International Journal of Scientific Research in Dental and Medical Sciences

www.ijsrdms.com

Megakaryocytic Alterations in Cases of Thrombocytopenia on Bone Marrow Examination at a Tertiary Care Centre

Ishita Choudhary *, Sonal Bhati, Seema Meena, Monika Lukkad

Department of Pathology, Rabindranath Tagore Medical College, Udaipur, India

ARTICLE INFO

Article history:
Received 07 April 2025
Received in revised form 25 May 2025
Accepted 03 June 2025
Available online 05 June 2025

Keywords:
Bone Marrow Cells
Hematopoiesis
Platelet Count

ABSTRACT

Background and aim: Thrombocytopenia is a common hematological disorder characterized by the abnormal development of megakaryocytes, a crucial component of bone marrow. This study aims to analyze age-wise distribution, causes, megakaryocytic alterations, and dysplastic and non-dysplastic changes.

Material and methods: This was a cross-sectional observational study conducted at the Department of Pathology, RNT Medical College, Udaipur, over six months. Bone marrow aspiration smears from 68 cases of thrombocytopenia were received and stained with Giemsa stain for 15-20 minutes. The examination was conducted under a light microscope to determine the number and morphology of megakaryocytes, and the findings were analyzed.

Results: The commonest cause of thrombocytopenia was found to be acute leukemia (35.3%), followed by megaloblastic anemia (25%). The age-wise distribution of all cases showed a maximum number of cases belonging to the 21-30-year age group (26.5%). Cases with ITP presented with an increased number of megakaryocytes (100%). The decreased number was seen in the majority of cases of MDS (75%) and acute leukemia (62.5%). The total number of cases with dysplastic changes was 18 (26.5%), and that of non-dysplastic changes was 33 (48.5%).

Conclusions: Megakaryocyte alterations in bone marrow aspirates from patients with thrombocytopenia underscore their clinical significance despite their small proportion in cellularity. A comprehensive evaluation is crucial for understanding the relationship between megakaryocyte alterations and the factors that cause thrombocytopenia, thereby enabling the development of effective treatment options.

1. Introduction

Megakaryocytes (MKs), which arise from hematopoietic stem cells (HSCs), are the precursor cells responsible for producing and releasing platelets into the bloodstream. Mature MKs produce circulating platelets by acquiring the necessary cytoplasmic structural and functional characteristics for platelet function.[1] Thrombocytopenia is characterized by a platelet count of less than the normal range (150,000 – 450,000 per cubic millimeter). This hematological condition can be caused by various factors, including megaloblastic anemia, acute leukemia, dimorphic anemia, idiopathic thrombocytopenic purpura (ITP), chronic myeloid leukemia (CML), lymphoproliferative disorder, myelodysplastic syndromes (MDS), multiple myeloma, and bone marrow metastasis.[2] Although megakaryocytes constitute only a small fraction (0.5%) of the marrow cellularity, their maturation is closely linked to their natural microenvironment. The number of megakaryocytes is expressed as a number per 10 low power field (LPF) and is further subdivided into absent (no megakaryocytes seen in 10 LPF), decreased (1/5–10 LPF), normal (1/1–3 LPF), and increased (>2/LPF).[2] Any defect in the stages of megakaryopoiesis can result in dysmegakaryopoiesis and thrombocytopenia. Dysmegakaryopoiesis is characterized by various megakaryocytic alterations in the bone marrow aspirates and includes both non-dysplastic and dysplastic features.[3] Nondysplastic features included immature forms, emperipolesis, platelet budding, cytoplasmic vacuolization, and bare megakaryocyte nuclei. Dysplastic features included hyperlobated nuclei, micromegakaryocytes, and hypogranular forms.[4] Dysplastic changes are seen in megakaryocytes in non-myelodysplastic hematological conditions such as megaloblastic anemia, immune thrombocytopenic purpura (ITP), infection-associated thrombocytopenia (IAT), hypersplenism, dimorphic anemia, acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), bone marrow metastasis and blast crisis of chronic myeloid leukemia. These changes are exceptionally well documented in thrombocytopenia related to myelodysplastic syndrome (MDS).[5] Minimum of 30 megakaryocytes have to be evaluated on BMA smears, and dysplastic alterations are considered significant only when 10% or more of megakaryocytes observed show the changes. Despite this, there is limited data on the prevalence of dysplastic changes in megakaryocytes in non-myelodysplastic hematological conditions.[6] Although megakaryocytes make

