Original research article

Clinico Morphological Spectrum of Bone Marrow in A Tertiary Care Centre

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Abstract

Introduction: Bone marrow examination plays an important role in diagnosis of haematological as well as non-haematological disorders. It is one of the diagnostic investigations of cases of Pyrexia of unknown origin, cytopenia, abnormal red cell indices, malignant haematological disorder and suspected bone marrow metastasis as its leads to an etiological diagnosis in most of the cases. BMA is mainly performed for cytomorphological examination.

Aim: The aim was to study the Clinico-morphological spectrum of bone marrow aspiration and Biopsy examination and its correlation with biochemical parameters;and to assess the diagnostic value of bone-marrow examination.

Material and methods: It is an observational study with retrospective and prospective design. The study was conducted at in Department of Pathology, Heritage Institute of Medical Sciences, Varanasi. All eligible participants age group 3 month to 85 years were included. Data collection was done from November 2018 to April 2022. Bone marrow examination was performed for all cases. The parameters assessed after bone marrow examination were cellularity, myeloid to erythroid ratio, cytomorphological details of all cell lineage.

Results: In present study, commonest indication of bone marrow examination was unexplained anaemia followed by cytopenia and malignant haematological disorder. Distribution of bone marrow cellularity was normocellular in most of the cases. Dimorphic anaemia (26.21%) was most common finding followed by Micro normoblastic picture (22.33%) & Megaloblastic changes in 18.45% cases. Other finding was Acute leukaemia in which AML was most common finding.

Conclusion: Bone marrow study reproducible procedure used for the evolution of Haematological and non-haematological condition. Various studies shows the BME is an essential investigation for the diagnosis and management of many disorders of blood and BM.

Keyword: Bone Marrow Aspiration, Bone Marrow Trephine Biopsy, Haematological Disorders, Anaemia, Erythroid Hyperplasia, Idiopathic Thrombocytopenic Purpura, Leukaemia

Introduction

Bone marrow examination (BME) plays an important role in diagnosis of haematological as well as non-haematological disorders. It is a simple and safe procedure and is particularly useful in the investigation of pyrexia of unknown origin as it leads to an etiological diagnosis in most of the cases.[1,2]

Bone marrow aspiration (BMA) is mainly performed for cytomorphological examination of bone marrow cells, but also to proceed to other analyses such as immunophenotypic, flow cytometry, cytogenetic, molecular genetics, and microbiological tests. BMA is an important medical procedure for the diagnosis, staging, and follow-up of patients with haematological diseases and for investigating various non-haematological conditions including storage diseases, inborn errors of metabolism, metastatic cancer, and infection that has spread to the bone marrow.[3]

With our rapidly expanding knowledge of the clinical and biologic diversity of leukaemia and other hematologic neoplasms, and an increasing variety of therapeutic options, the bone marrow examination has become more critical for therapeutic monitoring and planning optimal therapy. Sensitive molecular techniques, in vitro drug sensitivity testing, and a number of other special assays are available to provide valuable data to assist these endeavours. Fortunately, improvements in bone marrow aspirate and needle technology has made the procurement of adequate specimens more reliable and efficient, while the use of conscious sedation has improved patient comfort.[7]

The yield of bone marrow examination in the diagnosis of infections has been extensively studied and its usefulness has been well established. Hence, a prospective study will be performed to investigate the role of BME along with Clinico-haematological analysis; and to help clarify its role in the diagnosis of various haematological and non-haematological disorders.[7]

Aim

To describe Clinico-morphological spectrum of bone marrow aspiration and biopsy examination and its correlation with biochemical parameters.

Material & Methods

Study participants:

It was descriptive study done from November 2018 to October 2022 in Department of Pathology, Heritage Institute of Medical Sciences, Varanasi. Bone marrow examination was performed in 103 cases for different indications of haematological and non-haematological abnormalities. This study was approved by the Departmental Ethics Committee. The written consents were obtained from all the patients for their participation in the study.

Clinical-analysis: Clinical details like age, clinical signs and symptoms, various haematological parameters, biochemical parameters (Vitamin B12, Serum ferritin, serum iron) and indications of bone marrow aspiration had been recorded. Clinical details regarding drug intake, weakess, fever, weight loss, organomegaly, lymphadenopathy, bone pain were also recorded. A peripheral smear had been made just prior to performing bone marrow aspiration.

