

Megakaryocytic Alterations in Thrombocytopenia: A Bone Marrow Aspiration Study

Abstract

Thrombocytopenia is defined as a platelet count of less than 1,50,000 per cubic millimeter. It is a hematological presentation which could have a multitude of causes. This study was conducted with an objective to identify the alterations in number and morphology of megakaryocytes in different hematological disorders causing thrombocytopenia. A prospective bone marrow aspiration study was conducted on 100 patients. Bone marrow aspiration was done, and smears were examined for quantitative as well as qualitative changes. Bone marrow aspirate films were studied by two pathologists separately and megakaryocytic alterations were documented and analyzed using Fischer's Exact Test. Out of a total of 100 cases of thrombocytopenia, 49% were megaloblastic anaemia, followed by ITP (13%), Dimorphic anaemia (11%), CML-blast crisis (7%) and AML (6%) among others. We observed an increase in the number of megakaryocytes in 28% (n=14) cases of megaloblastic anaemia, and 77% (n=10) cases of ITP. 67.35% (n=33) cases of megaloblastic anemia and 72.73% (n=8) cases of dimorphic anaemia showed hyperlobated megakaryocytes. 61.54% (n=8) cases of ITP showed hypolobated megakaryocytes. Cases of AML, Aplastic anaemia and hairy cell leukaemia showed normal number of nuclear lobes. 51.02 % (n=25) and 61.53 % (n=8) cases of megaloblastic anaemia and ITP respectively showed presence of dysplastic megakaryocytes. Detailed evaluation is key to establish the relationship between megakaryocytic alterations with the different causes of thrombocytopenia.

Keywords: Bone marrow, Haematology, Megakaryocyte, Thrombocytopenia

Introduction

Megakaryocytes are thrombocyte precursors that are present in the bone marrow along with other hematopoietic cells. Thrombocytopenia is defined as a platelet count of less than 1,50,000 per cubic millimetre. It is a hematological presentation that could have a multitude of causes including megaloblastic anaemia, myelodysplastic syndromes (MDS), nutritional anemia, idiopathic thrombocytopenic purpura (ITP), Leukaemia, bone marrow metastasis, and megakaryocytic thrombocytopenia.^[1] Although megakaryocytes make up a small percentage of the marrow cellularity, their maturation is intricately connected to their natural microenvironment.^[2] A defect at any stage of megakaryopoiesis may lead to dysmegakaryopoiesis and thrombocytopenia

This study was conducted to identify the alterations in the number and morphology of megakaryocytes in different hematological

disorders causing thrombocytopenia. This study evaluates if these alterations have any significant association with the different causes of thrombocytopenia.

Further studies on the evaluation of megakaryocytic alteration and their contribution to thrombocytopenia can provide knowledge on the pathogenesis of numerous hematopoietic disorders that may identify broader clinical applications of the newer strategies to regulate platelet count and functioning.

Materials and Methods

This prospective bone marrow aspiration study was conducted on patients reporting for thrombocytopenia in the Department of Pathology, in a tertiary care hospital in western Maharashtra. A total of 100 cases were included in this study. An institutional ethics committee clearance (IECC) was obtained before the start of the study. The

**Banyameen Iqbal^{1*},
Rajeshwari
Ravishankar¹,
Meesha Zaheer¹,
Shrish S.
Chandanwale¹,
Charusheela R. Gore¹**

¹Department of Pathology, Dr D.Y Patil Medical College, Hospital and Research Centre, Dr. D.Y Patil Vidyapeeth, Pimpri, Pune – 411018, India.

Address for correspondence:

Banyameen Iqbal,
Department of Pathology, Dr D.Y Patil Medical College, Hospital and Research Centre, Dr. D.Y Patil Vidyapeeth, Pimpri, Pune – 411018, India.
E-mail: banzey@gmail.com

Access this article online

Website: www.cci-online.org

DOI: [10.51847/jNE8SWyDAW](https://doi.org/10.51847/jNE8SWyDAW)

Quick Response Code:



How to cite this article: Iqbal B, Ravishankar R, Zaheer M, Chandanwale SS, Gore CR. Megakaryocytic Alterations in Thrombocytopenia: A Bone Marrow Aspiration Study. Clin Cancer Investig J. 2022;11(1):21-7. <https://doi.org/10.51847/jNE8SWyDAW>

patient's informed and written consent was taken in English and/or the local language.

