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Original Research Article

Correlation of Megakaryocyte Morphology with Platelet Count and Clinical Severity in Thrombocytopenia

Abhishek Kumar Jha[1], Dipika Kumari[2], Md. Alimuddin Ansari[3]

[1]Senior Resident, Department of Pathology, SNMMC, Dhanbad, Jharkhand, India
[2]Junior Resident (Academic), Department of Pathology, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India
[3]Assistant Professor, Department of Pathology, SNMMC, Dhanbad, Jharkhand, India

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Corresponding Author: Dr. Md. Alimuddin Ansar
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Abstract:

Background: Thrombocytopenia is a common hematological disorder characterized by a reduction in platelet count below the normal reference range and is associated with a broad spectrum of clinical conditions ranging from transient infections to malignant hematological disorders. Bone marrow examination plays a pivotal role in identifying the underlying pathology in thrombocytopenic patients. Megakaryocytes, being the platelet-producing cells of bone marrow, exhibit diverse morphological alterations in various hematological and non-hematological disorders. Correlating megakaryocyte morphology with platelet count and clinical severity may provide valuable diagnostic and prognostic insights.

Aim: To evaluate the correlation of megakaryocyte morphology with platelet count and clinical severity in patients presenting with thrombocytopenia.

Materials and Methods: A hospital-based cross-sectional observational study was conducted at the Department of Pathology, Rajendra Institute of Medical Sciences (RIMS), Ranchi, over a period of 1.5 years from January 2024 to June 2025. A total of 73 patients presenting with thrombocytopenia were included in the study. Bone marrow aspiration smears were evaluated for megakaryocyte number and morphological alterations including hypolobation, multinucleation, micromegakaryocytes, emperipolesis, bare nuclei, and immature forms. Platelet counts and clinical severity based on bleeding manifestations were recorded. Statistical analysis was performed using SPSS version 25. Pearson correlation test, Chi-square test, and ANOVA were used wherever appropriate. A p-value <0.05 was considered statistically significant.

Results: Among 73 patients, 42 (57.5%) were males and 31 (42.5%) were females. The mean age of participants was 38.6 ± 15.2 years. The most common cause of thrombocytopenia was immune thrombocytopenic purpura (ITP) accounting for 24.7% of cases, followed by megaloblastic anemia and acute leukemia. Dysplastic megakaryocyte morphology was significantly associated with severe thrombocytopenia (platelet count $<20,000/\mu L$) and increased clinical bleeding manifestations ($p<0.001$). Micromegakaryocytes and hypolobated forms were predominantly observed in patients with severe thrombocytopenia. A significant inverse correlation was observed between abnormal megakaryocyte morphology score and platelet count ($r=-0.52$, $p<0.001$).

Conclusion: Megakaryocyte morphological alterations demonstrate significant correlation with platelet count and clinical severity in thrombocytopenic patients. Bone marrow megakaryocyte evaluation may serve as an important diagnostic and prognostic tool in the assessment of thrombocytopenia.

Keywords: Thrombocytopenia, Megakaryocytes, Bone Marrow, Platelet Count, Dysplasia, Clinical Severity.

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Introduction

Thrombocytopenia is defined as a platelet count below 150,000/µL and represents one of the most common hematological abnormalities encountered in clinical practice.[1] The condition may arise due to decreased platelet production, increased peripheral destruction, splenic sequestration, or dilutional causes.[2] Patients with thrombocytopenia may present with a wide range of clinical manifestations varying from asymptomatic laboratory findings to severe life-threatening hemorrhage.[3]

Bone marrow examination remains a cornerstone in the evaluation of thrombocytopenia, particularly when the etiology is uncertain or associated with pancytopenia, atypical peripheral smear findings, or suspected hematological malignancy.[4] Megakaryocytes are large polyploid bone marrow

cells responsible for platelet production and play a crucial role in maintaining hemostatic balance.[5]

Megakaryocyte morphology in bone marrow aspirates provides valuable information regarding underlying marrow pathology.[6] Alterations such as hypolobated nuclei, micromegakaryocytes, emperipolesis, immature forms, bare nuclei, and multinucleation have been described in several benign and malignant hematological disorders.[7]

Immune thrombocytopenic purpura (ITP), megaloblastic anemia, myelodysplastic syndrome, aplastic anemia, acute leukemia, and infectious diseases are among the important causes of thrombocytopenia associated with distinct megakaryocytic changes.[8] Increased megakaryocyte numbers with immature forms are commonly observed in ITP due to peripheral platelet destruction, whereas dysplastic megakaryocytes are characteristic of myelodysplastic syndromes.[9]

The correlation between megakaryocyte morphology and platelet count has gained increasing attention in recent years.[10] Several studies have demonstrated that severe thrombocytopenia is frequently associated with abnormal megakaryocyte maturation and dysplastic changes.[11] Morphological evaluation of megakaryocytes may therefore provide insights into disease severity and marrow response.