Bone marrow analysis: Bone marrow was aspirated from posterior superior iliac spine and slides were prepared according to the standard procedures. For the assessment of bone marrow cellularity and of iron stores, aspirates were stained with May Grunwald-Giemsa and

Perl's stain, respectively. The bone marrow trephine biopsy samples were taken from the same site and stained with Haematoxylin and eosin. Interpretation of biopsy material was done according to the cellularity comparison of the relative proportions of myeloid, erythroid and megakaryocytic cells, other bone elements and reticulin. Special stain was used whenever indicated.

Results

Table 1: Age and gender distribution

Age (Years)	Number of cases	Male	Female
≤10	3	2	1
11 - 20	11	5	6
21 - 30	18	12	6
31 - 40	17	15	2
41 - 50	11	8	3
51- 60	16	12	4
61- 70	22	11	11
71- 80	03	03	00
81- 90	02	02	00
Total	**103**	**70**	**33**

Age of the patients in this study ranged from 7 months to 85 years. Most common age group undergoing bone marrow examination was 61-70 years. Out of total of 103 cases 70 were male and 33 cases were female. (Figure 1)

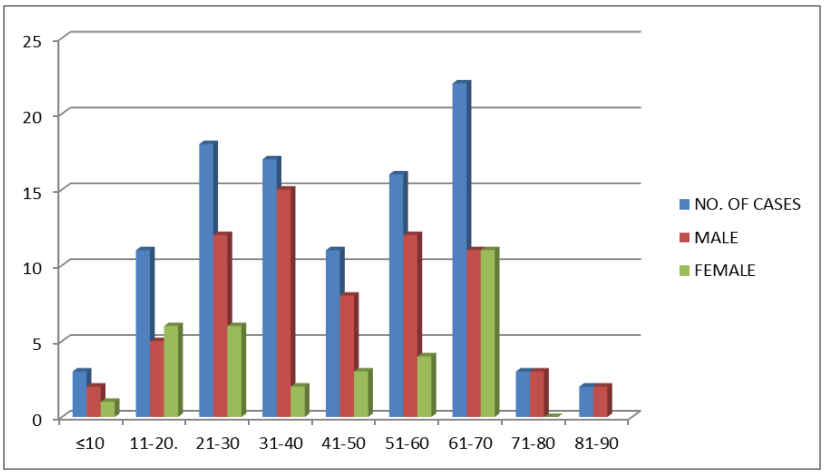

Figure 1: Age and gender wise distribution of patients

The commonest indication of bone marrow examination was unexplained anemia (43.68%) followed by unexplained pancytopenia (18.37%). Other indications were unexplained leuco-thrombocytopenia, splenomegaly, fever and suspected leukaemia's. (Table 1)

Table 2: Clinical indication for bone marrow examination

Indications	Number of cases	Percentage (%)
Unexplained anemias	45	43.68
Unexplained leuco-thrombocytopenia	9	8.75
Unexplained pancytopenia	21	20.38
Suspected leukemia	8	7.77
Unexplained splenomegaly	8	7.77

Unexplained fever	12	11.65
Total	**103**	**100%**

The distribution of bone marrow cellularity showed normocellular marrow in 55.34% cases, though 23.30% were hypercellular and 21.36% cases showed hypocellular marrow. (Figure 2)