Each patient's clinical details including history and physical findings were documented. Complete blood counts, peripheral smears, and other relevant laboratory investigations required were performed and documented. Peripheral smears were prepared and stained using Leishman stain. Cases with proven pseudo thrombocytopenia on peripheral smear examination and those with evidence of viral infections like dengue were excluded from the study.

Bone marrow aspiration (BMA) was done under standard aseptic conditions from Posterior Superior Iliac Spine or Shin of Tibia (in patients less than 8 years of age) and smears were stained with Leishman's stain. The BMA smears were examined (using the Olympus CH20i model) by two pathologists separately, and the findings were documented and analyzed.

The bone marrow smears were examined for changes in megakaryocytes in thrombocytopenia (platelet count less than 1,50,000 / μ L of blood). The number of megakaryocytes was considered normal (1 megakaryocyte per one to three low power fields), increased (more than two megakaryocytes per low power field), or decreased (one megakaryocyte per five to ten low power fields). The morphological changes of megakaryocytes that were studied included nuclear segmentation, dysplastic forms, presence of immature forms, micro megakaryocytes, emperipolesis, bare megakaryocytic nuclei, hypogranular forms, platelet budding, and cytoplasmic vacuolization.

It was considered that normal megakaryocytes have four to sixteen nuclear lobes. Immature megakaryocytes were defined as young forms of megakaryocytes with scanty bluish cytoplasm and lacking nucleus lobulation, which occupied most of the cell. Dysplastic megakaryocytes were defined as those with single or multiple separate nuclei. Micro megakaryocytes were defined as those whose size was that of a monocyte or large lymphocyte and which had a single or bilobed nucleus. The megakaryocytes were considered to show platelet budding if there was the budding of cytoplasmic processes from their surfaces. Hypogranular forms were defined as megakaryocytes with water-clear or pale grey cytoplasm and sparse granules. The type of cell seen within the megakaryocyte in emperipolesis was also documented. The bone marrow smears were examined for changes in the number and morphology of megakaryocytes in the various disorders causing thrombocytopenia.

The morphological changes of megakaryocytes that were studied include, Number of nuclear lobes of megakaryocytes, presence of immature forms, presence of dysplastic forms, presence of micro megakaryocytes, and evidence of platelet budding and cytoplasmic vacuolization, presence of hypogranular forms and bare nuclei and evidence of emperipolesis.

Results and Discussion

As per standard guidelines, bone marrow aspirate films were studied by two pathologists separately and megakaryocytic alterations were documented and analyzed using Fischer's Exact Test. Based on the analysis of data, the results obtained in our study revealed the following:

A total of 100 cases of thrombocytopenia were included in the present study, predominated by megaloblastic anaemia (49%), followed by ITP (13%), Dimorphic anaemia (11%), CML-blast crisis (7%), and AML (6%) among others (**Table 1**).

Out of the total 100 cases, 16% (n=16), belonging to the age group category 21-30 years and 9% (n=9) of the total cases belonging to the age group category ' \leq 10 years' were diagnosed to be Megaloblastic anemia.

6% (n=6) of ITP cases were found in the age group category ' \leq 10 years. Female: Male ratio was 1.7:1.

Table 1. Incidence Of Cases

Sr. No:	Bone Marrow Diagnosis	Number of Cases	% Cases
1.	Megaloblastic Anaemia	49	49%
2.	ITP	13	13%
3.	Dimorphic Anaemia	11	11%
4.	CML (blast crisis)	7	7%
5.	AML	6	6%
6.	Multiple myeloma	4	4%
7.	ALL	3	3%
8.	MDS	2	2%
9.	Aplastic Anaemia	2	2%
10.	BM Metastasis	2	2%
11.	Hairy cell leukemia	1	1%
Grand Total		100	100%

Out of the total 100 cases of thrombocytopenia, 35% (n=35) diagnosed with megaloblastic anemia were females. ITP and dimorphic anemia also showed female preponderance. CML (blast crisis) however showed male preponderance, with a male: female ratio being 1.3:1 (**Figure 1**).