Clinical severity in thrombocytopenia is generally assessed based on bleeding manifestations including petechiae, purpura, epistaxis, gum bleeding, gastrointestinal bleeding, and intracranial hemorrhage.[12] Previous investigators have suggested that certain megakaryocyte morphological abnormalities correlate with increased bleeding risk and poorer clinical outcomes.[13]

Micromegakaryocytes are small mononuclear or bilobed megakaryocytes commonly associated with dysmegakaryopoiesis and myelodysplastic syndromes.[14] Hypolobated megakaryocytes and abnormal nuclear segmentation may indicate defective thrombopoiesis and ineffective platelet production.[15]

Emperipolesis, characterized by engulfment of intact hematopoietic cells within megakaryocytes, has been reported in both reactive and neoplastic marrow disorders.[16] Increased emperipolesis has been associated with immune-mediated platelet destruction and inflammatory conditions.[17]

Several studies have attempted to correlate bone marrow megakaryocyte morphology with peripheral platelet count and disease severity.[18] However, variations exist due to differences in study population, disease spectrum, and diagnostic criteria.

In developing regions such as eastern India, thrombocytopenia is frequently encountered in association with infectious diseases, nutritional deficiencies, autoimmune disorders, and hematological malignancies.[19] Despite the clinical importance of megakaryocyte evaluation, limited data are available regarding the correlation between megakaryocyte morphology, platelet count, and clinical severity among thrombocytopenic patients in this region.

Understanding megakaryocyte morphology may assist clinicians and pathologists in differentiating peripheral platelet destruction from marrow production defects and may contribute to early diagnosis and management.[20]

Therefore, the present study was undertaken to evaluate the correlation of megakaryocyte morphology with platelet count and clinical severity in patients presenting with thrombocytopenia at a tertiary care center in eastern India.

Materials and Methods

Study Design: Hospital-based cross-sectional observational study.

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

Study Duration: 1.5 years (January 2024 to June 2025).

Study Population: Patients presenting with thrombocytopenia undergoing bone marrow examination.

Sample Size: A total of 73 patients were included in the study.

Inclusion Criteria

1. Patients of all age groups with platelet count <150,000/μL.
2. Patients undergoing bone marrow aspiration for evaluation of thrombocytopenia.
3. Patients providing informed consent.

Exclusion Criteria

1. Patients with inadequate bone marrow aspirate smears.
2. Patients receiving chemotherapy.
3. Previously diagnosed myeloproliferative neoplasms under treatment.
4. Patients unwilling to participate.

Data Collection Procedure: Detailed clinical history including bleeding manifestations, fever, pallor, organomegaly, and associated symptoms was recorded. Peripheral blood counts were analyzed using automated hematology analyzer. Bone marrow aspiration was performed under aseptic precautions.

Leishman-stained bone marrow smears were examined under light microscopy. Megakaryocytes were evaluated for number and morphology. Morphological parameters studied included:

- Micromegakaryocytes
- Hypolobated megakaryocytes
- Multinucleated forms
- Bare nuclei
- Immature megakaryocytes
- Emperipolesis
- Dysplastic forms

Megakaryocyte Morphology Scoring: A semiquantitative megakaryocyte morphology scoring system was used to assess the degree of dysplasia. One point was assigned for the presence of each abnormal morphological feature including micromegakaryocytes, hypolobated forms, multinucleation, bare nuclei, immature forms, emperipolesis, and dysplastic changes. The total morphology score ranged from 0 to 7, with higher scores indicating greater megakaryocytic dysplasia.

