



Original Research Article

MORPHOLOGICAL VARIATIONS IN MEGAKARYOCYTES: INSIGHTS FROM BONE MARROW CYTOLOGY

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ABSTRACT

Background: Megakaryocytes are specialised haematopoietic cells responsible for platelet production. Their quantitative and qualitative morphological abnormalities provide valuable diagnostic information in various haematological disorders. Although dysplastic megakaryocytic changes are characteristic of myelodysplastic syndromes, similar features may occur in several non-MDS conditions. Therefore, systematic evaluation of megakaryocyte morphology is essential for accurate interpretation of bone marrow aspirates.

Materials and Methods: A retrospective observational study reviewed 40 archived bone marrow aspiration smears received between August 2023 and July 2025 at the Department of Pathology, ESIC Medical College and Hospital, Kalaburagi. Leishman-stained smears and clinical records were evaluated for megakaryocyte number, size, nuclear configuration, and cytoplasmic features. Dysplastic features and non-dysplastic changes were assessed.

Results: In the present study of 40 cases, megaloblastic anaemia was the predominant diagnosis (16 cases/40%), followed by iron deficiency anaemia (8 cases/20%) and immune thrombocytopenic purpura (4 cases/10%). Megakaryocyte counts showed variation across different disorders, with increased numbers observed in megaloblastic anaemia, immune thrombocytopenic purpura, chronic myeloid leukaemia, and myeloproliferative neoplasms. Among the dysmegakaryopoietic features, hypolobated forms were the most common (14 cases/35.0%), whereas immature forms were the predominant non-dysplastic feature (17 cases/42.5%).

Conclusion: Megakaryocyte morphology in bone marrow aspiration smears demonstrates considerable variation across haematological disorders. Assessment of megakaryocyte number and morphology, including both dysplastic and non-dysplastic features, provide valuable diagnostic insights. A comprehensive evaluation integrating megakaryocyte morphology with clinical, haematological, and laboratory findings is essential for establishing the underlying diagnosis.

Keywords: Megakaryocytes; Bone marrow aspiration; Megakaryopoiesis; Megakaryocytic dysplasia; Haematological disorders; Cytomorphology.

INTRODUCTION

Megakaryocytes are specialised haematopoietic cells responsible for the production of platelets.

They originate from pluripotent haematopoietic stem cells (HSCs), which differentiate into committed progenitor cells through sequential stages of maturation. Early progenitor cells, including burst-forming unit-

megakaryocyte (BFU-MK) and colony-forming unit-megakaryocyte (CFU-MK), express the CD34 surface antigen and subsequently develop into mature megakaryocytes through a tightly regulated process of differentiation and endomitosis.^[1,2] Thrombopoietin (TPO) is the principal cytokine regulating megakaryocyte proliferation, maturation, and platelet production. It maintains normal platelet homeostasis by stimulating megakaryopoiesis and acts synergistically with several cytokines, including interleukin (IL)-3, IL-6, and IL-11, to support the growth and differentiation of megakaryocytic progenitor cells.^[3,4] During maturation, megakaryocytes undergo extensive cytoplasmic development and form specialised membrane systems that ultimately generate thousands of circulating platelets from a single cell. Any disruption in this complex process may result in quantitative or qualitative platelet abnormalities and contribute to a variety of haematological disorders.^[5,6]

Morphological evaluation of megakaryocytes in bone marrow aspirates provides valuable diagnostic information in several benign and malignant haematological conditions. Alterations in megakaryocyte number, size, nuclear configuration, and cytoplasmic features reflect the underlying bone marrow pathology and assist in differentiating reactive from neoplastic disorders. Dysplastic megakaryocytic changes are considered characteristic of myelodysplastic syndromes (MDS); however, similar abnormalities may also be encountered in several non-MDS conditions. These include immune thrombocytopenic purpura (ITP), megaloblastic anaemia, aplastic anaemia, iron deficiency anaemia, chronic myeloid leukaemia (CML), multiple myeloma, and acute leukaemia. Therefore, careful assessment of megakaryocyte morphology should always be interpreted in conjunction with the clinical presentation and other haematological findings to establish an accurate diagnosis.^[7,8]

Aims

1. To evaluate the morphological characteristics of megakaryocytes in bone marrow aspiration smears.
2. To identify qualitative and quantitative abnormalities of megakaryocytes in various haematological disorders.