* *Corresponding author. Ishita Choudhary*
E-mail address: *ishita.choudhary@gmail.com*
Department of Pathology, Rabindranath Tagore Medical College, Udaipur, India
https://doi.org/10.30485/IJSRDMS.2025.513248.1655

up only a small portion of bone marrow cells, they are just as critical as erythroid and myeloid cells in bone marrow assessments. Recognizing their significance could enhance clinical approaches to regulating platelet production and function. A comprehensive evaluation is essential for identifying how changes in megakaryocytes contribute to different causes of thrombocytopenia, enabling more effective treatment strategies. Therefore, the current study aimed to identify the various causes of thrombocytopenia and to gain a better understanding of megakaryocytic alterations in various conditions that lead to thrombocytopenia, thereby improving diagnostic accuracy.

2. Material and Methods

Study design

This was a cross-sectional observational study that was conducted after approval by the Ethics Committee of Rabindranath Tagore Medical College and MB Hospital, Udaipur.

Study site

Department of Pathology, Rabindranath Tagore Medical College and MB Hospital, Udaipur.

Study period

Six months.

Inclusion criteria

All the cases of thrombocytopenia diagnosed on a HORIBA hematology analyzer (Platelet count <1,50,000/mm^3) and confirmed subsequently by peripheral blood smear examination.

Exclusion criteria

Cases showing evidence of pseudo-thrombocytopenia, inadequate material, or receiving chemo/radiotherapy.

Procedure

• Prior informed consent was taken from all the patients. Detailed clinical histories, physical examinations, past medical histories, family histories, and radiological investigations were also collected for these patients. Diagnosis of thrombocytopenia was made after evaluation of CBC and PBF.

• Corresponding bone marrow aspiration smears were received in our department and stained by Giemsa stain for 15-20 mins. After rinsing in distilled water, the slides were examined under a light microscope according to standard guidelines.

• The number of megakaryocytes was assessed by counting them across 10 low-power fields (LPFs). They were classified as absent if no megakaryocytes were seen in 10 LPFs, decreased if one was observed in 5-10 LPFs, normal if one was observed in 1-3 LPFs, and increased if more than two were seen per LPF.

• Morphological features of megakaryocytes were studied at 100X magnification. A minimum of 30 megakaryocytes were examined for alterations, including non-dysplastic features like immature forms and cytoplasmic vacuolization, as well as dysplastic features such as multiple separate nuclei, micromegakaryocytes and hypogranular forms.

• The findings of the BMA smears were documented in a tabular form. The age-wise distribution of cases presenting with thrombocytopenia, their causes, as well as the number and morphology of the megakaryocytes were studied and tabulated after detailed microscopic examination.

3. Results

In the present study, out of the 68 patients, 41 (60.3%) were males and 27 (39.7%) were females. The majority of cases were observed in the 21–30 years age group, accounting for 18 cases (26.5%), followed by the 0–10 years group with 16 cases (23.5%). The 11–20 years age group comprised 11 cases (16.2%). Cases in the 41–50 and 51–60 years age groups were 8 (11.8%) and 6 (8.8%), respectively. The 31–40 years group contributed 5 cases (7.3%). At the same time, only 5.9% of the cases were seen in individuals above 60 years of age, including 3 cases (4.4%) in the 61–70 years group and 1 case (1.5%) in the 71–80 years group. The most typical cause of thrombocytopenia for which bone marrow aspiration was sought was acute leukemia (35.3%) followed by megaloblastic anemia (25%), dimorphic anemia (10.3%), idiopathic thrombocytopenic purpura (8.8%), myelodysplastic syndrome (5.9%), multiple myeloma (4.4%), lymphoproliferative disorder (4.4%), CML – Blast Crisis (2.9%) and metastatic deposits (2.9%) (Table 1).

Table 1. Causes of thrombocytopenia.

