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RESEARCH ARTICLE

Comprehensive Evaluation of Megakaryocyte Morphology and Its Correlation with Different Etiologies of Thrombocytopenia: A Bone Marrow Aspirate Study

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ABSTRACT

Background: Thrombocytopenia is a common hematological abnormality encountered in clinical practice and may arise from diverse etiologies including peripheral platelet destruction, impaired platelet production, bone marrow infiltration, nutritional deficiencies, infections, and hematological malignancies. Bone marrow examination remains an essential diagnostic tool in evaluating unexplained thrombocytopenia. Megakaryocytes, the platelet-producing cells of the bone marrow, exhibit distinct morphological alterations in various pathological conditions. Detailed assessment of megakaryocyte morphology can therefore provide valuable clues regarding the underlying etiology of thrombocytopenia.

Aim: To evaluate megakaryocyte morphology in bone marrow aspirates and correlate the morphological patterns with different etiologies of thrombocytopenia.

Methods: This prospective observational study was conducted in the Department of Pathology at Rajendra Institute of Medical Sciences (RIMS), Ranchi, over a duration of 1.5 years. A total of 73 patients presenting with thrombocytopenia and undergoing bone marrow aspiration were included. Bone marrow aspirate smears were stained with Leishman stain and examined for megakaryocyte number and morphology. Morphological parameters assessed included immature forms, dysplastic forms, bare nuclei, hypolobated megakaryocytes, micromegakaryocytes, emperipolesis, and platelet budding. Statistical analysis was performed using SPSS version 25.0. Chi-square test and ANOVA were applied wherever appropriate. A p-value <0.05 was considered statistically significant.

Results: Among the 73 cases, immune thrombocytopenic purpura (ITP) was the most common etiology (31.5%), followed by megaloblastic anemia (21.9%), acute leukemia (15.1%), aplastic anemia (12.3%), dengue-associated thrombocytopenia (9.6%), and myelodysplastic syndrome (9.6%). Increased megakaryocytes were predominantly observed in ITP cases, while reduced megakaryocytes were significantly associated with aplastic anemia and acute leukemia ($p<0.001$). Dysplastic megakaryocytes and micromegakaryocytes were significantly associated with myelodysplastic syndrome ($p=0.002$). Hypolobated forms were commonly observed in megaloblastic anemia and MDS. Emperipolesis was most frequent in ITP.

Conclusion: Megakaryocyte morphology provides important diagnostic insights in thrombocytopenia and correlates significantly with underlying etiologies. Bone marrow examination with careful morphological assessment of megakaryocytes remains an invaluable diagnostic approach for differentiating causes of thrombocytopenia.

Keywords: Thrombocytopenia, megakaryocyte morphology, bone marrow aspiration, immune thrombocytopenic purpura, megaloblastic anemia, myelodysplastic syndrome

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INTRODUCTION

Thrombocytopenia is a commonly encountered hematological abnormality characterized by a platelet count below 150,000/µL and may result from decreased platelet production, increased peripheral destruction, splenic sequestration, or abnormal platelet distribution [1]. It is associated with a wide spectrum of clinical manifestations ranging from asymptomatic laboratory findings to life-threatening hemorrhagic complications. Accurate identification of the underlying etiology is essential for appropriate management and prognostication.

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Bone marrow examination remains one of the most important diagnostic tools in the evaluation of thrombocytopenia, particularly in cases with unexplained cytopenias, suspected marrow pathology, or nonresponsive peripheral thrombocytopenia [2]. Among the various marrow elements, megakaryocytes play a pivotal role because they are directly responsible for platelet production. Detailed assessment of megakaryocyte morphology in bone marrow aspirates provides valuable insight into the pathophysiology and etiology of thrombocytopenia [3].

Megakaryocytes are large polyploid marrow cells derived from hematopoietic stem cells through thrombopoietin-mediated differentiation [4]. Under normal conditions, megakaryocytes exhibit multilobulated nuclei and abundant granular cytoplasm. Alterations in their number, maturation pattern, nuclear morphology, and cytoplasmic characteristics may reflect specific hematological disorders and marrow responses [5].