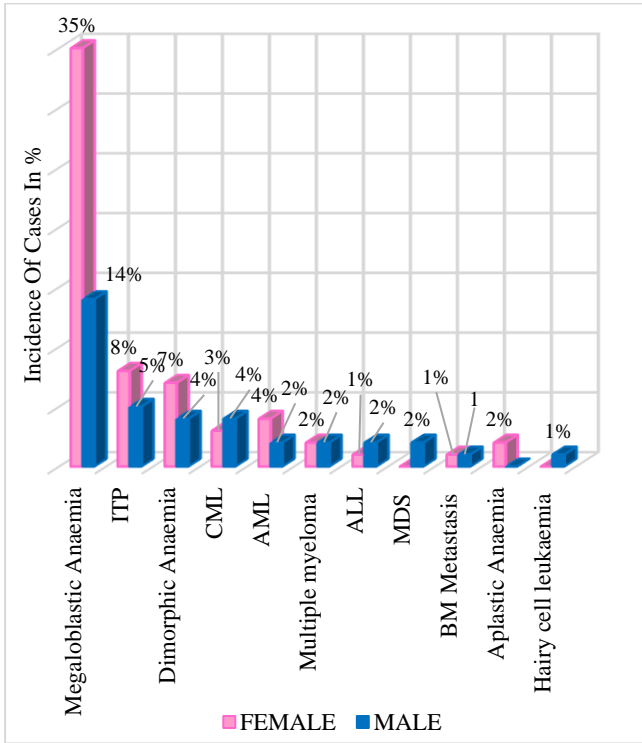


Figure 1. Gender-Wise Distribution Of Individual Cases

The quantitative and qualitative megakaryocytic alterations were studied. The number of megakaryocytes was rated as normal when there was 1 megakaryocyte/1-3 LPFs increased when there were >2 megakaryocytes/LPF or decreased when there were 1 megakaryocyte/5-10 LPFs.^[1] **Table 2** represents the quantitative megakaryocytic alterations seen among all the cases (n=100) in our study. We observed an increase in the number of megakaryocytes in 28% (n=14) cases of megaloblastic anemia and 77% (n=10) cases of ITP. Cases of AML, CML, and ALL among others, showed a decrease in the number of megakaryocytes on bone marrow examination.

Table 2. Quantitative Megakaryocytic Alterations

Bone Marrow Diagnosis	Normal	Increased	Decreased
Megaloblastic Anaemia (n=49)	61.22%	28.57%	10.20%
ITP (n=13)	23.08%	76.92%	-
Dimorphic Anaemia (n=11)	45.45%	27.27%	27.27%
CML-blast crisis (n=7)	14.29%	-	85.71%
AML (n=6)	-	-	100%
Multiple myeloma (n=4)	25%	25%	50%
ALL (n=3)	33.33%	-	66.67%
MDS (n=2)	-	100%	-
BM Metastasis (n=2)	-	-	100%
Aplastic Anaemia (n=2)	-	-	100%
Hairy cell leukaemia (n=1)	-	-	100%
Grand Total	41%	30%	29%

Megakaryocytes with 4 to 16 lobes were considered as having the normal number of nuclear lobes. 67.35% (n=33) cases of megaloblastic anemia and 72.73% (n=8) cases of dimorphic anemia showed hyperlobated megakaryocytes. 61.54% (n=8) cases of ITP showed hypolobated megakaryocytes. All 100% (n=7) of the total cases of CML (blast crisis) showed hypolobated megakaryocytes. Cases of AML, Aplastic anemia and hairy cell leukemia showed the normal number of nuclear lobes (**Table 3**).

Table 3. Qualitative Megakaryocytic Alterations: Number of Nuclear Lobes

Bone Marrow Diagnosis	Hyperlobated	Normal	Hypolobated	Grand Total
Megaloblastic Anaemia	67.35%	30.61%	2.04%	100%
ITP	-	38.46%	61.54%	100%
Dimorphic Anaemia	72.73%	27.27%	0%	100%
CML (blast crisis)	-	-	100%	100%
AML	-	100%	-	100%
Multiple myeloma	-	75%	25%	100%
ALL	-	100%	-	100%
MDS	-	-	100%	100%
BM Metastasis	-	100%	-	100%
Aplastic Anaemia	-	100%	-	100%
Hairy cell leukemia	-	100%	-	100%
Grand Total	41%	40%	19%	100%