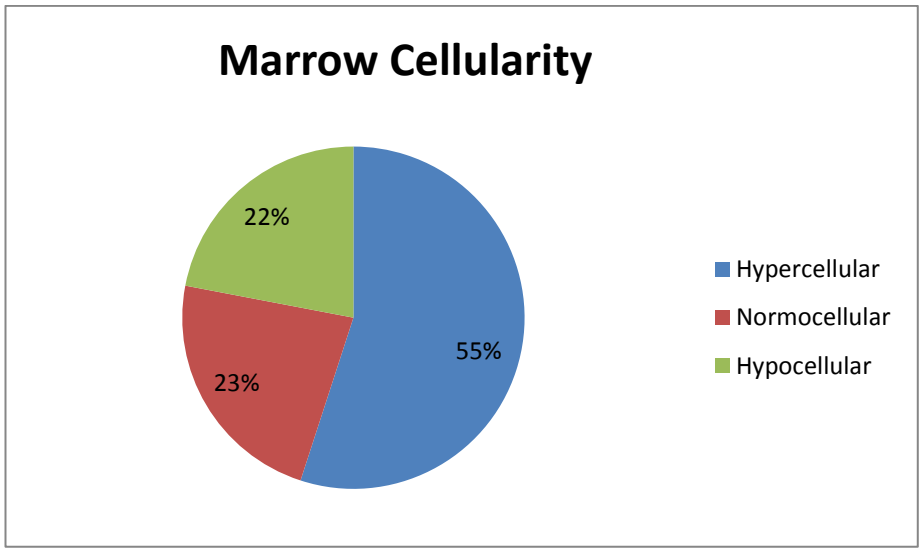

Figure 2: cellularity of bone marrow in aspirated smear

Table 14: Hematological disorder diagnosed with BMA cytology

Clinical indication	BMA Finding	Number of cases	Percentage (%)
Unexplained anemia	Micronormoblastic	23	22.33
	Megaloblastic	19	18.45
	Dimorphic	27	26.21
	Normal bone marrow	1	0.97
Unexplained pancytopenia	Aplastic anemia	6	5.83
	hypoplastic MDS	1	0.97
Unexplained splenomegaly	CML	4	3.88
Suspected malignancy	AML	5	4.85
	ALL	1	0.97
	CLL	1	0.97
Unexplained leuco-thrombocytopenia	ITP	8	7.77
Others	HLH	1	0.97
	MDS EB1	1	0.97
	Plasma cell dyscrasia	3	2.92
	Hypersplenism	1	0.97
Infection	Reactive myeloid hyperplasia	1	0.97
Total		**103**	**100%**

Dimorphic anemia was seen in 27 (26.21%) of the cases, thus it was the most common finding in this study. Apart from this; 23 (22.33%) cases showed micro normoblastic picture

and 19 (18.45%) cases showed megaloblastic changes. Aplastic anemia was diagnosed in 6 (5.83%) of cases and 8 cases showed leuco-thrombocytopenia. Among cases of suspected malignancies; 5 (4.85%) cases were diagnosed as AML, 1 (0.97%) was of ALL and 1 (0.97%) was of CLL. There were single case of each of HLH (0.97%), MDS EB1 (0.97%) and Hypersplenism (0.97%). 3 (2.92%) were of plasma cell dycrasia. Among infectious indication 1 (0.97%) case showed reactive myeloid hyperplasia. Single case (0.97%) showed normal bone marrow picture.

Correlation of anaemia with dimorphic blood picture with blood indices and biochemical parameters:

In present study 27 cases were diagnosed as anaemia with dimorphic blood picture, out of 27 cases, MCV was within normal in 13 cases and decreased in 14 cases. MCH was normal in 12 cases and decreased in 15 cases, MCHC was normal in 22 cases and decreased in 5 cases, RDW was increased in 25 cases and normal in 2 cases.

In dimorphic blood picture iron, ferritin, B12 & folic acid were decreased in all 27 cases.

Special stain finding: Perl's stain was done on bone marrow aspirate of all 27 cases, in which, cases associated with iron deficiency, showing lack of iron in marrow.

Correlation of anaemia with micro normoblastic blood picture with blood indices and biochemical parameters: Out of 23 cases, in all cases MCH was below normal range and MCHC was decreased in 22 cases and MCV was below normal range in 20 cases.

Serum IRON and FERRITIN levels were decreased in all 23 cases of anaemia with micro normoblastic and B12 & FOLIC ACID levels were normal.

Special stain finding - Special stain, Perl's Prussian blue performed on all 23 cases, showing lack of iron granules.

Correlation of Anaemia with Megaloblastic blood picture with blood indices and biochemical parameters:

In our study, 19 cases were diagnosed as anaemia with megaloblastic blood picture, MCV, MCH was increased and MCHC was normal in all these cases.

Biochemical parameters serum B12& FOLIC ACID were decreased in all 19 cases.

Special stain finding: Perl's stain on BM aspirates was performed on all 19 cases showing increased iron stores with many abnormal sideroblastic population.

Out of 103 cases 6 cases were aplastic anaemia showing increased iron stores in marrow aspirates, reticulin stain was negative for reticular fibres.

Hypo plastic MDS positive for reticulin stain due to increase reticular fibres.

One case was MDS, showing positive for Perl's stain due to ring sideroblastic population.

In our study bone marrow biopsy was performed in 6 cases of aplastic anaemia. Diagnosis in all cases correlated with Bone marrow aspiration finding.