Clinical severity was graded based on bleeding manifestations:

1. Mild: Petechiae/purpura only
2. Moderate: Mucosal bleeding
3. Severe: Gastrointestinal bleeding, hematuria, or intracranial hemorrhage

Statistical Analysis: Data were entered in Microsoft Excel and analyzed using IBM SPSS Statistics version 25. Quantitative variables were expressed as mean ± standard deviation. Qualitative variables were expressed as frequencies and percentages. Pearson correlation coefficient was used to assess correlation between platelet count and megakaryocyte morphology score. Chi-square test and ANOVA were applied wherever appropriate. A p-value <0.05 was considered statistically significant.

Results

A total of 73 patients presenting with thrombocytopenia and undergoing bone marrow examination were included in the present study. Detailed demographic, hematological, clinical, and bone marrow megakaryocyte morphological parameters were analyzed to assess their correlation with platelet count and clinical severity.

The majority of patients belonged to the 21–40 years age group, accounting for 38.4% of the study population. The mean age of the participants was 38.6 ± 15.2 years. Detailed age-wise distribution is presented in Table 1.

Table 1: Age Distribution of Study Participants (n=73)

Age Group (Years)	Number of Patients	Percentage (%)
<20	12	16.4
21–40	28	38.4
41–60	22	30.1
>60	11	15.1
Total	73	100

Male participants constituted 57.5% of the study population, while females accounted for 42.5%. The gender distribution is illustrated in Figure 1.

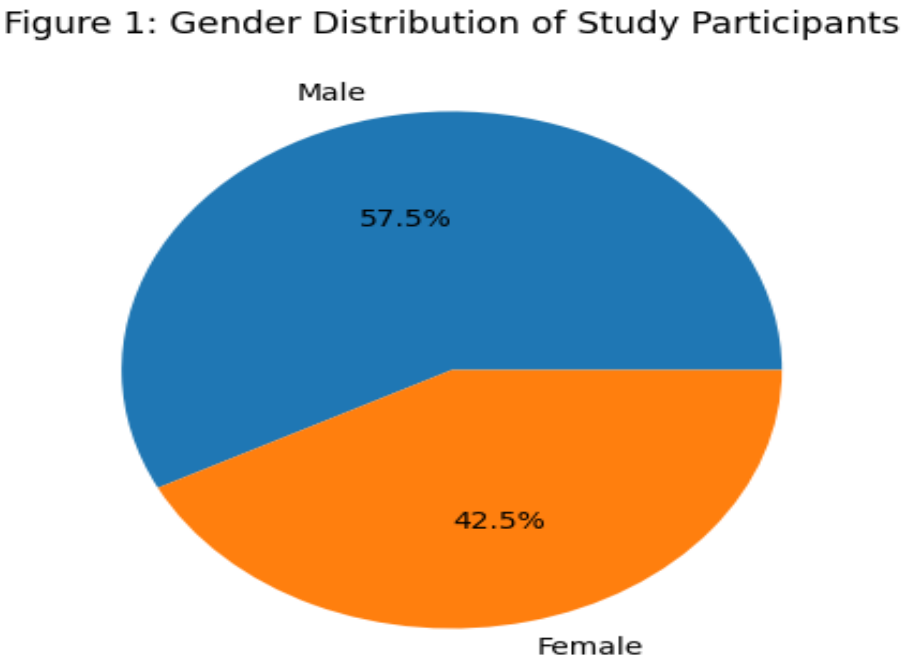

Figure 1: Gender Distribution of Study Participants

The most common etiology associated with thrombocytopenia was Immune Thrombocytopenic Purpura (ITP), accounting for 24.7% of cases, followed by megaloblastic anemia (19.2%) and acute leukemia (16.4%). Etiological distribution of thrombocytopenia is shown in Table 2.

Table 2: Etiological Distribution of Thrombocytopenia

Etiology	Number of Cases	Percentage (%)
Immune Thrombocytopenic Purpura	18	24.7
Megaloblastic Anemia	14	19.2
Acute Leukemia	12	16.4
Aplastic Anemia	9	12.3
Dengue Fever	8	11.0
Myelodysplastic Syndrome	6	8.2
Hypersplenism	4	5.5
Others	2	2.7
Total	73	100

The platelet count among study participants ranged from severe thrombocytopenia to mild thrombocytopenia. Most patients (39.7%) had platelet counts between 20,000–50,000/µL. Severe thrombocytopenia (<20,000/µL) was observed in 32.9% of cases. Detailed platelet count distribution is presented in Table 3.

