41-50	8	8.9		
51-60	8	8.9		
60-70	12	13.3		
More than 70	8	8.9		

Clinical Presentation: The most common symptom was generalized weakness (90%), followed by pallor (88.9%). Dyspnea was present in 28.9% and fever in 20%. On examination, splenomegaly was noted in 21.1%, lymphadenopathy in 14.4%, and hepatomegaly in 12.2% of patients (Table 2).

Table 2: Tabular presentation of clinical features (N = 90 patients)

Clinical Feature	Present (n)	Percentage (%)	Absent (n)	Percentage (%)
Fever	18	20.0%	72	80.0%
Weakness	81	90.0%	9	10.0%
Dyspnoea	26	28.9%	64	71.1%
Pallor	80	88.9%	10	11.1%
Hepatomegaly	11	12.2%	79	87.8%
Splenomegaly	19	21.1%	71	78.9%
Lymphadenopathy	13	14.4%	77	85.6%

Peripheral Blood Parameters: The mean hemoglobin was markedly low at 5.61 g/dL, indicating severe anemia. The mean total leukocyte count (TLC) was 7,561/mm³, within the normal range. The mean platelet count was 116.41 x 10^3/µL, indicating thrombocytopenia. The mean reticulocyte count was 2.64%.

Spectrum of Bone Marrow Diagnoses: A wide morphological spectrum was observed. Megaloblastic Anemia (MA) was the single most common diagnosis, found in 28 patients (31.1%). Aspirate smears showed hypercellular marrow with erythroid hyperplasia, megaloblastic changes, giant metamyelocytes, and dysplastic features (Figure 1).

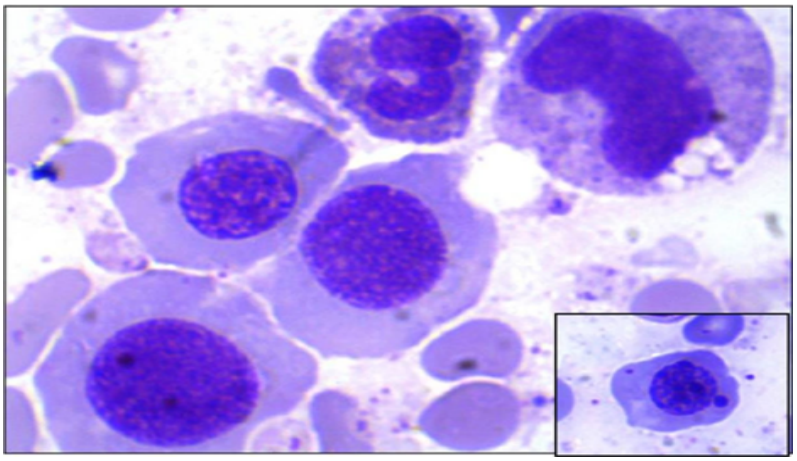

Figure 1: BMA shows megaloblast and giant metamyelocytes. Leishman's stain (100 X).

Mixed Deficiency Anemia (MDA) and Iron Deficiency Anemia (IDA) were diagnosed in 18 (20.0%) and 10 (11.1%) patients, respectively. MDA marrow showed dimorphic erythroid populations (micronormoblastic and megaloblastic) (Figure 2A, B).

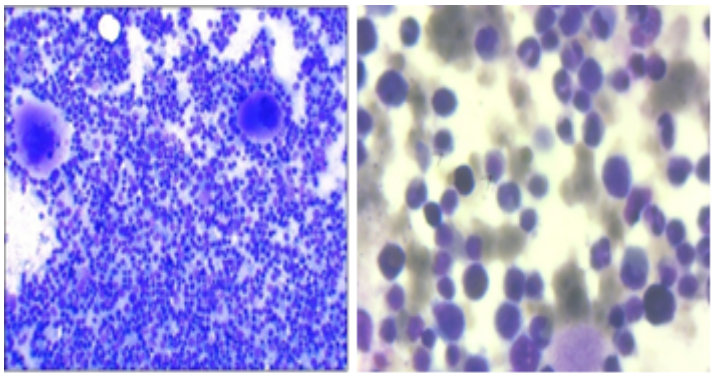

Figure 2: BMA shows erythroid hyperplasia with miro-normoblastic reaction. Leishman's stain ((A): 100X and (B): 400X).

Immune Thrombocytopenic Purpura (ITP) was seen in 6 patients (6.7%), with marrow showing increased or normal megakaryocytes, often with immature forms.

Acute Leukemia and Aplastic Anemia (AA) were each diagnosed in 4 patients (4.4%). AA was characterized by a hypocellular marrow with increased fat spaces and decreased hematopoietic cells.

Myelofibrosis was diagnosed in 3 patients (3.3%), where BMA resulted in a dry tap, and BMB revealed dense reticulin fibrosis (MF-2/MF-3).

Other diagnoses included Essential Thrombocythemia (ET, 2.2%) with marked megakaryocytic hyperplasia, Chronic Granulomatous Lesion (CGL, 2.2%), and Hypoproliferative Marrow (HPM, 2.2%).

Neoplastic vs. Non-Neoplastic Disorders: Non-neoplastic disorders, predominantly nutritional anemias, constituted the vast majority (85.5%, n=77). Neoplastic disorders (acute leukemia, myeloproliferative neoplasms, aplastic anemia*) accounted for 14.4% (n=13). This difference was highly statistically significant (χ^2=114.02, $p<0.001$).

