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Diagnostic Utility of Bone Marrow Examination in Routine Haematology Practice



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ABSTRACT

Aims and objectives-To determine the utility of bone marrow aspiration and bone marrow biopsy examination in routine hematological practice. **Materials and methods-**The study included 151 cases of bone marrow examination, referred to the department of pathology, DUPMC, Jalgaon during the period of June 2017 to May 2020. Bone marrow aspiration slides were stained by Leishman and Perl's Prussian Blue, the biopsy was routinely processed for histopathology and stained by H&E, Special stains were used wherever needed. **Results -** In all 151 cases, bone marrow aspiration & bone marrow biopsy were available. The age ranged from 6 years to 80 years. The commonest clinical indication for aspiration was anaemia 107 cases (70.8%), followed by malignancy 13 cases (8.6%), thrombocytopenia 11 cases (7.2%), pancytopenia and hepatosplenomegaly in 8 cases (5.2%), backache and staging in 2 cases (1.3%). Most of the cases had hypercellular marrow 97 cases (64.2%) followed by normocellular 43 (28.4%) and hypocellular marrow 11 cases (7.2%). The diagnostic accuracy of aspiration was 96.02% whereas 100% for biopsy. **Conclusion-** Bone marrow aspiration and biopsy complement each other, the advantage of the two procedures helps us study the cytomorphology of cells and pattern distribution of cells depending on the cases, hence helping inaccurate diagnosis.

INTRODUCTION

“The fountain of life and the primary seat of the soul. The marrow of our bones is the seedbed of our blood.” described blood correctly by Sir William Harvey. Bone marrow is the site of myeloid, erythroid and megakaryocytic as well as lymphoid cell development.¹Careful assessment of blood elements is often the first step in the assessment of hematological function and diagnosis². Bone marrow examination is an invasive, simple, safe, and cost-effective procedure that helps in the diagnosis of hematological and nonhematological disorders which include nutritional deficiency anemia, Acute leukemia, Myeloproliferative disorders, hematological neoplasm, and non-hematological disorders including diseases infiltrating the marrow such as parasite infection, tuberculosis, and metastatic deposits.³Bone marrow aspiration(BMA) is important in eliciting individual cell structure properly whereas bone marrow biopsy(BMB) helps to provide bone marrow architectural structures and distribution.⁴ The present study was conducted for assessing bone marrow examination findings amongst subjects with hematological disorders.

MATERIALS AND METHODS

The study was conducted in the department of pathology, DUPMC Jalgaon during period of June 2017 to May 2020. A total of 151 cases were included in this study. All patients who underwent simultaneous BMA and BMB after taking written consent were included in this study and cases where the biopsy was not obtained were excluded. 0.5 to 1 ml of bone marrow aspirate was taken from the posterior superior iliac spine by using spinal needles no 16 & 18 following standard technique. BMA smears were made using the wedge smear technique. Leishman stain was used for all BMA slides, Perls Prussian blue stain was done for assessing iron content. BMB was taken using Jamshidi needles no 11 and 12. BMB obtained was decalcified and then processed for routine H&E stain. Special stain-reticulin was used in cases of fibrosis for grading by the WHO grading system. Complete blood evaluation, peripheral smear, a recount was done along with a recording of patients detailed information, clinical history with the indication for a procedure for all the cases. All slides were examined by expert pathologists and data was entered in an MS excel sheet and analyzed for diagnostic accuracy.

RESULTS

The present study included 151 cases wherein BMA and BMB were done. Table 1 shows the age and sex distribution of the patients. The age ranged from 6 years to 80 years. 78 cases (51.6%) were males and 73 cases (48.3%) were females with Male to Female ratio:1.06:1. Maximum cases of hematological disorders who underwent Bone marrow examination were 68 cases (45.03%) in the age group of 21 to 40 years.

Table 1: AGE AND SEX DISTRIBUTION

AGE(YEARS)	MALE	FEMALE	TOTAL
0 -20	5	3	8
21 - 40	35	33	68
41 - 60	29	31	60
61-80	9	6	15
Total	78(51.6%)	73(48.3%)	151

The commonest clinical indication for BMA was anemia 107 cases (70.8%), followed by malignancy 13 cases (8.6%), while least common indications were backache and staging for lymphoma in 2 cases (1.3%) each.