Dysplastic and Non-Dysplastic megakaryocytic changes were observed in our study. Common dysplastic features included micromegakaryocytes, multiple segmented nuclei, and hypogranular forms. 51.02% (n=25) and 61.53% (n=8) cases of megaloblastic anaemia and ITP respectively showed the presence of dysplastic megakaryocytes. Micromegakaryocyte were seen in 76.92% (n=10) cases of ITP and 42.85% (n=3) cases of CML (blast crisis). Among the non-dysplastic features, immature forms were the most common. 75.51% (n=37), 100% (n=13) and 85.71% (n=6) cases of megaloblastic anaemia, ITP, and CML (blast crisis) respectively showed presence of immature forms of megakaryocytes, including megakaryoblasts. Bare nuclei were also commonly seen in cases of megaloblastic anemia, ITP, Dimorphic anemia, and CML (blast crisis).

In 100% (n=2) cases of MDS, immature forms, dysplastic forms, and micromegakaryocytes were seen. Cytoplasmic vacuolation, hypogranular forms, emperipolesis, and bare megakaryocytic nuclei were seen in 50% (n=1) cases each (**Table 4**).

Table 4. Qualitative Megakaryocytic Alterations: Dysplastic And Non-Dysplastic Features

Bone Marrow Diagnosis	Total Number of Cases	Immature Forms	Dysplastic Forms	Micromega Karyocytes	Platelet Budding	Cytoplasmic Vacuolation	Hypogranular Forms	Emperipolesis	Bare Nuclei
Megaloblastic Anaemia	49	75.51% (N=37)	51.02% (n=25)	2.04% (n=1)	-	46.93% (n=23)	-	4.08% (n=2)	61.22% (n=30)
ITP	13	100% (n=13)	61.53% (n=8)	76.92% (n=10)	61.50% (n=8)	15.38% (n=2)	46.15% (n=6)	46.15% (n=6)	76.92% (n=10)
Dimorphic Anaemia	11	45.45% (n=5)	63.63% (n=7)	-	-	45.45% (n=5)	-	-	63.63% (n=7)
CML (Blast crisis)	07	85.71% (n=6)	71.42% (n=5)	42.85% (n=3)	-	-	28.57% (n=2)	-	85.71% (n=6)
AML	06	-	-	-	-	-	-	-	-
Multiple Myeloma	04	50% (n=2)	50% (n=2)	25% (n=1)	-	50% (n=2)	-	25% (n=1)	25% (n=1)
Aplastic Anaemia	03	-	-	-	-	-	-	-	-
ALL	02	-	-	-	-	-	-	50% (n=1)	-
MDS	02	100% (n=2)	100% (n=2)	100% (n=2)	-	50% (n=1)	50% (n=1)	50% (n=1)	50% (n=1)
Bone Marrow Metastasis	02	-	-	-	-	-	-	-	-
Hairy Cell Leukaemia	01	-	-	-	-	-	-	-	-

A maximum of 49% (n=49) cases of thrombocytopenia were diagnosed on bone marrow examination as megaloblastic anaemia. Female preponderance was observed. The mean age observed was 24.9. In our study, megakaryocytes were normal in 61.22% cases, increased in 28.57% cases, and reduced in

10.20% cases. Dysmegakaryopoiesis in form of nuclear separation was seen in 51.02% of cases, hypersegmented forms were seen in 67.20% cases, and bare megakaryocyte nuclei were seen in 61.22% of cases (Figure 2).