MATERIALS AND METHODS

The present retrospective observational study was conducted in the Department of Pathology, ESIC Medical College and Hospital, Kalaburagi, using archived bone marrow aspiration (BMA) cases received between August 2023 and July 2025. Bone marrow aspiration reports, Leishman-stained smears, and relevant clinical records were retrieved from departmental archives to evaluate the quantitative and qualitative morphological changes

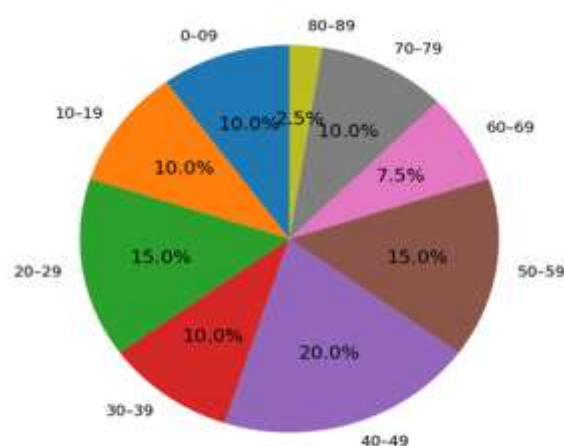
of megakaryocytes in various haematological disorders.

Patients of all age groups with adequately cellular and well-stained BMA smears were included. Poorly preserved or inadequately stained smears, severely haemodiluted or acellular aspirates, and cases receiving chemotherapy or other disease-modifying treatment were excluded.

The retrieved Leishman-stained BMA smears were examined under light microscopy. Megakaryocyte numbers were assessed by examining 10 low-power fields (LPF) and categorised as decreased (1 megakaryocyte/5–10 LPF), normal (1 megakaryocyte/1–3 LPF), or increased (>2 megakaryocytes/LPF). Qualitative evaluation included dysplastic features such as micromegakaryocytes, hypolobated forms, multiple separated nuclei (pawn-ball megakaryocytes), and hypogranular forms, along with non-dysplastic features including immature forms, emperipoiesis, cytoplasmic vacuolization, and bare megakaryocyte nuclei. Whenever feasible, at least 30 megakaryocytes were evaluated per smear, and dysplastic changes were considered significant when present in $\geq 10\%$ of the megakaryocytes examined.⁹ Data were analysed using descriptive statistics. Categorical variables were expressed as frequencies and percentages. The distribution of megakaryocyte frequency and morphological features was assessed across the different diagnostic categories.

RESULTS

A total of 40 cases were included in the study, comprising a wide range of haematological disorders. Bone marrow aspirates from all cases were evaluated for overall cellularity, and detailed megakaryocyte morphology.



Graph 1: Distribution of cases according to the age group

Among 40 cases, highest proportion of cases was observed in the 40–49 years age group, accounting

for 20% of the cases. The 20–29 years and 50–59 years age groups each constituted 15%. The 0–09, 10–19, 30–39, and 70–79 years age groups each contributed 10% of the cases. The 60–69 years age group accounted for 7.5%, while the

80–89 years age group represented the smallest proportion, at 2.5%. Overall, the distribution indicates that the study population was predominantly in the adult age groups, particularly 40–49 years.

Table 1: Distribution of Cases According to Diagnosis

Cases	Total cases	Peripheral Smear findings
Iron Deficiency Anaemia (IDA)	8	Microcytic hypochromic RBCs, (5 cases) Marked microcytosis and hypochromia with anisopoikilocytosis (3 cases)
Megaloblastic Anaemia	16	Macro-ovalocytes, anisopoikilocytosis, hypersegmented neutrophils (11 cases) Dimorphic population of macrocytes & normocytes (5 cases)
ITP	4	Thrombocytopenia with increased large platelets
Multiple Myeloma	2	Rouleaux formation, normocytic normochromic anaemia & occasional circulating plasma cells
Aplastic Anaemia	2	Pancytopenia (Normocytic normochromic RBCs, markedly reduced leukocytes and platelets)
Chronic Myeloid Leukaemia (CML)	2	Leucocytosis with left shift, increased myelocytes & metamyelocytes; basophilia
Chronic Lymphocytic Leukaemia (CLL)	1	Marked absolute lymphocytosis with predominance of small mature lymphocytes & smudge cells
Acute Myeloid Leukaemia (AML)	1	Leucocytosis with few circulating blast cells, high N:C ratio, fine chromatin & prominent nucleoli
Myeloproliferative Neoplasms (MPN)	2	Normocytic normochromic cells with teardrop & pencil shaped cells
Pyrexia of Unknown Origin (PUO)	2	Normocytic normochromic RBCs

Among the 40 cases, megaloblastic anaemia was the most common diagnosis (16 cases, 40%), followed by IDA (8 cases, 20%). Peripheral smear findings

were consistent with the respective haematological disorders.