Bone Marrow Aspiration Impression	No. of Cases (Total-68)	Percentage (%)
Acute Leukemia	24	35.3
Megaloblastic Anemia	17	25
Dimorphic Anemia	7	10.3
ITP	6	8.8
MDS	4	5.9
Multiple Myeloma	3	4.4
Lymphoproliferative Disorder	3	4.4
CML – Blast Crisis	2	2.9
Metastatic Deposits	2	2.9

Cases of acute leukemia presented with either a decreased number (62.5%) or absent megakaryocytes (37.5%), whereas megaloblastic anemia cases showed either normal (58.8%) or increased (41.2%) number. Most cases of dimorphic anemia (71.4%) and multiple myeloma (66.7%) showed a normal number, whereas all cases of ITP presented with an increased number of megakaryocytes. The decreased number was observed in the majority of MDS cases (75%) and all cases of Lymphoproliferative disorder, CML-Blast Crisis, as well as metastasis (Table 2).

Table 2. Number of megakaryocytes seen in LPF (10x)

Bone Marrow Aspiration Impression	Normal	Increased	Decreased	Absent	Total
Acute Leukemia	0(0%)	0(0%)	15(62.5%)	9(37.5%)	24
Megaloblastic Anemia	10(58.8%)	7(41.2%)	0(0%)	0(0%)	17
Dimorphic Anemia	5(71.4%)	0(0%)	1(14.3%)	1(14.3%)	7
ITP	0(0%)	6(100%)	0(0%)	0(0%)	6
MDS	1(25%)	0(0%)	3(75%)	0(0%)	4
Multiple Myeloma	2(66.7%)	0(0%)	0(0%)	1(33.3%)	3
Lymphoproliferative Disorder	0(0%)	0(0%)	3(100%)	0(0%)	3
CML – Blast Crisis	0(0%)	0(0%)	2(100%)	0(0%)	2
Metastatic Deposits	0(0%)	0(0%)	2(100%)	0(0%)	2

Our study identified both dysplastic and non-dysplastic alterations in megakaryocytes. (Table 3). Among the dysplastic features commonly observed were micromegakaryocytes, hypermutated nuclei, and forms that were hypogranular. Commonly observed nondysplastic features included hypolobated forms and cytoplasmic vacuolation. Hypolobated forms were observed in cases of acute leukemia (37.5%), ITP (33.3%), MDS (25%), and multiple myeloma (66.7%), whereas hyperlobated megakaryocytes were seen in cases of megaloblastic anemia (29.4%). Hypogranulation was noted in cases of acute leukemia (8.3%), multiple myeloma (33.3%), metastatic deposits (50%), and in all cases of CML-Blast Crisis. Micromegakaryocytes were a feature of the majority of cases of MDS (75%) and ITP (66.7%), as well as all cases of CML-Blast Crisis. Cytoplasmic vacuolization, which was present in a total of 20 cases, suggests heightened megakaryocyte turnover.

Table 3. Morphological changes in megakaryocytes.

Bone Marrow Aspiration Impression	Normal	Hypolobation	Hyperlobation	Hypogranular Forms	Micro Megakaryocytes	Cytoplasmic Vacuolation
Acute Leukemia (n=24)	4(16.7%)	9(37.5%)	0(0%)	2(8.3%)	0(0%)	9(37.5%)
Megalo-blastic Anemia (n=17)	6(35.3%)	0(0%)	5(29.4%)	0(0%)	0(0%)	6(35.3%)
Dimorphic Anemia (n=7)	3(42.8%)	0(0%)	0(0%)	0(0%)	0(0%)	4(57.1%)
ITP (n=6)	0(0%)	2(33.3%)	0(0%)	0(0%)	4(66.7%)	0(0%)
MDS (n=4)	0(0%)	1(25%)	0(0%)	0(0%)	3(75%)	1(25%)
Multiple Myeloma (n=3)	0(0%)	2(66.7%)	0(0%)	1(33.3%)	0(0%)	0(0%)
Lymphoproliferative Disorder (n=3)	3(100%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
CML –Blast Crisis (n=2)	0(0%)	0(0%)	0(0%)	2(100%)	2(100%)	0(0%)
Metastatic Deposits (n=2)	1(50%)	0(0%)	0(0%)	1(50%)	0(0%)	0(0%)

