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RESEARCH ARTICLE

Spectrum and Frequency of Megakaryocyte Morphological Alterations in Thrombocytopenia: A Cross-Sectional Study from a Tertiary Care Centre in Eastern India

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ABSTRACT

Background: Thrombocytopenia is a commonly encountered hematological abnormality associated with diverse etiologies ranging from transient infections to primary bone marrow disorders. Bone marrow examination remains an important diagnostic tool in evaluating thrombocytopenia, particularly through assessment of megakaryocyte morphology. Alterations in megakaryocyte number, maturation, and nuclear characteristics often provide important clues regarding the underlying pathology.

Objective: To evaluate the spectrum and frequency of megakaryocyte morphological alterations in patients presenting with thrombocytopenia.

Materials and Methods: A hospital-based cross-sectional observational study was conducted in the Department of Pathology at Rajendra Institute of Medical Sciences (RIMS), Ranchi, over a period of 1.5 years. A total of 73 patients with thrombocytopenia undergoing bone marrow examination were included. Bone marrow aspiration smears were stained with Leishman stain and examined for megakaryocyte morphology. Morphological alterations including hypolobation, micromegakaryocytes, bare nuclei, immature forms, emperipolesis, cytoplasmic vacuolization, and dysplastic changes were evaluated. Statistical analysis was performed using SPSS version 25.0. Chi-square test and Student's t-test were used where appropriate, and p-value <0.05 was considered statistically significant.

Results: The mean age of study participants was 41.8 ± 15.6 years, with a male predominance (58.9%). Immune thrombocytopenic purpura (ITP) was the most common cause of thrombocytopenia (32.9%), followed by megaloblastic anemia (20.5%) and aplastic anemia (13.7%). Increased megakaryocytes were observed in 57.5% of cases, while decreased megakaryocytes were noted in 24.7%. Hypolobated megakaryocytes were the most frequent morphological abnormality (50.7%), followed by bare megakaryocytic nuclei (45.2%), immature megakaryocytes (39.7%), micromegakaryocytes (28.8%), and emperipolesis (19.2%). Dysplastic changes were significantly more common in myelodysplastic syndrome and leukemia cases (p = 0.002).

Conclusion: Megakaryocyte morphological evaluation provides valuable diagnostic information in thrombocytopenia. Specific alterations such as hypolobation, micromegakaryocytes, and dysplastic forms may help differentiate reactive from neoplastic and marrow failure conditions.

Keywords: Thrombocytopenia, Megakaryocytes, Bone marrow aspiration, Morphological alterations, Dysplasia, Immune thrombocytopenic purpura

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INTRODUCTION

Thrombocytopenia, defined as a platelet count below 150,000/µL, is a frequently encountered hematological abnormality in clinical practice and may arise from decreased platelet production, increased peripheral destruction, splenic sequestration, or dilutional causes (1). The condition may present with manifestations ranging from asymptomatic laboratory abnormalities to severe bleeding complications. Accurate etiological diagnosis is

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essential for timely management and prognostic assessment.

Megakaryocytes are large polyploid bone marrow cells responsible for platelet production. Their morphology and distribution within the bone marrow provide critical insight into the pathogenesis of thrombocytopenia (2). Bone marrow examination remains one of the most informative investigations in evaluating unexplained thrombocytopenia, especially when peripheral smear findings and clinical features are inconclusive.

Megakaryopoiesis involves a highly regulated process of cellular maturation, endomitosis, and cytoplasmic fragmentation resulting in platelet formation (3). Alterations in these processes can lead to characteristic morphological abnormalities in megakaryocytes. These changes may include micromegakaryocytes, hypolobated nuclei, multinucleation, emperipolesis, immature forms, and cytoplasmic vacuolization (4).

The pattern of megakaryocyte morphology often varies depending on the underlying disease process. In immune thrombocytopenic purpura (ITP), increased megakaryocytes with immature forms are commonly observed due to compensatory marrow response (5). In contrast, myelodysplastic syndromes (MDS) typically demonstrate dysplastic megakaryocytes with hypolobation and micromegakaryocyte formation (6). Megaloblastic anemia may show giant metamyelocytes and abnormal megakaryocyte maturation due to ineffective hematopoiesis (7).