Table 2: Megakaryocytes (Mk) per low power field (lpf)

Cases	Normal	Increased	Decreased
	(1 Mk /1–3 LPF)	(>2 Mk /LPF)	(1Mk /5–10 LPF)
Iron Deficiency Anaemia (IDA)	6	2	0
Megaloblastic Anaemia	5	11	0
ITP	0	4	0
Multiple Myeloma	2	0	0
Aplastic Anaemia	0	0	2
Chronic Myeloid Leukaemia (CML)	0	2	0
Chronic Lymphocytic Leukaemia (CLL)	1	0	0
Acute Myeloid Leukaemia (AML)	1	0	0
Myeloproliferative Neoplasms (MPN)	0	2	0
Pyrexia of Unknown Origin (PUO)	2	0	0

Increased megakaryocytes were predominant in megaloblastic anaemia (11/16), ITP (4/4), CML (2/2) and MPN (2/2). Most IDA cases showed normal megakaryocyte numbers (6/8). The aplastic

anaemia case showed decreased megakaryocytes. Overall, megakaryocyte frequency varied according to the underlying haematological disorder.

Table 3: Distribution of Dysmegakaryopoietic Features According to the Cases

Diseases	Multiple Segmented Nuclei	Hypogranular Forms	Hypoblated Forms	Micro Megakaryocytes	Cytoplasmic vacuolations
IDA	0	2	1	0	0
Megaloblastic Anaemia	2	1	2	0	0
ITP	2	1	1	1	1
Multiple Myeloma	2	0	0	0	0
Aplastic Anaemia	0	1	1	1	0
CML	1	1	2	3	0
CLL	0	0	1	0	0
AML	0	2	2	1	0
MPN	1	1	4	1	0
PUO	0	0	0	0	1

Hypolobated and hypogranular forms were the most frequently observed dysmegakaryopoietic features, occurring in 14 cases (35.0%) and 9 cases (22.5%), respectively. Multiple/segmented nuclei were observed in 8 cases (20.0%), while micromegakaryocytes were identified in 7 cases (17.5%). Cytoplasmic vacuolations were the least frequently observed feature, occurring in 2 cases (5.0%). Dysmegakaryopoietic changes were observed across various haematological disorders,

with the greatest number of feature observations noted in CML and MPN (7 observations each), followed by ITP (6 observations), megaloblastic anaemia and AML (5 observations each). These findings indicate that dysmegakaryopoietic changes, particularly hypolobated and hypogranular forms, were not confined to a single haematological disorder but occurred across a broad spectrum of haematological conditions. [Figure 2A & 2B]

Table 4: Distribution of Non-Dysplastic Features According to the Cases

Diseases	Immature Forms	Emperipolesis	Cytoplasmic Budding	Bare Nuclei
IDA	4	0	0	1
Megaloblastic Anaemia	3	2	2	4
ITP	2	1	1	1
Multiple Myeloma	1	0	1	1
Aplastic Anaemia	1	0	0	0
CML	2	1	1	0
CLL	0	0	0	1
AML	2	0	1	0
MPN	2	3	2	1
PUO	0	0	0	0

Immature forms were the most frequently observed non-dysplastic megakaryocytic feature, occurring in 17 cases (42.5%), followed by bare nuclei in 9 cases (22.5%), cytoplasmic budding in 8 cases (20.0%), and emperipolesis in 7 cases (17.5%). Non-dysplastic megakaryocytic features were observed across a range of haematological disorders. The greatest number of feature observations was noted in megaloblastic anaemia (11), followed by MPN (8), IDA and ITP (5 each), CML (4), multiple myeloma and AML (3 each), aplastic anaemia and CLL (1 each). No non-dysplastic features were observed in the PUO cases. Overall, immature forms constituted the predominant non-dysplastic megakaryocytic feature, while emperipolesis was the least frequently observed feature. [Figure 2C & 3A]