The diseases were further analyzed based on the percentage of dysplastic and non-dysplastic changes observed (Table 4). The total number of cases with dysplastic changes was 18 (26.5%), and that of non-dysplastic changes was 33 (48.5%). Both (100%) cases of CML – Blast Crisis showed dysplastic changes, followed by 75% cases of MDS, 66.7% cases of ITP, 50% cases with metastatic deposits, 33.3% cases of multiple myeloma, 29.4% cases of megaloblastic anemia and 8.3% cases of acute leukemia. In contrast, conditions like dimorphic anemia and lymphoproliferative disorder showed no dysplastic changes.

Table 4. Frequency of dysplastic and non-dysplastic changes in various hematological conditions.

Bone Marrow Aspiration Impression	Dysplastic Changes	Non-Dysplastic Changes	Megakaryocytes Showing no Alterations	Total
Acute Leukemia	2(8.3%)	18(75%)	4(16.7%)	24
Megaloblastic Anemia	5(29.4%)	6(35.3%)	6(35.2%)	17
Dimorphic Anemia	0(0%)	4(57.1%)	3(42.8%)	7
ITP	4(66.7%)	2(33.3%)	0(0%)	6
MDS	3(75%)	1(25%)	0(0%)	4
Multiple Myeloma	1(33.3%)	2(66.7%)	0(0%)	3
Lymphoproliferative Disorder	0(0%)	0(0%)	3(100%)	3
CML – Blast Crisis	2(100%)	0(0%)	0(0%)	2
Metastatic Deposits	1(50%)	0(0%)	1(50%)	2
Total Cases	18(26.5%)	33(48.5%)	17(25%)	68

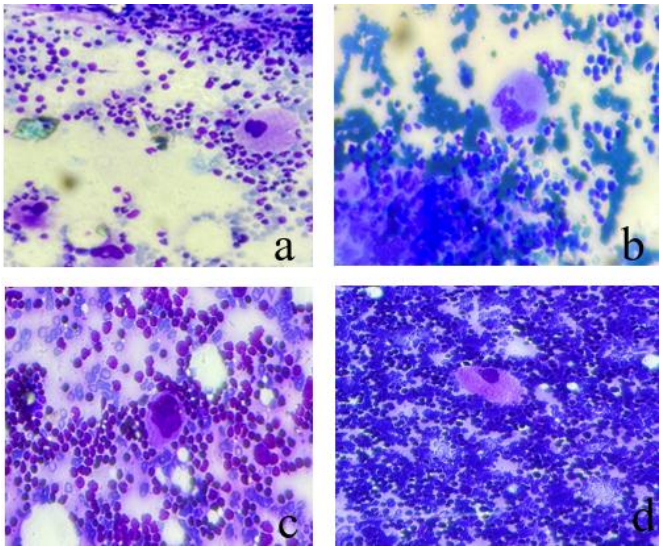

Fig. 1. (a) Increased number of megakaryocytes, (b) A hyperlobated megakaryocyte seen in a case of megaloblastic Anemia, (c) A micro micromegakaryocyte seen in a case of CML – Blast Crisis, and (d) Hypolobated megakaryocyte (100x).