Table 2: INDICATIONS OF BONE MARROW

Indication	Number of cases
Anemia	107(70.8%)
Pancytopenia	8(5.2%)
Thrombocytopenia	11(7.2%)
Malignancy	13(8.6%)
Hepatosplenomegaly	8(5.2%)
Backache	2(1.3%)
Staging	2(1.3%)
Total	151

Most of the cases had hypercellular marrow 97 cases (64.2%) followed by normocellular 43(28.4%) and hypocellular marrow 11 cases (7.2%) as shown in Table 3.

Table 3: CELLULARITY OF BONE MARROW

Marrow cellularity	Number of cases
Hypercellular	97(64.2%)
Normocellular	43(28.4%)
Hypocellular	11(7.2%)
TOTAL	151

The spectrum of hematological disorders diagnosed on bone marrow cytology is shown in Table 4. Maximum cases encountered in the study were of nutritional anaemia 100 cases(79.01%) of which 54 cases were of Iron deficiency anaemia(35.7%),25 cases were of Megaloblastic anaemia(16.55%)and 21 cases were of Mixed deficiency anaemia(13.9%).Of the remaining cases commoner were Idiopathic thrombocytopenic purpura(ITP) 11 cases 7.2%,Acute Leukemias 9 cases(5.96%) and Dry tap 6 cases(3.9%). The diagnostic accuracy for bone marrow aspiration was found to be 96.02%. Figure 1 and 2 shows BMA findings.

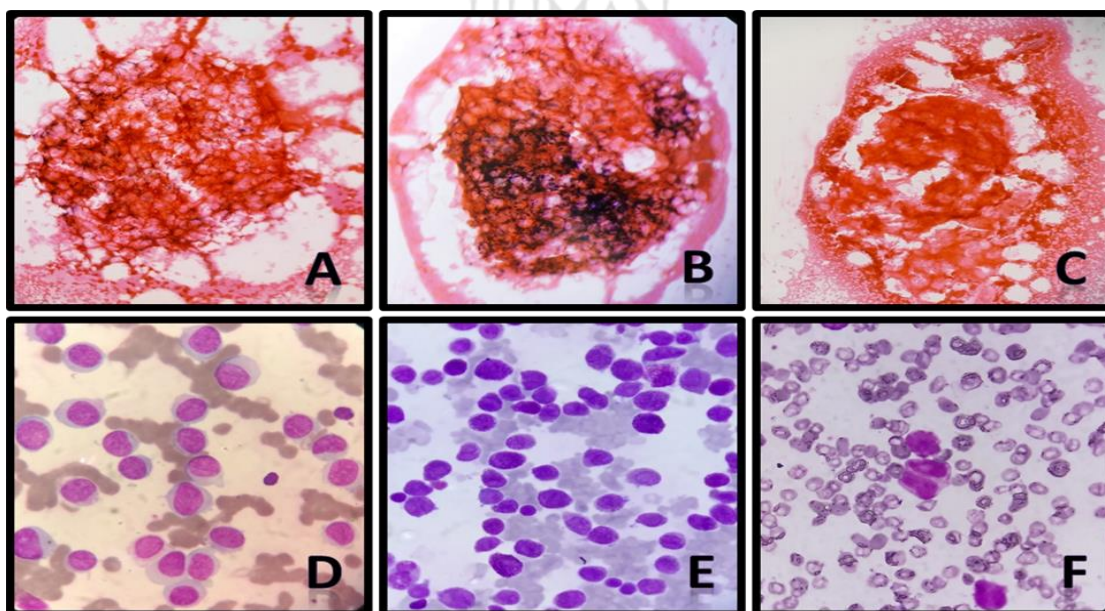


Figure 1-A) Normal Iron stores (Prussian blue stain -100X)B)Increased iron stores(Prussian blue stain -100X) C)Absent Iron stores. (Prussian blue stain -100X) D)AML- M5 Leishman

stain(100X) E)AML-M3-(APML-Hypergranular variant)Leishman stain(100X) F)AML-M3V(Hyopgranular variant)Leishman stain(100X)