Various benign and malignant hematological disorders demonstrate characteristic megakaryocytic changes. Immune thrombocytopenic purpura (ITP) commonly shows increased megakaryocytes with immature forms and hypolobated nuclei due to compensatory marrow response [6]. In contrast, aplastic anemia frequently demonstrates markedly reduced or absent megakaryocytes reflecting marrow hypoplasia [7]. Megaloblastic anemia may reveal giant megakaryocytes with nuclear maturation defects secondary to impaired DNA synthesis [8].

Myelodysplastic syndromes (MDS) are associated with dysplastic megakaryocytes including micromegakaryocytes, multiple separated nuclei, and hypogranular forms [9]. Acute leukemias and marrow infiltrative disorders may suppress normal megakaryopoiesis and produce abnormal megakaryocytic morphology [10]. Therefore, systematic evaluation of megakaryocyte morphology can substantially aid in differentiating reactive from neoplastic causes of thrombocytopenia.

Bone marrow aspiration is considered a rapid, minimally invasive, and highly informative procedure for evaluating hematological abnormalities [11]. Careful examination of marrow smears allows assessment of megakaryocyte number, morphology, distribution, and maturation stages. Correlation of these findings with peripheral blood counts and clinical features enhances diagnostic accuracy [12].

Several studies have highlighted the importance of megakaryocyte morphology in thrombocytopenia. Changes such as bare nuclei, immature megakaryocytes, emperipolesis, cytoplasmic vacuolization, hypogranularity, and dysplastic nuclear forms have shown significant association with specific disease categories [13]. Recognition of these features may reduce diagnostic ambiguity and facilitate early therapeutic intervention.

Immune-mediated thrombocytopenia remains one of the most common causes of isolated thrombocytopenia across all age groups [14]. Increased peripheral platelet destruction stimulates compensatory megakaryocytic hyperplasia within the marrow. Conversely, disorders affecting marrow production generally exhibit decreased megakaryocyte counts and defective maturation [15]. Thus, marrow morphology serves as an important indicator of the underlying pathogenic mechanism.

In developing countries, infectious diseases such as dengue fever, malaria, septicemia, and viral illnesses contribute substantially to thrombocytopenia burden [16]. Reactive marrow changes associated with these conditions may mimic primary hematological disorders, necessitating careful morphological interpretation. Nutritional deficiencies including vitamin B12 and folate deficiency also significantly influence megakaryocyte morphology [17].

Recent advances in hematopathology have improved understanding of megakaryocyte biology and its diagnostic implications. Nevertheless, bone marrow morphology continues to remain a cornerstone investigation in resource-limited settings where advanced molecular diagnostics may not be readily available [18]. Standardized morphological evaluation can therefore provide clinically meaningful diagnostic guidance even in peripheral centers.

Despite the recognized value of megakaryocyte assessment, relatively few studies from eastern India have comprehensively evaluated megakaryocyte morphology across different etiologies of thrombocytopenia [19]. Regional studies are important because infectious, nutritional, and hematological disease patterns vary considerably across populations and may influence marrow morphology.

The present study was undertaken to comprehensively evaluate megakaryocyte morphology in bone marrow aspirates of thrombocytopenic patients and to correlate the

observed morphological patterns with different etiologies of thrombocytopenia at Rajendra Institute of Medical Sciences, Ranchi over a study duration of one and a half years [20].

MATERIALS AND METHODS

Study Design

Prospective observational study.

Study Place

Department of Pathology, Rajendra Institute of Medical Sciences (RIMS), Ranchi.

Study Duration

1.5 years.

Sample Size

A total of 73 patients with thrombocytopenia undergoing bone marrow aspiration were included in the study.

Study Population

Patients presenting with thrombocytopenia and referred for bone marrow aspiration evaluation.

Inclusion Criteria

- Patients with platelet count <150,000/µL.
- Patients undergoing bone marrow aspiration for evaluation of thrombocytopenia.
- Patients of all age groups and both genders.
- Patients providing informed consent.

Exclusion Criteria

Patients with inadequate bone marrow aspirate smears.
Patients with known platelet disorders already on definitive therapy.
Patients unwilling to participate.

Data Collection

Detailed clinical history, demographic profile, laboratory investigations, and bone marrow findings were recorded in a structured proforma.