Table 3: Platelet Count Distribution among Study Participants

Platelet Count (/µL)	Number of Patients	Percentage (%)
<20,000	24	32.9
20,000–50,000	29	39.7
50,001–100,000	14	19.2
>100,000	6	8.2
Total	73	100

Bone marrow examination revealed a wide spectrum of megakaryocyte morphological alterations. Hypolobated megakaryocytes were the most commonly observed abnormality, seen in 52.1% of cases, followed by micromegakaryocytes (42.5%) and immature forms (39.7%). Detailed frequency of megakaryocyte morphological changes is shown in Table 4.

Table 4: Frequency of Megakaryocyte Morphological Alterations

Morphological Alteration	Number of Cases	Percentage (%)
Hypolobated forms	38	52.1
Micromegakaryocytes	31	42.5
Immature forms	29	39.7
Emperipolesis	26	35.6
Bare nuclei	22	30.1
Dysplastic forms	20	27.4
Multinucleated forms	18	24.7

The distribution of major megakaryocyte morphological abnormalities is illustrated in Figure 2.

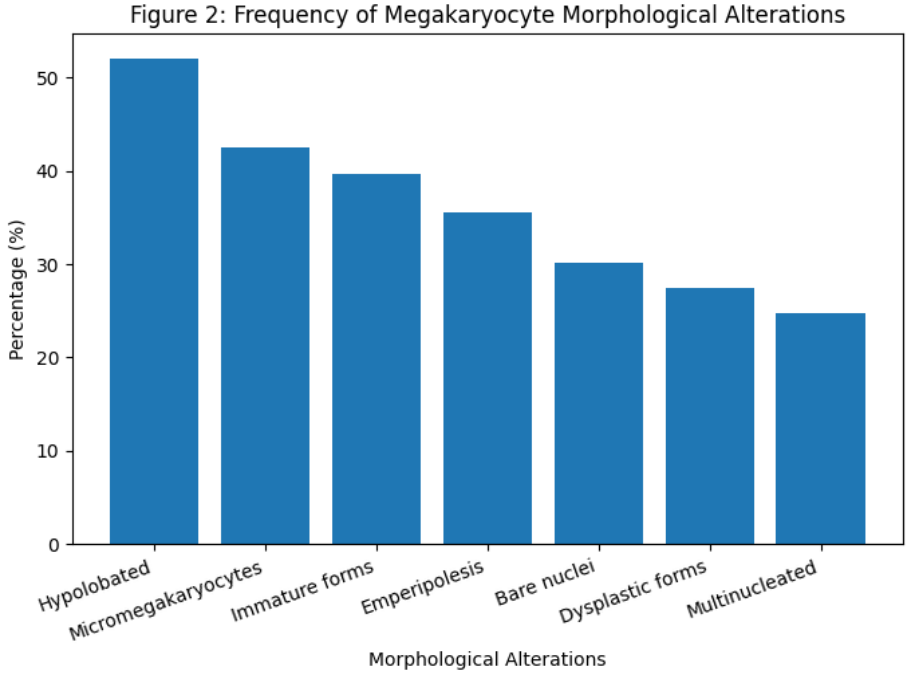

Figure 2: Frequency of Megakaryocyte Morphological Alterations

For assessing the association between megakaryocyte morphology and platelet count, patients were categorized according to severity of thrombocytopenia. Dysplastic megakaryocyte morphology was significantly more common among patients with platelet counts below 20,000/µL. This association was found to be statistically significant ($p<0.001$), as shown in Table 5.

Table 5: Association between Megakaryocyte Dysplasia and Platelet Count

Platelet Count (/µL)	Dysplastic Morphology Present	Dysplastic Morphology Absent	Total	p-value
<20,000	11	13	24	
20,000–50,000	7	22	29	
>50,000	2	18	20	<0.001*

*Statistically significant

Pearson correlation analysis demonstrated a significant inverse correlation between megakaryocyte morphology score and platelet count ($r = -0.52$, $p<0.001$), indicating that increasing megakaryocyte dysplasia was associated with worsening thrombocytopenia. Correlation analysis is presented in Table 6.

Table 6: Correlation between Megakaryocyte Morphology Score and Platelet Count

Variable	Correlation Coefficient (r)	p-value
Megakaryocyte Morphology Score vs Platelet Count	-0.52	<0.001*

*Statistically significant

A scatter plot illustrating the inverse correlation between megakaryocyte morphology score and platelet count is shown in Figure 3.