Several infectious diseases, including dengue fever, malaria, and sepsis, may also cause thrombocytopenia through marrow suppression or peripheral destruction mechanisms (8). In such cases, marrow examination may reveal transient suppression of megakaryopoiesis or reactive changes. Similarly, acute leukemias and aplastic anemia may present with marked reduction or dysplastic changes in megakaryocytes due to marrow infiltration or failure (9).

The evaluation of megakaryocyte morphology has gained increasing importance in hematopathology due to its diagnostic and prognostic significance. Morphological abnormalities may help distinguish reactive thrombocytopenia from clonal hematological disorders (10). Furthermore, the World Health Organization (WHO) classification of hematological malignancies includes megakaryocytic dysplasia as an important criterion in diagnosing myelodysplastic syndromes (11).

Previous studies have demonstrated variable frequencies of megakaryocyte abnormalities in thrombocytopenia. Muhury et al. reported dysplastic megakaryocytes in a substantial proportion of patients with marrow disorders (12). Bhasin et al. observed increased immature megakaryocytes and emperipolesis predominantly in ITP cases (13). Studies from different geographic regions have also highlighted differences in etiological patterns depending on endemic infections and nutritional deficiencies (14).

In developing countries such as India, thrombocytopenia is commonly associated with infectious diseases, nutritional anemia, and hematological malignancies (15). Despite the widespread prevalence of thrombocytopenia, limited studies from eastern India have systematically evaluated megakaryocyte morphology across different etiologies.

Careful morphological assessment of megakaryocytes not only aids diagnosis but may also provide clues regarding disease severity and marrow response. Features such as hypogranular cytoplasm, nuclear budding, separated nuclear lobes, and micromegakaryocytes are considered indicators of dysmegakaryopoiesis (16). Reactive conditions, on the other hand, often show increased cellularity with preserved maturation patterns.

The role of bone marrow aspiration in thrombocytopenia remains particularly important when peripheral smear findings are ambiguous or when patients fail to respond to empirical therapy (17). Bone marrow examination can exclude malignant infiltration, marrow fibrosis, aplastic anemia, and myelodysplastic syndromes.

Recent advances in understanding megakaryocyte biology have also emphasized the role of cytokines, thrombopoietin signaling, and marrow microenvironment in platelet production (18). Disturbances in these pathways may manifest morphologically as altered megakaryocyte maturation.

In ITP, autoantibody-mediated platelet destruction stimulates compensatory megakaryocytic hyperplasia, often associated with immature and atypical forms (19). In contrast, marrow suppression due to chemotherapy or viral infections may lead to decreased megakaryocyte numbers (20).

Megakaryocyte morphology is also useful in distinguishing inherited thrombocytopenias from acquired disorders. Certain congenital disorders may exhibit characteristic giant or hypolobated megakaryocytes (21). Therefore, morphological evaluation should always be interpreted in conjunction with clinical and laboratory findings.

Although automated hematology analyzers provide rapid platelet counts, they cannot replace direct morphological examination of bone marrow cells (22). Histopathological correlation remains essential in many complex cases.

Several Indian studies have emphasized the utility of bone marrow examination in thrombocytopenia; however, data regarding the spectrum of megakaryocyte abnormalities remain limited (23). Regional studies are important because infectious and nutritional etiologies vary significantly across populations.

The present study was therefore undertaken to evaluate the spectrum and frequency of megakaryocyte morphological alterations in thrombocytopenia among patients attending a tertiary care centre in Ranchi, Jharkhand.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based cross-sectional observational study was conducted in the Department of Pathology, Rajendra Institute of Medical Sciences (RIMS), Ranchi, Jharkhand.

Study Duration

The study was carried out over a period of 1.5 years from January 2024 to June 2025.

Study Population

Patients presenting with thrombocytopenia and undergoing bone marrow aspiration examination during the study period were included.

Sample Size

A total of 73 patients fulfilling the inclusion criteria were enrolled consecutively during the study period.

Inclusion Criteria

- Patients of all age groups with platelet count <150,000/µL
- Patients undergoing bone marrow aspiration for evaluation of thrombocytopenia
- Patients willing to provide informed consent

Exclusion Criteria

- Patients with inadequate bone marrow aspirate samples
- Patients already receiving chemotherapy
- Patients with known inherited platelet disorders
- Patients unwilling to participate

Data Collection

Detailed clinical history, demographic details, clinical examination findings, and laboratory parameters were recorded using a structured proforma.