Bone Marrow Examination

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

Megakaryocyte Assessment

- The following parameters were evaluated:
- Megakaryocyte number
- Immature megakaryocytes
- Dysplastic forms
- Hypolobated megakaryocytes
- Bare nuclei
- Micromegakaryocytes
- Emperipolesis
- Platelet budding

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 25.0. Quantitative variables were expressed as mean ± standard deviation. Qualitative variables were expressed as frequency and percentage. Chi-square test and ANOVA were applied for statistical comparisons. A p-value <0.05 was considered statistically significant.

Ethical Consideration

Institutional ethical committee approval was obtained from RIMS, Ranchi. Confidentiality of patient information was maintained throughout the study.

RESULTS

A total of 73 patients with thrombocytopenia undergoing bone marrow aspiration were included in the present study. Detailed evaluation of demographic characteristics, etiological spectrum, bone marrow cellularity, and megakaryocyte morphology was performed.

Demographic Characteristics

Among the 73 study participants, 41 (56.2%) were males and 32 (43.8%) were females, showing a male predominance. The mean age of participants was 34.7 ± 16.2 years. The majority of patients belonged to the 21–40 years age group (42.5%), followed by the 41–60 years age group (26.0%). The age distribution is summarized in Table 1 and illustrated in Figure 1.

The majority of thrombocytopenic patients belonged to the 21–40 years age group.

Male patients constituted the majority of the study population.

Etiological Distribution of Thrombocytopenia

Immune thrombocytopenic purpura (ITP) was identified as the most common etiology accounting for 31.5% of cases, followed by megaloblastic anemia (21.9%)

Table 1: Age Distribution of Study Participants

Age Group (Years)	*Frequency (n)*	*Percentage (%)*
≤20	14	19.2
21–40	31	42.5
41–60	19	26.0
>60	9	12.3
Total	73	100

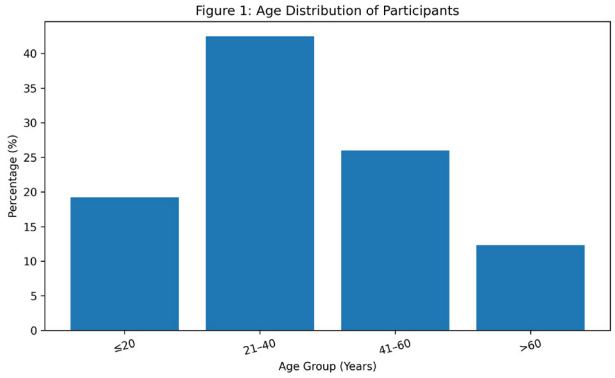

Figure 1: Age Distribution of Participants

Table 2: Gender Distribution of Study Participants

Gender	*Frequency (n)*	*Percentage (%)*
Male	41	56.2
Female	32	43.8
Total	73	100

Table 3: Etiological Distribution of Thrombocytopenia

Etiology	*Frequency (n)*	*Percentage (%)*
Immune thrombocytopenic purpura (ITP)	23	31.5
Megaloblastic anemia	16	21.9
Acute leukemia	11	15.1
Aplastic anemia	9	12.3
Dengue-associated thrombocytopenia	7	9.6
Myelodysplastic syndrome (MDS)	7	9.6
Total	73	100

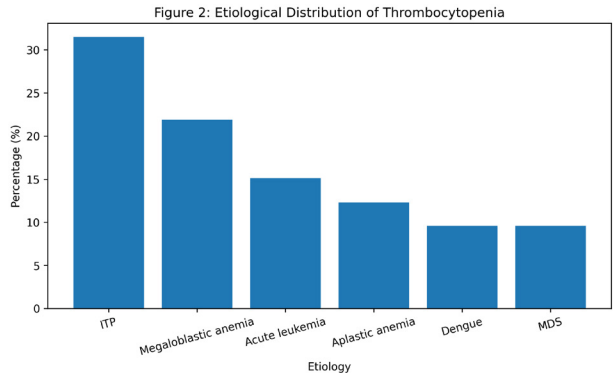

Figure 2: Etiological Distribution of Thrombocytopenia

Table 4: Megakaryocyte Number in Different Etiologies

Etiology	*Increased*	*Normal*	*Decreased*
ITP	18	5	0
Megaloblastic anemia	6	7	3
Acute leukemia	1	3	7
Aplastic anemia	0	2	7
Dengue-associated thrombocytopenia	3	4	0
MDS	2	2	3

and acute leukemia (15.1%). The etiological spectrum is shown in Table 3 and Figure 2.