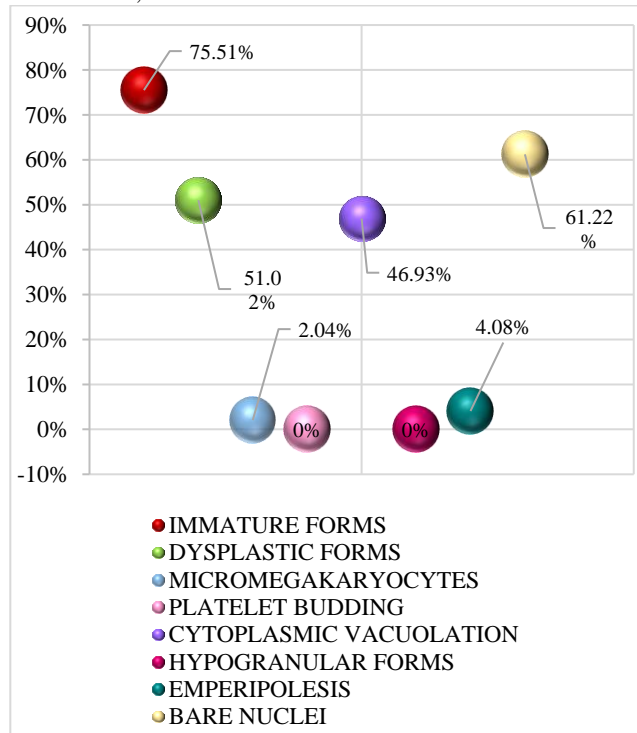


Figure 2. Qualitative Changes In Megakaryocytes In Megaloblastic Anaemia

This was followed by 13 % (n=13) cases of ITP, also showing female preponderance. 46% (n=6) cases were found in the age group category '≤10 years'. Megakaryocytes were increased in 76.92% (n=10) of the cases. Immature forms were seen in 100% (n=13) cases. 76.92% (n=10) of the cases showed the presence of micromegakaryocytes and bare megakaryocytic nuclei (Figure 3).

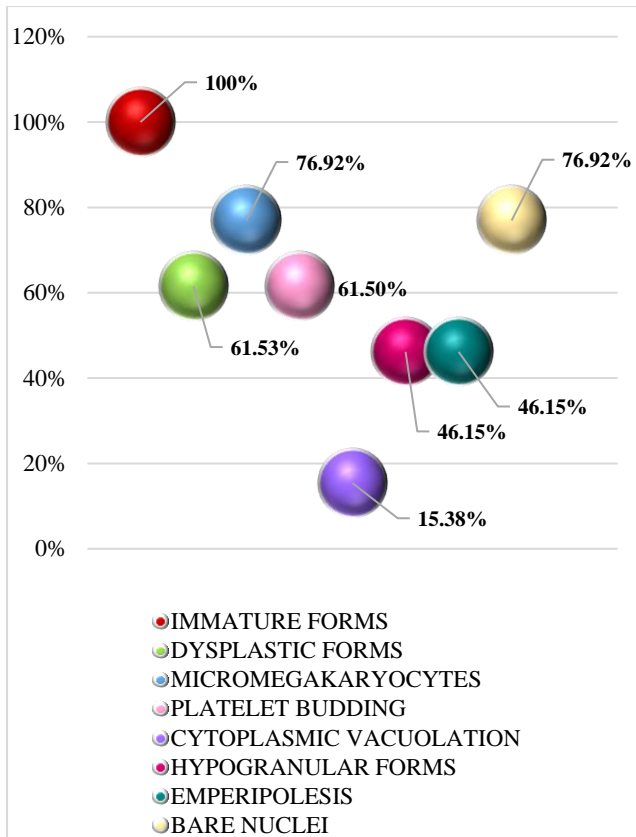


Figure 3. Qualitative Changes In Megakaryocytes In Itp Cases

Dimorphic Anaemia (11%) was the next incidence among cases of thrombocytopenia in our study. Female preponderance was observed with wide age distribution. Quantitatively, megakaryocytes were normal in about 50% of cases. Bare megakaryocytic nuclei and dysplastic forms were common findings amongst morphological alterations.

Cases of thrombocytopenia with raised leucocyte counts were also included in the study. The bone marrow aspiration films were then diagnosed to be CML (in blast crisis) in 7% of cases, AML (6%), and ALL (4%). The majority of the above-mentioned cases showed a drastically reduced number of megakaryocytes on bone marrow aspirate. Cases of CML (blast crisis) showed dysplastic megakaryocytic changes in approximately 85% (n=6) cases. Cases of AML and ALL, on the other hand, showed no significant morphologic alterations.

4% of the total cases were diagnosed as multiple myeloma. 50% of cases showed a decreased number of megakaryocytes. Morphologically, immature forms, dysplastic forms, and cytoplasmic vacuolation were seen in 50% of cases.