Bone Marrow Examination

Bone marrow aspiration was performed under aseptic precautions from the posterior superior iliac spine or sternum. Smears were stained using Leishman stain and examined under light microscopy.

Megakaryocytes were assessed for:

- Number (increased, normal, decreased)
- Nuclear morphology
- Cytoplasmic granularity
- Lobulation abnormalities
- Presence of micromegakaryocytes
- Emperipolesis
- Bare megakaryocytic nuclei
- Dysplastic features

Statistical Analysis

- Data were entered into Microsoft Excel and analyzed using SPSS version 25.0.
- Continuous variables were expressed as mean ± standard deviation.
- Categorical variables were expressed as frequency and percentage.
- Chi-square test was used for comparison between categorical variables.
- Student's t-test was used for continuous variables.
- A p-value <0.05 was considered statistically significant.

Ethical Considerations

Institutional Ethics Committee approval was obtained prior to commencement of the study. Written informed consent was obtained from all participants.

RESULTS

A total of 73 patients with thrombocytopenia were included in the study during the 1.5-year study period. All bone marrow aspirates were adequate for megakaryocyte morphology assessment.

Demographic Characteristics:

The age of the study participants ranged from 14 to 78 years, with a mean age of 41.8 ± 15.6 years. The majority of patients belonged to the 21–40 years age group. Males

Table 1: Demographic Profile of Study Participants (N = 73)

Variable	*Frequency*	*Percentage (%)*
Age <20 years	9	12.3
21–40 years	31	42.5
41–60 years	22	30.1
>60 years	11	15.1
Male	43	58.9
Female	30	41.1

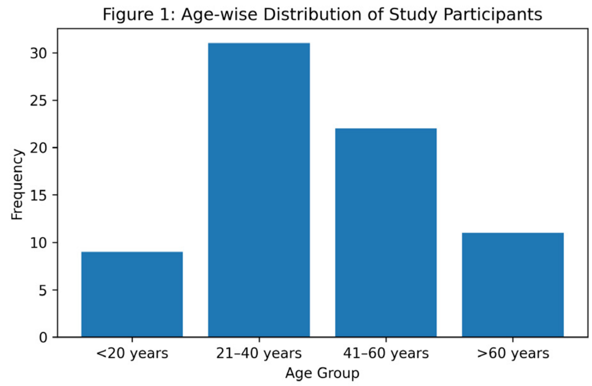

Figure 1: Age-wise Distribution of Study Participants

Table 2: Etiological Spectrum of Thrombocytopenia

Diagnosis	*Frequency*	*Percentage (%)*
Immune thrombocytopenic purpura (ITP)	24	32.9
Megaloblastic anemia	15	20.5
Aplastic anemia	10	13.7
Acute leukemia	8	11.0
Myelodysplastic syndrome	5	6.8
Dengue-associated thrombocytopenia	6	8.2
Hypersplenism	3	4.1
Others	2	2.8

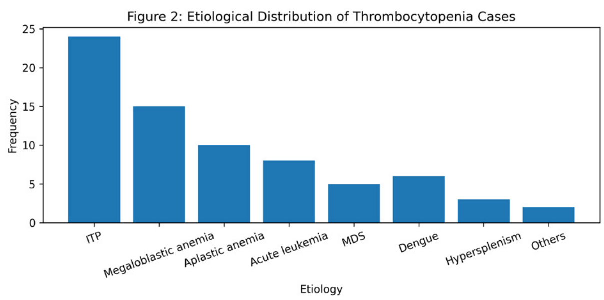

Figure 2: Etiological Distribution of Thrombocytopenia Cases

Table 3: Frequency of Megakaryocyte Morphological Alterations

Morphological Alteration	*Frequency (N = 73)*	*Percentage (%)*
Increased megakaryocytes	42	57.5
Decreased megakaryocytes	18	24.7
Hypolobated megakaryocytes	37	50.7
Micromegakaryocytes	21	28.8
Bare megakaryocytic nuclei	33	45.2
Immature megakaryocytes	29	39.7
Dysplastic forms	17	23.3
Emperipolesis	14	19.2
Cytoplasmic vacuolization	11	15.1

constituted 43 cases (58.9%), while females accounted for 30 cases (41.1%), giving a male-to-female ratio of 1.4:1.