4. Discussion

Normal platelet formation occurs through megakaryocyte DNA replication without cell division (endomitosis), resulting in a large, lobulated, and polyploid nucleus. Various growth factors, including thrombopoietin, work together with other hematopoietic cytokines and transcription factors to stimulate the maturation and development of megakaryocytes. A defect at any stage of megakaryopoiesis can lead to dysmegakaryopoiesis and thrombocytopenia.[7] Dysplastic megakaryocytes are characterized by having hyperlobated nuclei, micromegakaryocytes, and hypogranulation. Micromegakaryocytes are identified by their small size (<15 µ), comparable to a large lymphocyte or monocyte, and typically possess a single or bilobed nucleus. Hyperlobated nuclei refer to nuclei with an abnormal or excessive number of lobes. Hypogranular forms are defined by a pale grey or clear cytoplasm with few or no granules.[1] Immature forms, cytoplasmic vacuolization, emperipolesis, and budding are considered non-dysplastic features. Immature megakaryocytes are identified by their scant bluish cytoplasm and lack of lobulation. Cytoplasmic vacuolization indicates degenerative processes, such as apoptosis and para-apoptosis, which ultimately lead to vacuolization.[8] In the present study, out of the 68 patients, 41(60.3%) patients were males and 27(39.7%) patients were females. These findings were similar to those reported by Gupta et al.[8] The age incidence of cases in our study showed two peaks belonging to group categories 0-10 years and 21 to 30 years, which was in concordance with the study conducted by Iqbal et al.[2] The most common cause of thrombocytopenia for which bone marrow aspiration was sought was acute leukemia (35.3%). These findings are comparable with the study done by Vinayakamurthy et al. and Kutum et al.[4, 7] Megakaryocyte number was either decreased (62.5%) or absent (37.5%) in cases of acute leukemia and these findings were similar to those of Iqbal et al. and Deepika et al.[2, 9] A study conducted by Tejinder Singh Bhasin et al., revealed an increase in the number of megakaryocytes in all cases of ITP and similar findings were observed in the present study.[1] All cases of lymphoproliferative neoplasm (n=3) in our study showed a decrease in the number of megakaryocytes, which was in concordance with the study done by Sharma R et al.[6] Decrease in the number of megakaryocytes seen in both cases of metastatic deposits. This was in contrast to the observations made by Vinayakmurthy et al. In our study, as metastatic tumor cells infiltrate the bone marrow, replacing normal hematopoietic cells, megakaryocyte precursors are also replaced, leading to a decrease in their number. In the present study, a common dysplastic feature observed in megakaryocytes of ITP was the presence of micromegakaryocytes (66.7% of cases), similar to observations made by Tirumalasetti et al.[10] This may be a result of platelet production in response to immune-mediated destruction. The accelerated megakaryopoiesis leads to abnormal, smaller megakaryocytes as a compensatory mechanism. In contrast, Gupta et al. reported that the most frequent morphological changes in ITP cases were hypolobation and hypogranular forms.[8] Hyperlobated megakaryocytes were seen in 29.4% of cases of megaloblastic Anemia, which was in concordance with the findings of Sharma et al. and Tirumalasetti et al.[6, 10] This is due to delayed DNA

maturation than cytoplasmic maturation. Both cases of CML-Blast crisis exhibited dysplastic features, with micromegakaryocytes and hypogranular forms being evident. These findings were consistent with those reported by Gupta et al.[8] In the present study, hypolobated (immature) megakaryocytes were observed in 66.7% of cases of multiple myeloma, 37.5% of cases of acute leukemia, 33.3% of cases of ITP, and 25% of cases of MDS. Cases of the above disorders were also presented with hypolobated forms in a study conducted by Iqbal et al.[2] Such forms arise from abnormal megakaryocyte maturation due to bone marrow dysfunction. These conditions disrupt normal development, leading to fewer nuclear lobes in megakaryocytes. The above findings emphasize that specific morphological patterns, including dysplastic changes such as micromegakaryocytes in CML and ITP and hyperlobation in megaloblastic anemia, can serve as valuable clinical indicators. Furthermore, non-dysplastic changes, such as hypolobated forms, are also frequent findings in conditions like acute leukemia, multiple myeloma, and MDS. In addition to morphological abnormalities, the quantitative assessment of megakaryocytes also holds diagnostic significance, with an increase in their number often observed in conditions such as ITP and megaloblastic Anemia and a decrease typically noted in acute leukemia, MDS, and lymphoproliferative disorders. The morphological evaluation of megakaryocytes remains a crucial, cost-effective adjunct to ancillary investigations, particularly in resource-limited settings. Therefore, our results underscore the importance of meticulous bone marrow assessment in the diagnostic workup of thrombocytopenia, as thrombocytopenia itself can result from either increased peripheral destruction or decreased marrow production, making it essential to correlate platelet counts with underlying marrow findings.