ITP represented the most frequent cause of thrombocytopenia in the present study.

Megakaryocyte Number in Different Etiologies

Increased megakaryocytes were predominantly observed in cases of ITP, whereas markedly decreased megakaryocytes were associated with aplastic anemia and acute leukemia. Megakaryocyte distribution according to different etiologies is summarized in Table 4.

A statistically significant association was observed between megakaryocyte number and underlying etiology (Chi-square = 31.84, $p < 0.001$). Increased megakaryocytes were strongly associated with ITP, while decreased megakaryocytes were predominantly associated with aplastic anemia and acute leukemia.

Megakaryocyte Morphological Alterations

Various morphological alterations in megakaryocytes were identified during bone marrow examination. Immature megakaryocytes were the most frequent abnormality (39.7%), followed by emperipolesis (35.6%) and increased platelet budding (32.9%). Detailed morphological findings are shown in Table 5 and Figure 3.

Immature forms and emperipolesis were the most commonly observed megakaryocyte abnormalities.

Table 5: Megakaryocyte Morphological Features

Morphological Feature	*Frequency (n)*	*Percentage (%)*
Immature megakaryocytes	29	39.7
Dysplastic forms	18	24.7
Hypolobated megakaryocytes	21	28.8
Bare nuclei	14	19.2
Micromegakaryocytes	11	15.1
Emperipolesis	26	35.6
Increased platelet budding	24	32.9

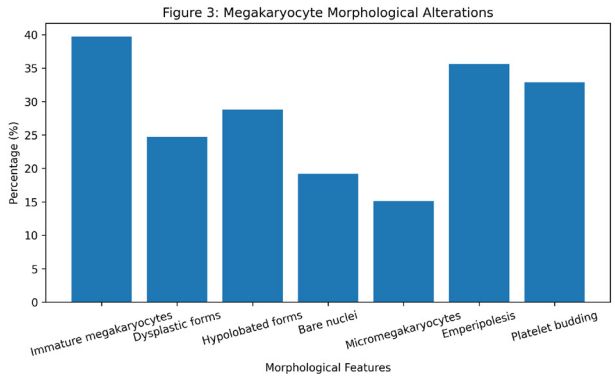

Figure 3: Frequency of Megakaryocyte Morphological Alterations

Table 6: Correlation of Megakaryocyte Morphology with Etiology

Morphological Feature	*Predominant Etiology*	*p-value*
Immature megakaryocytes	ITP	0.001
Emperipolesis	ITP	0.003
Dysplastic forms	MDS	0.002
Micromegakaryocytes	MDS	0.001
Hypolobated forms	Megaloblastic anemia/ MDS	0.012
Decreased megakaryocytes	Aplastic anemia	<0.001

Table 7: Mean Platelet Count in Different Etiologies

Etiology	*Mean Platelet Count (/µL) Mean ± SD*
ITP	38,000 ± 14,200
Megaloblastic anemia	54,000 ± 18,500
Acute leukemia	27,000 ± 10,600
Aplastic anemia	22,000 ± 8,400
Dengue-associated thrombocytopenia	46,000 ± 12,900
MDS	35,000 ± 11,300

Table 8: Bone Marrow Cellularity Patterns

Bone Marrow Cellularity	*Frequency (n)*	*Percentage (%)*
Hypercellular	34	46.6
Normocellular	21	28.8
Hypocellular	18	24.6
Total	73	100

Correlation of Megakaryocyte Morphology with Etiology

Distinct megakaryocyte morphological patterns were associated with specific etiologies of thrombocytopenia. Immature megakaryocytes and emperipolesis were predominantly observed in ITP, whereas dysplastic forms and micromegakaryocytes were significantly associated with MDS. The correlation is presented in Table 6.

Statistically significant correlations were identified between specific megakaryocyte morphological features and underlying disease etiologies.

Platelet Count in Different Etiologies

The mean platelet count varied significantly among different etiological groups. The lowest mean platelet count was observed in aplastic anemia followed by acute leukemia. Platelet count comparison is summarized in Table 7.

A statistically significant difference in platelet counts among different etiological groups was observed (ANOVA $F = 6.28$, $p = 0.001$).