As shown in Table 1, the highest proportion of thrombocytopenic patients belonged to the economically productive age group of 21–40 years.

Etiological Distribution of Thrombocytopenia

Among the 73 cases, immune thrombocytopenic purpura (ITP) was the most common diagnosis, followed by megaloblastic anemia and aplastic anemia.

Table 2 demonstrates that non-neoplastic causes constituted the majority of thrombocytopenia cases in the present study.

Megakaryocyte Morphological Alterations

Various megakaryocytic alterations were identified on bone marrow examination. The most common finding was increased megakaryocytes, followed by hypolobated forms and bare nuclei.

As illustrated in Table 3, hypolobation and bare

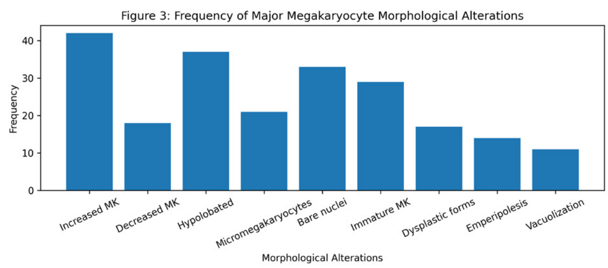

Figure 3: Frequency of Major Megakaryocyte Morphological Alterations

Table 4: Association Between Etiology and Major Megakaryocyte Alterations

Etiology	*Increased Megakaryocytes n (%)*	*Hypolobated Forms n (%)*	*Dysplastic Forms n (%)*
ITP (n=24)	19 (79.2)	10 (41.7)	2 (8.3)
Megaloblastic anemia (n=15)	8 (53.3)	9 (60.0)	3 (20.0)
Aplastic anemia (n=10)	2 (20.0)	3 (30.0)	1 (10.0)
Acute leukemia (n=8)	4 (50.0)	5 (62.5)	4 (50.0)
MDS (n=5)	2 (40.0)	4 (80.0)	4 (80.0)
Others (n=11)	7 (63.6)	6 (54.5)	3 (27.3)

Table 5: Association Between Platelet Count and Megakaryocyte Alterations

Platelet Count	*Immature Megakaryocytes Present*	*Immature Megakaryocytes Absent*	*p-value*
<50,000/mm³ (n=37)	18	19	
≥50,000/mm³ (n=36)	11	25	0.018*

megakaryocytic nuclei were among the predominant dysmorphic changes observed.

Correlation Between Etiology and Megakaryocyte Morphology

Increased megakaryocytes and bare nuclei were predominantly associated with ITP, whereas dysplastic forms and micromegakaryocytes were more common in myelodysplastic syndrome and leukemia cases.

Table 4 demonstrates that dysplastic megakaryocytes were significantly more frequent in myelodysplastic syndrome and acute leukemia cases.

Statistical Analysis

Statistical analysis showed a significant association between dysplastic megakaryocyte morphology and neoplastic causes of thrombocytopenia ($\chi^2 = 9.84$, $p = 0.002$). Increased megakaryocyte counts were significantly associated with immune thrombocytopenic purpura ($\chi^2 = 11.26$, $p = 0.001$).

Patients with peripheral platelet counts below 50,000/mm³ demonstrated significantly higher frequencies of immature megakaryocytes compared to patients with platelet counts above 50,000/mm³ (48.6% vs 30.6%, p = 0.018).

As shown in Table 5, severe thrombocytopenia was significantly associated with immature megakaryocytic forms.

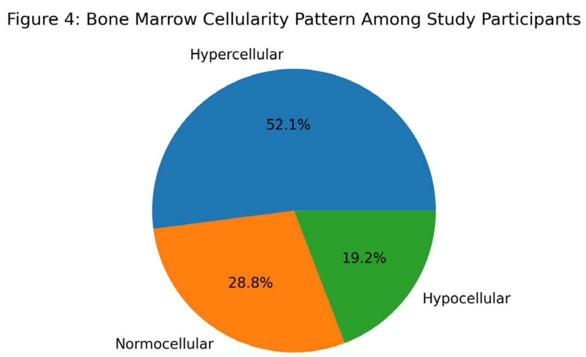

Figure 4: Bone Marrow Cellularity Pattern Among Study Participants

Bone Marrow Cellularity

Bone marrow examination revealed hypercellular marrow in 38 cases (52.1%), normocellular marrow in 21 cases (28.8%), and hypocellular marrow in 14 cases (19.2%). Hypercellularity was most frequently associated with ITP and megaloblastic anemia.