In the present study, 2% of cases were found to be MDS. Both the cases showed an increased number of megakaryocytes with micromegakaryocytes, dysplastic forms, immature forms, and a hypolobated megakaryocytic nucleus was seen in one of the cases. Emperipolesis, hypogranular form and cytoplasmic vacuolation were also observed in 50% of cases each. Platelet budding was not seen.

2 cases of metastatic deposits to the bone marrow were encountered during our study. One was a case of breast cancer metastasis to the bone marrow, and the other was a case of CNS lymphoma. In both cases, bone marrow examination revealed reduced megakaryocyte numbers. Dysplasia was however not appreciated.

A case of hairy cell leukemia in an 81-year-old male patient showed hypocellular marrow with a decrease in all three cell lines. No morphologic alterations were observed in the megakaryocytes.

A total of 100 cases of thrombocytopenia were studied, predominated by cases of megaloblastic anemia (49%), followed by those of ITP (13%), Dimorphic anaemia (11%), CML in blast crisis (7%), AML (6%), multiple myeloma and ALL 4% and 3% cases respectively, 2% each of MDS, Aplastic Anaemia and Bone Marrow Metastasis, and Hairy Cell Leukaemia (1%). Wide age distribution was seen in the cases of thrombocytopenia, ranging from 3 years to 81years, mean age being 29.46years. 2 peaks were observed in the age group categories '≤10years' and '21-30years'. Our study showed female preponderance with a Female: Male ratio being 1.7:1. The incidence of cases in the study conducted by *Muhury et al.*^[1] showed the predominance of cases of AML (27%), followed by those of ITP (13.5%) and then by cases of Dimorphic anemia and Multiple myeloma (12.5% cases each). The age incidence was in concordance with that of our study, with peak age groups of incidences being < 10 years and 21-30years. However, male preponderance was observed. The most common cause of thrombocytopenia in the study conducted by *Pokharel et al.*^[3] was Megakaryocytic Thrombocytopenia (44.7%), followed by Acute Leukaemia (26.3%) and then by aplastic anaemia (13.2%), MDS (5.3%), megaloblastic anaemia and myelofibrosis (2.6% each), which were the least common. Wide age distribution was seen, ranging from 3 years to 74 years, mean age being 25.9 years with a female preponderance, % female cases being 57.9%. In a study conducted by *Veerapaneni et al.*^[4], thrombocytopenia was most commonly seen in 40-49 years (26.5%) followed by the 50-59 years of age group, the mean age of incidence observed was 35.33years.

In our study, 49% of cases were that of megaloblastic anemia. A wide age range with a minimum of 3 years and a maximum of 57 years was observed, the mean age being 24.9. Of the 49 cases, 33% were found between the ages of 21-30 years. 35 out of 49 cases (71.43%) were females. BMA showed hypercellular marrow with dyserythropoiesis in the form of megaloblasts and dysmyelopoiesis in the form of giant metamyelocytes. Megakaryocytes were normal in 61.22%

cases, increased in 28.57% cases, and decreased in 10.2% cases. Dysmegakaryopoiesis in the form of immature megakaryocytes in 75.51% cases, dysplastic forms in 51.02% cases, hypersegmented forms in 33% cases, bare megakaryocyte nuclei in 61.22%, emperipolesis with nucleated RBCs and lymphocytes within the cytoplasm of megakaryocytes in 4.08% of the cases. Platelet budding and hypogranular forms were not seen in this study. *Muhury et al.*^[1] also described dysplastic forms of megakaryocytes and emperipolesis in megaloblastic anaemia on bone marrow aspirate in patients with thrombocytopenia.

13% of the total cases in our present study were that of ITP. Of them, 46% were found in the age group category '≤10 years'. Male: female ratio observed was 1: 2.1. In a study done by *Muhury et al.* 19 cases of ITP were diagnosed (13.15%).^[1] Most patients were children <20 years, commonly seen in males Normocellular BM was a common feature with normal erythropoiesis and myelopoiesis. Increased Megakaryocytes were seen in 76.92% of cases of ITP. Although the remaining cases showed the normal number of megakaryocytes on bone marrow aspirate, immature forms were seen in all the cases of ITP. Other megakaryocytic changes included micromegakaryocytes and bare nuclei (76.92% cases each), dysplastic forms, and platelet budding were seen in 61.50% of the cases each. Hypogranular forms (46.15%), cytoplasmic vacuolation (15.38% cases). The most striking feature observed in the study was Emperipolesis (46.15%) with lymphocytes, nucleated RBCs, and neutrophils within the cytoplasm of the megakaryocytes.