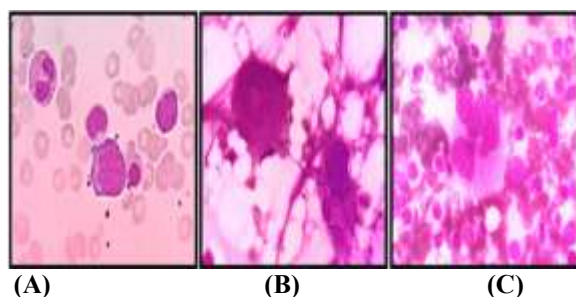


Figure 1: Bone marrow aspirates showing normal megakaryocytes at different stages of maturation. (A) Early megakaryocyte (megakaryoblast). (B) Immature megakaryocyte (promegakaryocyte). (C) Mature megakaryocyte

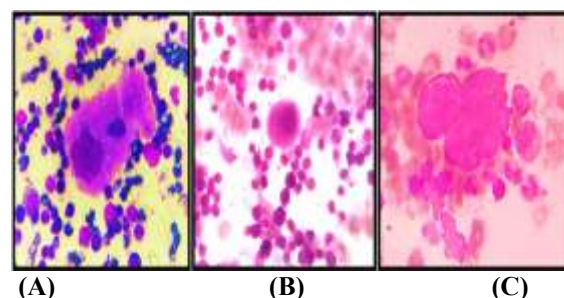


Figure 2: Bone marrow aspirates showing megakaryocytes with (A) Hypolobated form, (B) Micromegakaryocytes (C) Bare nuclei

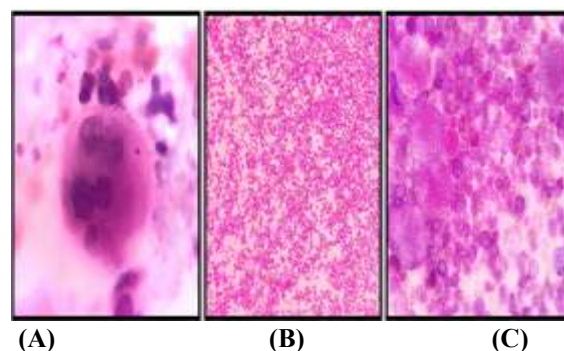


Figure 3: Bone marrow aspirates showing (A) Emperipolesis & Megakaryocytic hyperplasia (B) Low power view (C) High power view

DISCUSSION

Megakaryocytes constitute less than 1% of nucleated bone marrow cells but are the largest haematopoietic cells in the bone marrow. Assessment of their number, maturation, and morphology remains an integral component of bone marrow aspiration reporting. In the present study,

megakaryocyte morphology was evaluated in 40 adequate bone marrow aspiration smears representing a spectrum of haematological disorders.

Increased megakaryocyte numbers were predominantly observed in megaloblastic anaemia, ITP, chronic myeloid leukaemia (CML) and myeloproliferative neoplasms (MPN), whereas decreased megakaryocyte numbers were noted in aplastic anaemia. These findings are in agreement with the WHO Classification of Haematolymphoid Tumours (Loghavi et al., 2024),^[8] which recognises increased megakaryopoiesis as a characteristic feature of myeloproliferative neoplasms and reduced megakaryocytes in marrow failure syndromes. Recent work by Kana et al. (2024),^[10] also demonstrated heterogeneous megakaryocyte morphology with increased megakaryocytic proliferation in CML.

Immature megakaryocytes were encountered in cases of AML, CML, MPN, IDA and megaloblastic anaemia. In the present study, immature forms were the most frequently observed non-dysplastic megakaryocytic feature, occurring in 17 cases (42.5%), followed by bare nuclei in 9 cases (22.5%), cytoplasmic budding in 8 cases (20.0%), and emperipoiesis in 7 cases (17.5%). The highest number of non-dysplastic feature observations was noted in megaloblastic anaemia, followed by MPN, with IDA and ITP also showing several non-dysplastic changes. These observations are comparable with the review by Du et al. (2025),^[11] which emphasised that abnormal megakaryocyte maturation is a hallmark of both reactive and neoplastic disorders and reflects disturbed megakaryopoiesis.