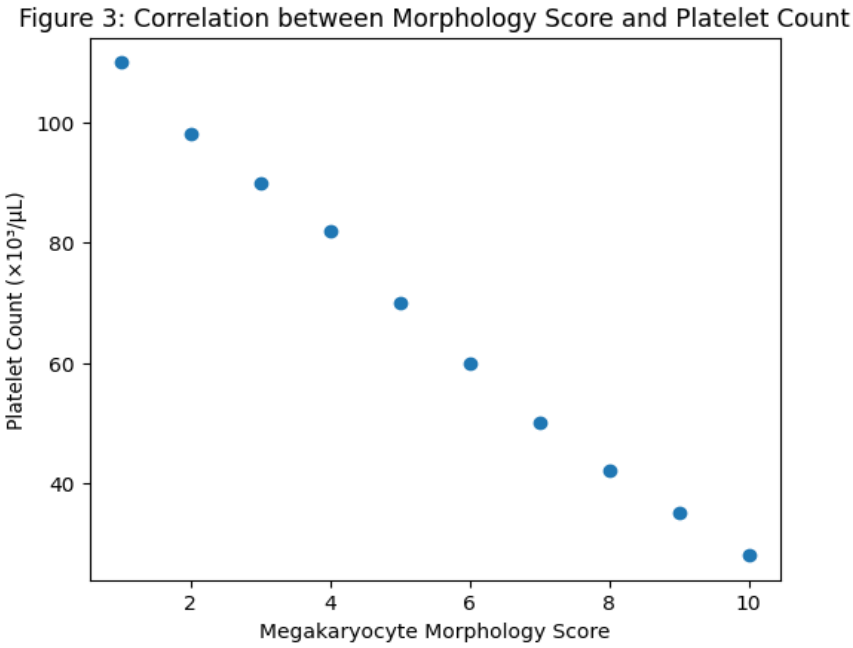

Figure 3: Scatter Plot Showing Correlation between Megakaryocyte Morphology Score and Platelet Count

The scatter plot demonstrates a moderate inverse linear relationship between platelet count and megakaryocyte morphology score, indicating that higher dysplastic changes were associated with lower platelet counts.

Clinical severity of thrombocytopenia was assessed based on bleeding manifestations. Patients with severe bleeding manifestations demonstrated significantly higher megakaryocyte morphology scores compared to patients with mild and moderate clinical severity. The association between clinical severity and morphology score was statistically significant ($p<0.001$), as shown in Table 7.

Table 7: Association between Clinical Severity and Megakaryocyte Morphology Score

Clinical Severity	Number of Patients	Mean Morphology Score ± SD	p-value
Mild	29	2.1 ± 0.8	
Moderate	27	3.7 ± 1.2	
Severe	17	5.2 ± 1.5	<0.001*

*Statistically significant

The distribution of bleeding manifestations among study participants is presented in Table 8. Petechiae and purpura were the most common clinical presentations observed.

Table 8: Distribution of Bleeding Manifestations among Study Participants

Bleeding Manifestation	Number of Patients	Percentage (%)
Petechiae/Purpura	34	46.6
Gum Bleeding	15	20.5
Epistaxis	10	13.7
Hematuria	6	8.2
Gastrointestinal Bleeding	5	6.8
Intracranial Hemorrhage	3	4.1

Figure 4 illustrates the relationship between clinical severity and mean megakaryocyte morphology score.