In a study conducted by *Muhury et al.*^[1], 18/19 cases had an increase in the number of megakaryocytes with hypolobated, normal, emperipolesis seen. Dysplastic forms were seen in 84.9%, bare megakaryocytic nuclei in 84.2%, micromegakaryocytes in 42.1%, emperipolesis in 84.2%, and cytoplasmic vacuolization seen in 47.4% cases.

Jubelirer *et al.*^[5], in their study on ITP, demonstrated that 82/86 cases had normal/increased megakaryocytes and 4/86 cases with decreased megakaryocytes.

In our study, 10% of the cases were found to be acute leukemia presenting with thrombocytopenia, showing a preponderance of AML. This finding correlates well with the studies conducted by *Kulshrestha et al.*^[6], *Muhury et al.*^[1], and *Kibria et al.*^[7], except *Pokharel et al.*^[3] in which ALL was predominant.

The age at presentation of AML in the present study varied from 39years-75years, the mean age being 51.5years with female preponderance. Megakaryocytes on bone marrow examination showed reduced numbers, but with normal morphology. No dysplastic features were observed.

Bhasin et al.^[2] observed normal or reduced numbers of megakaryocytes. Bare nuclei and hypogranular forms were also described. In a study by *Lee et al.* (1990)^[8], 32 patients with AML had normal or increased numbers of

megakaryocytes.

In our study, 3% of cases were that of ALL. Age ranging from 7 years to 30 years showing male preponderance. Quantitatively, megakaryocytes were normal in % and reduced in % cases. One of the cases showed emperipolesis of lymphocytes within a megakaryocytic cytoplasm. No other morphologic alteration was observed. *Muhury et al.* also described in their study immature megakaryocytes, dysplastic megakaryocytic changes, emperipolesis, and bare megakaryocyte nuclei in cases of ALL.^[1] *Pokharel et al.*^[3] also observed hypogranular megakaryocytes in 5 cases and emperipolesis in 1 case. Besides this, no other megakaryocytic alteration was detected.

4% of the total cases were diagnosed as multiple myeloma. 50% of cases showed a decreased number of megakaryocytes, while the rest showed a normal to the increased number of megakaryocytes. Morphologically, immature forms, dysplastic forms, and cytoplasmic vacuolation were seen in 50% of cases, micromegakaryocytes, emperipolesis, and bare megakaryocytic nuclei, and hypolobated nucleus were seen in 25% of cases. Platelet budding and hypogranular forms were not seen. *Bhasin et al.*^[2] had 3.33% cases of multiple myeloma in their study in which megakaryocytes were seen to have hypogranular as well as hypolobated forms. Hypolobated forms, micromegakaryocyte, bare nuclei, immature forms, dysplastic forms, emperipolesis, and cytoplasmic vacuolation were also described by *Muhury et al.*^[1]

In the present study, 2% of cases were found to be MDS. Both the cases showed an increased number of megakaryocytes with micromegakaryocytes, dysplastic forms, immature forms, and a hypolobated megakaryocytic nucleus was seen in one of the cases. Emperipolesis, hypogranular form and cytoplasmic vacuolation were also observed in 50% of cases each. Platelet budding was not seen. The study conducted by *Bhasin et al.*^[2] included 10% cases of MDS. Hypogranular forms were seen in all cases of MDS. Dysplastic forms and micromegakaryocytes were seen in 66.67% of cases.

2 cases of metastatic deposits to the bone marrow were encountered during our study. One was a case of breast cancer metastasis to the bone marrow, and the other was a case of CNS lymphoma. In both cases, bone marrow examination revealed reduced megakaryocyte numbers. The case of CNS lymphoma showed the presence of immature forms and dysplastic forms. Emperipolesis with lymphocytes was also observed. *Wong et al.* (1993)^[9] in their study on clinic-pathologic study of solid tumors described similar findings mean age of patients 61.6 years with anemia and thrombocytopenia. *Hennon et al.* (1976)^[10] in a study on Changes in bone marrow cellularity close to cancer metastases found that there is the alteration of surrounding hematopoietic tissue with the frequent presence of collagen fibrosis and hypoplasia of various cell lines, these alterations directly linked to the presence of cancerous cells. *Muhury et al.* (2009)^[1] in a similar study on megakaryocytic changes in thrombocytopenia showed 2 cases of metastasis with absent

Megakaryocytes.