Bone Marrow Cellularity

Bone marrow cellularity analysis demonstrated hypercellular marrow in 46.6% of cases, normocellular marrow in 28.8%, and hypocellular marrow in 24.6% of cases. Bone marrow cellularity patterns are shown in Table 8 and Figure 4.

Hypercellular marrow was the predominant bone marrow pattern observed in the study population.

Statistical Analysis

Statistically significant associations were observed between megakaryocyte morphology and specific etiologies of thrombocytopenia. Increased megakaryocytes showed a strong association with ITP (Chi-square = 16.74, $p = 0.001$). Micromegakaryocytes demonstrated significant association with MDS (Chi-square = 14.28, $p = 0.002$). Hypolobated megakaryocytes were significantly associated

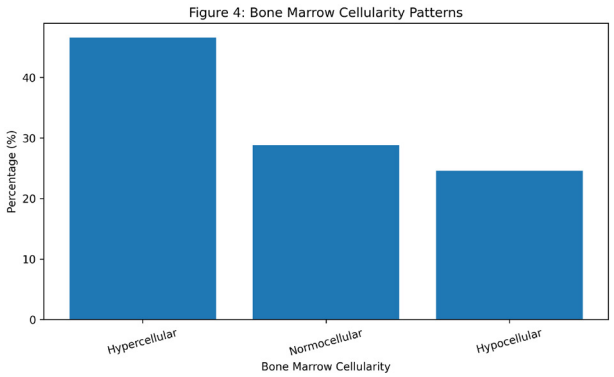

Figure 4: Bone Marrow Cellularity Patterns

with megaloblastic anemia and MDS (Chi-square = 9.63, p = 0.012). Reduced megakaryocytes were significantly associated with aplastic anemia and acute leukemia (Chi-square = 18.57, p <0.001).

DISCUSSION

Thrombocytopenia is a frequent hematological abnormality with diverse etiologies ranging from benign transient conditions to serious bone marrow disorders. Bone marrow examination remains an essential diagnostic modality in evaluating thrombocytopenic patients, particularly when peripheral smear findings are inconclusive. Megakaryocyte morphology provides important clues regarding platelet kinetics and marrow response patterns.

In the present study, the majority of patients belonged to the 21–40 years age group with a male predominance. Similar findings were reported by Muhury et al., who observed increased frequency of thrombocytopenia among young adults undergoing marrow evaluation [21].

Immune thrombocytopenic purpura was the most common etiology identified in our study. Increased megakaryocytes with immature forms and emperipolesis were predominantly observed in ITP cases. These findings are consistent with observations made by Bhasin et al., who demonstrated compensatory megakaryocytic hyperplasia in peripheral platelet destruction disorders [22].

Megaloblastic anemia represented the second most common etiology in the present study. Hypolobated megakaryocytes and dysplastic nuclear changes were frequently observed. Similar morphological abnormalities were described by Choudhary et al., who attributed these changes to defective DNA synthesis affecting hematopoietic maturation [23].

Acute leukemia and aplastic anemia demonstrated significantly reduced megakaryocyte numbers in our study. This finding reflects suppression of normal hematopoiesis due to marrow infiltration or stem cell failure. Comparable observations were reported by Kaur et al. in their evaluation of thrombocytopenic marrow disorders [24].

Myelodysplastic syndrome cases in the current study showed significant dysplastic megakaryocytes and micromegakaryocytes. These morphological alterations are considered characteristic of ineffective hematopoiesis and dysmegakaryopoiesis. Similar findings were documented by Gupta et al., who emphasized the diagnostic importance of micromegakaryocytes in MDS [25].

The present study highlights the importance of detailed megakaryocyte evaluation in differentiating peripheral platelet destruction from marrow production defects. Morphological assessment remains a valuable, cost-effective, and accessible diagnostic approach in routine hematopathology practice.

CONCLUSION

Megakaryocyte morphology demonstrates significant correlation with different etiologies of thrombocytopenia and provides valuable diagnostic information during bone marrow examination. Increased megakaryocytes with immature forms and emperipolesis are characteristic of ITP, whereas dysplastic forms and micromegakaryocytes are commonly associated with MDS. Reduced megakaryocytes strongly correlate with aplastic anemia and leukemic marrow infiltration. Detailed morphological assessment of megakaryocytes should therefore be considered an integral component of bone marrow evaluation in thrombocytopenic patients.

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