Overall, the study demonstrated that characteristic megakaryocytic morphological alterations were significantly associated with specific etiological categories of thrombocytopenia, thereby emphasizing the diagnostic utility of detailed bone marrow examination.

DISCUSSION

The present study evaluated the spectrum and frequency of megakaryocyte morphological alterations in thrombocytopenic patients attending a tertiary care centre in eastern India. Bone marrow examination remains an important diagnostic modality in thrombocytopenia, particularly in cases where peripheral smear findings are inconclusive or when hematological malignancies are suspected. The present study demonstrated that distinct megakaryocytic morphological patterns are associated with different etiological categories of thrombocytopenia.

In the present study, the majority of patients belonged to the 21–40 years age group, with a male predominance. Similar demographic findings have been reported in previous hematological studies evaluating thrombocytopenia patterns in hospital-based populations (24). The predominance of younger adults may be attributed to the higher occurrence of immune-mediated and infectious causes of thrombocytopenia in this age group.

Immune thrombocytopenic purpura (ITP) was identified as the most common cause of thrombocytopenia in the present study, followed by megaloblastic anemia and aplastic anemia. This observation is comparable with the findings of Agarwal et al., who reported ITP as a major non-neoplastic cause associated with increased megakaryopoiesis (25). Increased megakaryocyte numbers observed in ITP reflect compensatory marrow response to peripheral platelet destruction.

The present study identified increased megakaryocytes, hypolobated forms, bare megakaryocytic nuclei, and immature megakaryocytes as the predominant morphological alterations. Similar findings were documented by Bhasin et al., who reported increased immature megakaryocytes, hypolobated forms, and emperipolesis in various thrombocytopenic disorders, highlighting the diagnostic utility of megakaryocyte morphology (26). Increased megakaryocyte counts with active budding were especially common in immune-mediated thrombocytopenia, indicating increased platelet turnover.

Hypolobated megakaryocytes and micromegakaryocytes were observed more frequently in myelodysplastic syndrome (MDS) and acute leukemia cases. These findings are consistent with observations by Dutta et al., who emphasized the diagnostic importance of dysplastic megakaryocytic morphology in clonal hematological disorders (27). Dysplastic forms are considered indicators of abnormal megakaryocyte maturation and defective thrombopoiesis.

The present study also demonstrated a statistically significant association between dysplastic megakaryocytes and neoplastic causes of thrombocytopenia ($p = 0.002$). Chandra and Chandra similarly reported that megakaryocytic dysplasia is more frequently associated with malignant and pre-malignant marrow disorders than with reactive thrombocytopenia (28). Therefore, careful evaluation of megakaryocyte morphology can help differentiate benign from malignant etiologies.

Another important finding of the study was the significant association between severe thrombocytopenia and immature megakaryocytic forms. Increased immature forms may indicate accelerated marrow stimulation secondary to peripheral platelet destruction or ineffective thrombopoiesis. Hypercellular marrow was most commonly observed in ITP and megaloblastic anemia, whereas hypocellular marrow predominated in aplastic anemia cases. These marrow cellularity patterns are in agreement with standard hematopathological descriptions of thrombocytopenic disorders (29).

The findings of this study reinforce the importance of bone marrow examination in evaluating thrombocytopenia, particularly in resource-limited settings where advanced molecular investigations may not be readily available. Detailed assessment of megakaryocyte morphology not only aids in diagnosis but may also provide prognostic information in selected hematological disorders.

Overall, the study demonstrates that characteristic megakaryocytic alterations show significant association with specific etiologies of thrombocytopenia. Recognition of these patterns can substantially improve diagnostic accuracy and facilitate early clinical management.

CONCLUSION

Megakaryocyte morphological evaluation is an important component of bone marrow examination in thrombocytopenia. Hypolobation, immature forms, micromegakaryocytes, and emperipolesis were among the most common abnormalities observed. Increased megakaryocytes were predominantly associated with ITP, whereas decreased megakaryocytes were more common in aplastic anemia and leukemia. Dysplastic changes showed significant association with myelodysplastic syndrome and leukemic disorders. Careful assessment of megakaryocyte morphology can substantially aid etiological diagnosis and guide clinical management.

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