5. Conclusion

Megakaryocyte alterations observed in bone marrow aspirates from patients with thrombocytopenia across various hematological disorders indicate that, despite representing a small fraction of the bone marrow's cellularity, megakaryocytes should be regarded as equally important as erythroid and myeloid cells during bone marrow evaluations as they provide a cost-effective and efficient approach to diagnosing various thrombocytopenic disorders allowing for targeted management. Although this study offers significant insights, further research with a larger sample size would help validate these findings and facilitate a more comprehensive and detailed analysis.

Limitations

A key limitation of our study is the relatively small sample size, which may limit the statistical power of our findings.

Conflict of Interest

The authors declared that there is no conflict of interest.

Acknowledgments

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

[1] Bhasin TS, Sharma S, Manjari M, Mannan R, Kansal V, Chandey M, et al. Changes in megakaryocytes in cases of thrombocytopenia: bone marrow aspiration and biopsy analysis. Journal of clinical and diagnostic research: JCDR. 2013;7(3):473-9. https://doi.org/10.7860/JCDR/2013/5085.2801.

[2] Iqbal B, Ravishankar R, Zaheer M, Chandanwale SS, Gore CR. Megakaryocytic Alterations in Thrombocytopenia: A Bone Marrow Aspiration Study. Clinical Cancer Investigation Journal. 2022;11(1):21-7. https://doi.org/10.51847/jNE8SWyDAW.

[3] Sandeep V, Sasturkar RC, Prabhu MH. Megakaryocytic Alterations in Thrombocytopenia: a Bone Marrow Aspiration Study. International Journal of Science and Research (IJSR). 2020 Jan;9(1):220-6. https://doi.org/10.21275/ART20203873.

[4] Vinayakamurthy S, Potluri R, Shivajirao P, Singh R, Pujahari R, Maniketh I. A study of megakaryocyte morphology in bone marrow aspiration smears of cases of thrombocytopenia. Medical Journal of Dr. DY Patil University. 2017;10(1):51-7. https://doi.org/10.4103/0975-2870.197922.

[5] Pokharel S, Upadhyaya P, Karki S, Paudyal P, Pradhan B, Poudel P. Megakaryocytic alterations in thrombocytopenia: a bone marrow aspiration study. Journal of Pathology of Nepal. 2016;6(11):914-21. https://doi.org/10.3126/jpn.v6i11.15673.

[6] Sharma R, Kiran CM, Ramdas A. Morphological Alterations in Megakaryocytes in Bone Marrow Aspirate of Thrombocytopenia Cases. J Blood Lymph. 2019;9(1):235-9.

[7] Kutum P, Laishram RS, Devi KA, Ali MY, Chanamthabam TR, Das P. Megakaryocytic Alteration In Cases Of Thrombocytopenia- A Bone Marrow Aspiration Study. J. Evid. Based Med. Healthc. 2017 Sep 21;4(76):4460–4. https://doi.org/10.18410/jebmh/2017/889.

[8] Gupta P, Goswami A, Chavda J, Goswami N, Shah S. Study of Megakaryocytes in Bone Marrow Aspiration Smears in Patients with Thrombocytopenia. IOSR Journal of Dental and Medical Sciences. 2015 Jun;14(6):30–3.

[9] Deepika RK, Singh H, Bhatia L, Chakma S, Kaur N. Bone Marrow Findings in Cases of Thrombocytopenia. Annals of International Medical and Dental Research. 2017;3(4):7. https://doi.org/10.21276/aimdr.2017.3.4.PT2.

[10] Tirumalasetti N, Challa NR. Bone marrow aspiration study of megakaryocytic alterations in non myelodysplastic syndrome related thrombocytopenia. Ind J Pathol Oncol. 2016;3:587-92. https://doi.org/10.5958/2394-6792.2016.00109.5.

How to Cite this Article: Choudhary I, Bhati S, Meena S, Lukkad M. Megakaryocytic Alterations in Cases of Thrombocytopenia on Bone Marrow Examination at a Tertiary Care Centre. International Journal of Scientific Research in Dental and Medical Sciences. 2025;7(2):53-57. https://doi.org/10.30485/IJSRDMS.2025.513248.1655.