Conclusion

Megakaryocyte Changes studied in various hematological conditions in bone marrow aspirates associated with thrombocytopenia were statistically significant suggesting that megakaryocytes through forming a small percentage of cells in Bone marrow need to be given equal importance as that given to erythroid and myeloid cells in BMA evaluation. An attempt is made in this study to elucidate the changes in the megakaryocyte, numerical and morphological as well. These changes were reviewed with the literature and tried to correlate with pathogenetic mechanisms. In addition, a statistically significant association was established between the presence of immature megakaryocytes and micro-megakaryocytes in BMA films and the diagnosis of ITP. The results obtained in our study were in line and corroborated well with the findings of various other studies on this subject.

Morphologic changes in megakaryocytes seen in MDS are also seen in various non-MDS conditions which should also be considered during diagnostic evaluation. An in-depth analysis of megakaryocytic alterations and their role in thrombocytopenia can shed some light on the pathogenesis of various hematopoietic disorders, which may find broad clinical applications to regulate platelet count and functioning. Few studies have analyzed the significance of the alterations in the number and morphology of megakaryocytes in different hematological disorders, which causes thrombocytopenia. A detailed evaluation is a key to establishing the relationship between megakaryocytic alterations with the different causes of thrombocytopenia.

Acknowledgments

The authors are highly obliged to the Department of Pathology and Hematology for giving us permission to conduct this study.

Conflict of interest

None.

Financial support

None.

Ethics statement

Institutional Ethics Sub-Committee permission number: IESC/PGS/2019/179.

Consent was taken prior to the start of study.

References

1. Muhury M, Mathai AM, Rai S, Naik R, Pai MR, Sinha R. Megakaryocytic alterations in thrombocytopenia: a bone marrow aspiration study. *Indian J Pathol Microbiol.* 2009;52(4):490-4.
2. 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. *J Clin Diagn Res.* 2013;7(3):473-9.
3. Pokharel S, Upadhyaya P, Karki S, Paudyal P, Pradhan B, Poudel P. Megakaryocytic alterations in thrombocytopenia: A bone marrow aspiration study. *JPN.* 2016 6(11):914-21.
4. Veerpaneni S, Radhika C, Prabhu M. Megakaryocytic alterations in thrombocytopenia: a bone marrow aspiration study. *IJSR* 2020;9(1):220-6.
5. Jubelirer SJ, Harpold R. The role of the bone marrow examination in the diagnosis of immune thrombocytopenic purpura: case series and literature review. *Clin Appl Thromb Hemost.* 2002;8(1):73-6.
6. Kulshrestha R, Sah SP. Pattern of occurrence of leukemia at a teaching hospital in eastern region of Nepal - A six-year study. *J Nepal Med Assoc.* 2009;48(173):35-40.
7. Kibria SG, Islam MDU, Chowdhury AS, Ali MY, Haque MR, Mustanzid SM, et al. Prevalence of hematological disorder: a bone marrow study of 177 cases in a private hospital at Faridpur. *Faridpur Med Coll J.* 2010;5(1):11-3.
8. Lee EJ, Schiffer CA, Tomiyasu T, Testa JR. Clinical and cytogenetic correlations of abnormal megakaryocytopoiesis in patients with acute leukemia and chronic myelogenous leukemia in blast crisis. *Leukemia.* 1990;4(5):350-3.
9. Wong KF, Chan JK, Ma SK. Solid tumor with initial presentation in the bone marrow--a clinicopathologic study of 25 adult cases. *Hematol Oncol.* 1993;11(1):35-42.
10. Henon P, Marsan C, Gerota I, Zitouna M, Palacios S. Changes in bone marrow cellularity close to cancer metastases. *Cyto-histologic Study. Sem Hop.* 1976;52(11):695-700.