Role of Bone Marrow Biopsy: BMB was instrumental in cases where BMA was inadequate. It provided a definitive diagnosis in all cases of myelofibrosis (dry tap), allowed for accurate cellularity assessment in aplastic anemia, and helped detect granulomas and atypical infiltrates.

Discussion

This prospective study from the Bundelkhand region highlights the pivotal role of bone marrow examination in unraveling the etiology of diverse hematological presentations. The predominance of young adults (20-29 years) in our patient cohort aligns with studies from other developing regions of India, where hematological disorders significantly impact the economically productive population [9]. The near-equal gender distribution suggests that both sexes are equally vulnerable to the prevalent nutritional and hematological challenges in this region.

The overwhelming prevalence of nutritional deficiency anemias (MA, MDA, IDA), accounting for over 62% of all diagnoses, is the most striking finding of our study. This echoes similar patterns reported from various parts of India, where megaloblastic anemia has consistently been identified as a leading cause of pancytopenia and marrow abnormalities [10, 11]. The high burden of MA points towards widespread deficiencies of vitamin B12 and/or folate in the population, likely stemming from inadequate dietary intake, vegetarian diets, malabsorption syndromes, or socioeconomic factors. This underscores an urgent need for public health interventions focused on nutritional education, food fortification, and supplementation programs in this region.

The clinical presentation dominated by weakness and pallor is a direct reflection of the severe anemia prevalent in our cohort, with a mean hemoglobin of 5.61 g/dL. The associated thrombocytopenia (mean platelet count 116.41 x $10^3/\mu L$) often seen in megaloblastic anemia contributes to the bleeding tendency, while leukopenia can increase infection risk [12]. The finding of pancytopenia on peripheral smear in a large subset of these patients (e.g., DA + Pancytopenia, 18.9%) often raises the suspicion of more sinister disorders like aplastic anemia or leukemia, making bone marrow examination indispensable for correct diagnosis and avoiding unnecessary, potentially harmful treatments.

Bone Marrow Aspiration vs. Biopsy: Our study reinforces the complementary roles of BMA and BMB. BMA was excellent for detailing cytomorphology, assessing dysplasia in megaloblastic anemia, and grading iron stores. However, BMB was critical in several scenarios:

Dry Tap**:** In all three cases of myelofibrosis, BMA yielded a dry tap. BMB with reticulin staining was diagnostic, revealing MF-2/MF-3 grade fibrosis.

Cellularity Assessment: In aplastic anemia, BMB provided an unambiguous assessment of hypocellularity (often <10%), which is more reliable than aspirate smears that can be hemodiluted.

Architectural Evaluation: BMB detected granulomatous lesions and atypical infiltrates that were not apparent on aspiration.

This synergy is well-established in hematology practice; while aspirates are superior for cell detail, biopsy is the gold standard for assessing overall cellularity, fibrosis, and focal pathology [3, 4].

Among the neoplastic disorders, acute leukemia and aplastic anemia were equally prevalent (4.4% each). The diagnosis of acute leukemia was straightforward on BMA, showing >20% blasts. Aplastic anemia, a bone marrow failure syndrome, was characterized by a hypocellular biopsy with increased fat spaces and lymphocytosis. Distinguishing hypoplastic MDS or hypocellular AML from AA can be challenging and requires careful morphology and often ancillary tests [13]. Cases like Essential Thrombocythemia and myelofibrosis highlight the spectrum of myeloproliferative neoplasms where BMB is crucial for diagnosis and fibrosis grading.

Lessons from Morphology: The study provided classic morphological examples:

Megaloblastic Anemia: Hypercellular marrow, megaloblastic erythroid precursors with nuclear-cytoplasmic asynchrony, giant metamyelocytes, and hypersegmented neutrophils on peripheral smear.

Iron Deficiency: Absent marrow iron stores (Perls' stain grade 0), erythroid hyperplasia with micronormoblastic maturation (small, densely stained nuclei).

Mixed Deficiency Anemia: A dimorphic picture with both microcytic hypochromic and macrocytic cells, reflected in the marrow as a dual erythroid population.

Limitations: This study is a single-center study; the findings may not be fully generalizable. The lack of routine advanced diagnostic modalities like flow cytometry, cytogenetics, and molecular studies limited the sub-classification of leukemias and MDS. Future studies incorporating these techniques would provide a more comprehensive molecular profile of hematological malignancies in this region.

Conclusion

This study delineates the clinico-morphological spectrum of hematological disorders in the Bundelkhand region of Madhya Pradesh. The overwhelming preponderance of nutritional deficiency anemias, particularly megaloblastic anemia, calls for targeted public health strategies to address vitamin B12 and folate deficiencies.

Bone marrow examination, combining both aspiration and biopsy, proves to be an irreplaceable, cost-effective diagnostic tool in this resource-constrained setting. It accurately differentiates between benign nutritional deficiencies, marrow failure syndromes, and hematological malignancies, thereby guiding appropriate and timely management. This study establishes a baseline profile for hematological disorders in Bundelkhand and emphasizes the continued relevance of meticulous morphological examination in the diagnostic hematology armamentarium.

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