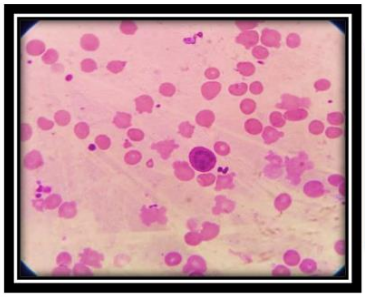

Fig 3: MEGALOBLASTIC ANEMIA (PBS, Leishman, 100 X)

PBS - RBCs show macro-ovalocytes with multilobed neutrophil

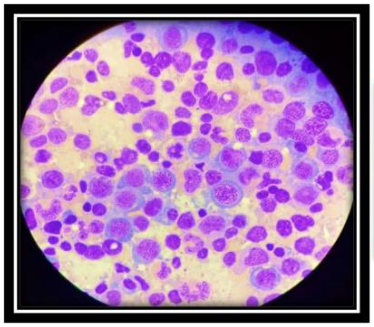

Fig 4: MEGALOBLASTIC ANAEMIA(BMA,Giemsa,100X)

Bone marrow smear shows large number of megaloblast cells

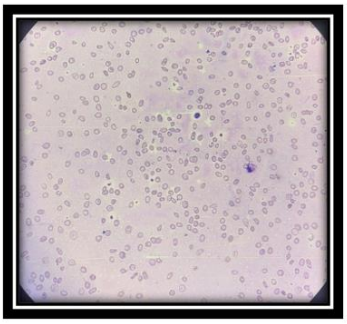

Fig 5: MICRONORMOERYTHOID HYPERPLASIA (PBS, Leishman, 40X)

Smear shows Tear drop cells, target cells & pencil cells

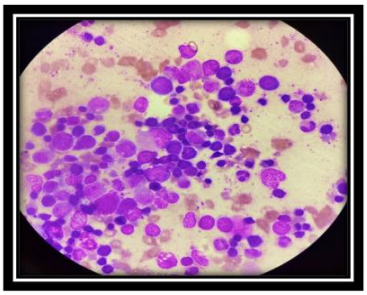

Fig 6: MICRO NORMO ERYTHROID HYPERPLASIA (BMA, Giemsa 100X)

Metamyelocyte surrounded by Erythroid island

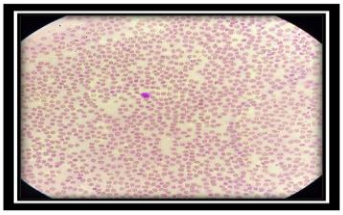

Fig 7: IMMUNE THROMBOCYTOPENIA (PBS,Leishman,40X)

Showing low platelets count

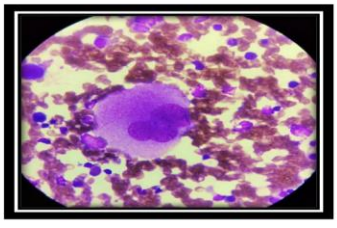

Fig 8: ITP (BMA, Giemsa,100X)

Megakaryocytes showing lobated nucleus with smooth border

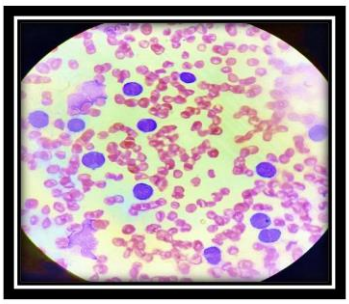

Fig 9: Acute myeloid leukemia-M3 (PBS,Leishman stain, 40X)

Shows immature bilobed cells

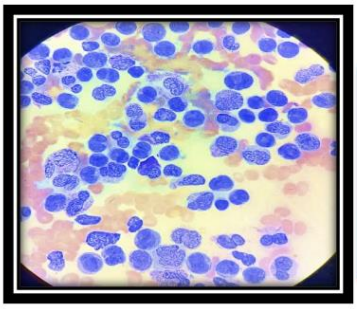

Fig 10: AML (BMA, Giemsa,100X) Shows bilobed promyelocytes, Faggot cell, Auer rods

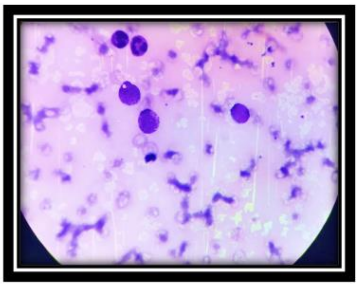

Fig 11: CML (PBS, Leishman, 100X)

Shows basophil

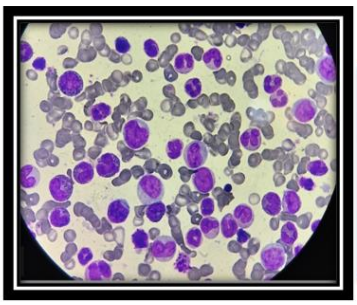

Fig 12: CML (BMA, Giemsa, 100X)

Shows blastoid population with basophils spectrum of lymphoid evolution

Discussion:

BMA is an important medical procedure for the diagnosis, staging, and follow-up of patients with haematological diseases and for investigating various non-haematological conditions including storage diseases, inborn errors of metabolism, metastatic cancer, and infection that has spread to the bone marrow.