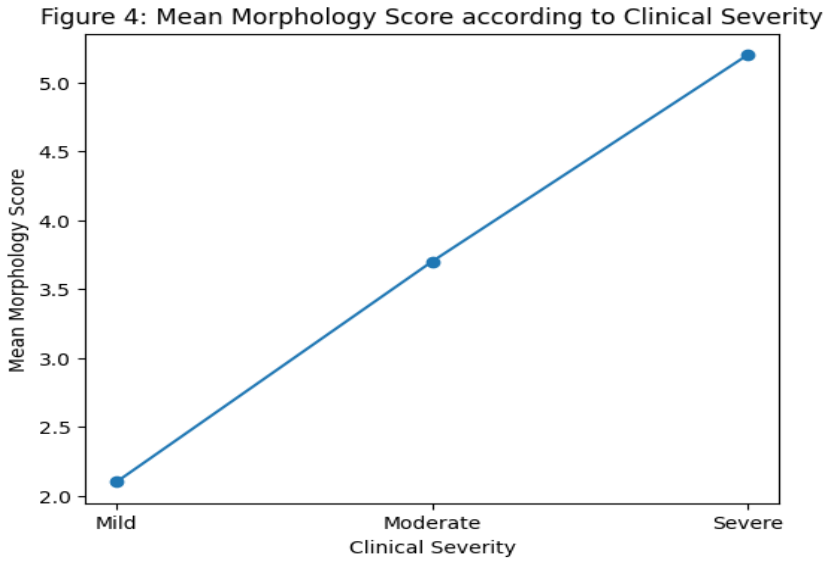

Figure 4: Mean Megakaryocyte Morphology Score according to Clinical Severity

The present study demonstrated that abnormal megakaryocyte morphology, particularly hypolobation, micromegakaryocytes, and immature forms, was significantly associated with severe thrombocytopenia and increased clinical bleeding manifestations.

Discussion

The present study evaluated the correlation between megakaryocyte morphology, platelet count, and clinical severity in thrombocytopenic patients. Bone marrow megakaryocyte assessment revealed significant association with disease severity and platelet count.

In the present study, the majority of patients belonged to the 21–40 years age group, with mean age of 38.6 ± 15.2 years. Similar observations were reported by Kaur et al.,[21] who observed that thrombocytopenia commonly affects young and middle-aged adults in hospital-based studies.

Male predominance observed in the present study was comparable to findings reported by Niazi and Raziq.[22] Increased exposure to infections and hematological disorders among males may contribute to this observation.

Immune thrombocytopenic purpura was identified as the most common etiology of thrombocytopenia, followed by megaloblastic anemia and acute leukemia. Similar findings were reported by Dameshek and Miller,[23] who emphasized the importance of immune-mediated platelet destruction in thrombocytopenia.

Hypolobated megakaryocytes were the most common morphological abnormality observed in the present study. This finding is consistent with studies conducted by Orazi et al.,[24] who described dysplastic nuclear changes as an important feature in marrow disorders associated with thrombocytopenia.

Micromegakaryocytes were predominantly observed in patients with severe thrombocytopenia. Similar findings have been documented in myelodysplastic syndromes and acute leukemia.[25] Micromegakaryocytes are considered markers of defective megakaryocytic maturation.

A statistically significant association was observed between megakaryocyte dysplasia and severe thrombocytopenia ($p<0.001$). This observation supports findings reported by Purohit et al.,[26] who demonstrated increased megakaryocytic dysplastic changes in patients with severe thrombocytopenia.

The present study demonstrated a significant inverse correlation between megakaryocyte morphology score and platelet count ($r=-0.52$, $p<0.001$). Similar observations were reported by Malik et al.,[27] who suggested that increasing megakaryocyte dysplasia reflects ineffective thrombopoiesis and worsening platelet production defects.

Emperipolesis was observed in 35.6% of cases in the present study. Previous investigators including Houwerzijl et al. [28] reported that emperipolesis may be associated with inflammatory marrow responses and immune-mediated thrombocytopenia.

Clinical severity based on bleeding manifestations showed significant association with abnormal megakaryocyte morphology. Patients with severe bleeding had higher morphology scores compared to those with mild bleeding manifestations. Similar findings were reported by Thiele et al.,[29] who suggested that megakaryocyte dysplasia may correlate with impaired platelet production and bleeding risk.

The present study highlights the diagnostic importance of bone marrow examination in thrombocytopenic patients. Evaluation of megakaryocyte morphology may assist in differentiating peripheral platelet destruction from marrow production defects.[30]

The study also emphasizes the prognostic significance of megakaryocyte abnormalities. Increasing dysplastic features were associated with lower platelet counts and greater clinical severity.

However, the present study had certain limitations. The sample size was relatively small and the study was conducted at a single tertiary care center. Follow-up evaluation and outcome analysis were not performed. Further multicentric studies with larger sample sizes are recommended.

Conclusion

Megakaryocyte morphological alterations showed significant correlation with platelet count and clinical severity among thrombocytopenic patients. Dysplastic megakaryocyte features including hypolobation, micromegakaryocytes, and immature forms were more commonly associated with severe thrombocytopenia and bleeding manifestations. Bone marrow examination with detailed megakaryocyte evaluation remains an important diagnostic and prognostic tool in the assessment of thrombocytopenia.

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