Hypolobated forms represented the most frequent dysmegakaryopoietic feature in the present study, occurring in 14 cases (35.0%), followed by hypogranular forms in 9 cases (22.5%). Multiple/segmented nuclei were observed in 8 cases (20.0%), while micromegakaryocytes were observed in 7 cases (17.5%). Hypolobated forms were most prominently represented in MPN, followed by CML, megaloblastic anaemia and AML, with additional occurrences in IDA, ITP, aplastic anaemia and CLL. Similar observations have been reported in the WHO Classification (Loghavi et al., 2024),^[8] and by Kana et al. (2024),^[10] who described micromegakaryocytes and abnormal megakaryocyte morphology as characteristic features of myeloid neoplasms.

Hypolobated forms and multiple/segmented nuclei were identified in several haematological disorders, including MPN, CML, AML, ITP and megaloblastic anaemia. In particular, MPN showed the highest representation of hypolobated forms, while CML showed prominent micromegakaryocytic changes. These findings are consistent with the observations of Thiele et al. (2023),^[12] who highlighted abnormal nuclear morphology and dysplastic megakaryocytes

as important morphological features in myeloproliferative disorders.

Hypogranular megakaryocytes were observed in 9 cases (22.5%) and constituted the second most frequent dysmegakaryopoietic feature in the present study. They were distributed across several disorders, with the highest number of observations in IDA and AML (2 observations each), while single observations were recorded in megaloblastic anaemia, ITP, aplastic anaemia, CML and MPN, indicating that hypogranularity was not restricted exclusively to clonal myeloid neoplasms. Recent reviews by Xu et al. (2024),^[13] have explained that defective cytoplasmic maturation and abnormal granule formation reflect disturbed megakaryocyte differentiation and are commonly encountered in myeloid neoplasms.

Reactive and nutritional disorders such as iron deficiency anaemia and megaloblastic anaemia demonstrated both dysmegakaryopoietic and non-dysplastic megakaryocytic features. In IDA, hypogranular forms were the predominant dysmegakaryopoietic finding, whereas megaloblastic anaemia showed multiple/segmented nuclei, hypolobated and hypogranular forms along with prominent non-dysplastic features. This indicates that megakaryocyte morphological alterations may occur in reactive and nutritional conditions as well, although the overall pattern and combination of abnormalities may differ from those seen in clonal disorders. Recent reviews by Du et al. (2025),^[11] and Wang et al. (2024),^[14] also emphasise that true dysplastic megakaryocytes are more frequent in clonal myeloid disorders than in reactive or nutritional conditions.

Overall, the findings of the present study demonstrate that dysmegakaryopoietic features were observed across a broad spectrum of haematological disorders, with hypolobated forms being the predominant abnormality, followed by hypogranularity, multiple/segmented nuclei and micromegakaryocytes. Among the disorders studied, MPN and CML showed the greatest representation of dysmegakaryopoietic features. In contrast, non-dysplastic features were also frequently encountered, with immature forms being the predominant finding, followed by bare nuclei, cytoplasmic budding and emperipoiesis. These findings indicate that megakaryocyte morphology may show considerable variation across both neoplastic and non-neoplastic haematological disorders. Megakaryocyte morphology reflects the complex interplay between thrombopoiesis, bone marrow microenvironment, and disease-related alterations, emphasizing its importance in understanding haematological disorders.^[15] Careful morphological evaluation of megakaryocytes on bone marrow aspiration smears, in conjunction with peripheral blood findings and clinical features, remains an essential diagnostic tool in the evaluation of haematological disorders.

CONCLUSION

According to international qualitative and quantitative guidelines, a harmonized evaluation of megakaryocyte morphology facilitates rapid diagnosis and aids in the prognostic stratification of patients. Optical microscopy (OM) remains a key tool for the assessment of megakaryocyte morphology. However, its interpretation is subject to interobserver variability and requires adequate expertise and training. Dysplastic megakaryocytes are not confined to myelodysplastic syndromes (MDS) and may also be observed in several non-MDS conditions. Therefore, morphological findings alone should not be used to establish a definitive diagnosis. A comprehensive approach that integrates clinical findings, haematological parameters, and bone marrow morphological features significantly improves diagnostic accuracy and contributes to appropriate patient management.

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