A total of 103 cases were included in this study. Age distribution of cases in the present study was 7 months - 85 years. Commonest age group affected was 61-70 years in the present study comparable with studies done by Sudhakar G et al (2021)[8], Chowdhary et al (2019)[9] and Kauser Z et al (2018)[10.]

In the present study, male preponderance was seen with male is to female ratio of 1.8:1 comparable with the other studies.[8,10,11]

The most common indication in our study was unexplained anaemia, similar to other study.[10,11,12,13.] But in contrast to these studies, pancytopenia was the most common indication in study done by Pudasaini S et al (2012)[14] and Sudhakar G et al (2021)[8].

The distribution of bone marrow cellularity showed mostly normocellular marrow in (55.34%) cases followed by hypercellular (23.30%) and hypocellular marrow (21.36%) cases. In contrast to this study, Pudasaini S et al (2012)[14] and Thiyagarajan P et al (2015)[13] showed hypercellular bone marrow as commonest finding.
Dimorphic anemia was seen in 27 (26.21%) of the cases, thus it was the most common finding in this study. Similar finding was there in a study conducted by Thiyagarajan P et al in (2015)[13] in which dimorphic maturation was confirmed in 56% of the cases. Apart from this; 23 (22.33%) cases showed micro normoblastic picture and 19 (18.45%) cases showed megaloblastic changes. Aplastic anemia was diagnosed in 6 (5.83%) of cases and 8 cases showed leuco-thrombocytopenia.

Table 2: Commonest finding in different studies [8,9,10,11,12,13]

Authors	Most common finding
Thiyagarajan P et al (2015)	Dimorphic anemia
Ekwere T A et al (2015)	Acute leukaemia
Ranabhat S et al (2017)	Megaloblastic anemia
Kauser Z et al (2018)	Megaloblastic anaemia
Chowdhary et al (2019)	Aplastic anemia
Sudhakar G et al (2021)	Bicytopenia and pancytopenia
Present study	Dimorphic anemia

In our study, megaloblastic anaemia was 3rd common finding in contrast to other studies.[10,11] Which showed megaloblastic anaemia as most common finding. Among cases of suspected malignancies, most common finding was AML (4.85%) followed by ALL (0.97%) and CLL (0.97%). In other studies occurrence of Acute Leukaemia ranged from 12 to 16%.[12,14] Out of these AML ranged from (9-11%).[12,14] and ALL ranged from (1-7%).[10,14] Similar findings were seen in other studies.[8,10,11] Immune thrombocytopenic purpura was diagnosed in total of 8 (7.77%) cases in present study. Similar finding was seen in other studies.[8,9,10,11,12,13]

Conclusion

The present study includes 103 cases of BME in Department of Pathology, Heritage Institute of Medical Sciences, Varanasi over a period of November 2018 to October 2022. The study was based on clinical correlation and its morphological spectrum of bone marrow examination. In our study, the commonest indication of bone marrow examination was unexplained anemia (43.68%) followed by unexplained pancytopenia (18.37%). Age of the patient in our study was ranged from 7 month to 85 years and most common age group undergoing bone marrow examination was 61-70 years. Out of total 103 cases 70 were male and 33 cases were female. The distribution of bone marrow cellularity showed normocellular marrow in 55.34% cases, though 23.30% were hypercellular and 21.36% cases showed hypocellular marrow. Dimorphic anaemia was seen in 27 (26.21%) of the cases, thus it was the most common finding in this study. Apart from this; 23 (22.33%) cases showed micro normoblastic picture and 19 (18.45%) cases showed megaloblastic changes.

Bone marrow study is a time-tested, reproducible procedure used for the evaluation of hematological and non-hematological conditions. When routine investigations fail to reach the final diagnosis, this can help in the diagnosis of the disease and subsequently can positively modify the outcome of the disease. This study shows that bone marrow examination is a useful diagnostic tool in the diagnosis of various non-hematological diseases in addition to hematological disorders and malignancies.

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