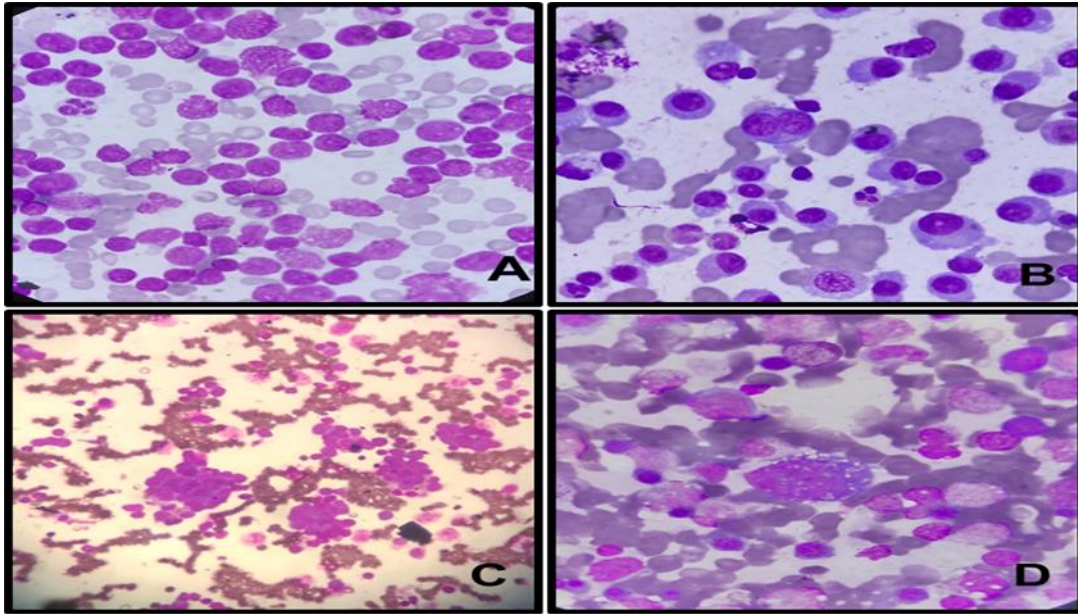


Figure 2-Leishman stain-A) ALL(100X) B)Multiple myeloma(100X) C)Metastasis in marrow(100X) D)NHL Infiltrate in marrow(100X)

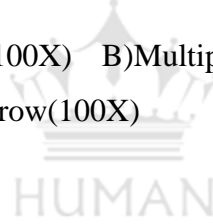


TABLE 4: SPECTRUM OF HAEMATOLOGICAL DISORDERS DIAGNOSED WITH BMA CYTOLOGY.

Broad category	Diagnosis	Number of cases
Nutritional anemia	Iron deficiency	54(35.7%)
	Megaloblastic anemia	25(16.55%)
	Mixed deficiency anemia	21(13.9%)
Anemia of chronic disease	Anemia of chronic disease	3(1.98%)
Aplastic anaemia	Aplastic anemia	3(1.98%)
Myeloproliferative and myelodysplastic diseases	Chronic myeloid leukemia	2(1.3%)
	Myelodysplastic syndrome	2(1.3%)
Acute Leukemia	Acute myeloid leukemia(AML)	6(3.9%)
	Acute lymphoid leukemia(ALL)	3(1.98%)
Chronic Leukemia	Chronic lymphoproliferative disorders(CLPD)	4(2.6%)
	Chronic Lymphoblastic lymphoma(CLL)	1(0.6%)
Plasma cell dyscrasias	Plasma cell leukemia	1(0.6%)
	Multiple myeloma	2(1.3%)
	Lymphoma	1(0.6%)
Idiopathic thrombocytopenic purpura	Idiopathic thrombocytopenic purpura	11(7.2%)
Others	Metastasis	1(0.6%)
	Hypersplenism	3(1.98%)
	Normal	1(0.6%)
	Eosinophilia	1(0.6%)
	Dry tap	6(3.9%)

Table 5 shows diagnoses made by bone marrow biopsies. Most commonly encountered were Erythroid hyperplasia 75 cases (49.6%), Megaloblastic anaemia 25 cases(16.5%),Acute leukemia

in 12 cases (7.94%) and ITP in 11 cases(7.28%). BMB was the gold standard and Diagnostic accuracy for BMB was 100%.

TABLE 5: DIAGNOSIS ON BONE MARROW BIOPSIES.

DIAGNOSIS	Number of cases
Erythroid hyperplasia	75(49.6%)
Megaloblastic anaemia	25(16.5%)
Acute Leukemia	12(7.94%)
Idiopathic thrombocytopenic purpura(ITP)	11(7.28%)
Chronic myeloid leukemia	4(2.64%)
Lymphoproliferative disorder	5(3.31%)
Myelodysplastic syndrome	2(1.32%)
Myelofibrosis	1(0.66%)
Plasma cell dyscrasia	3(1.98)
Metastasis	1(0.66%)
Eosinophilia	1(0.66%)
Lymphoma infiltration	2(1.32%)
Aplastic anemia	3(1.98%)
Normal	6(3.97%)
Total	151

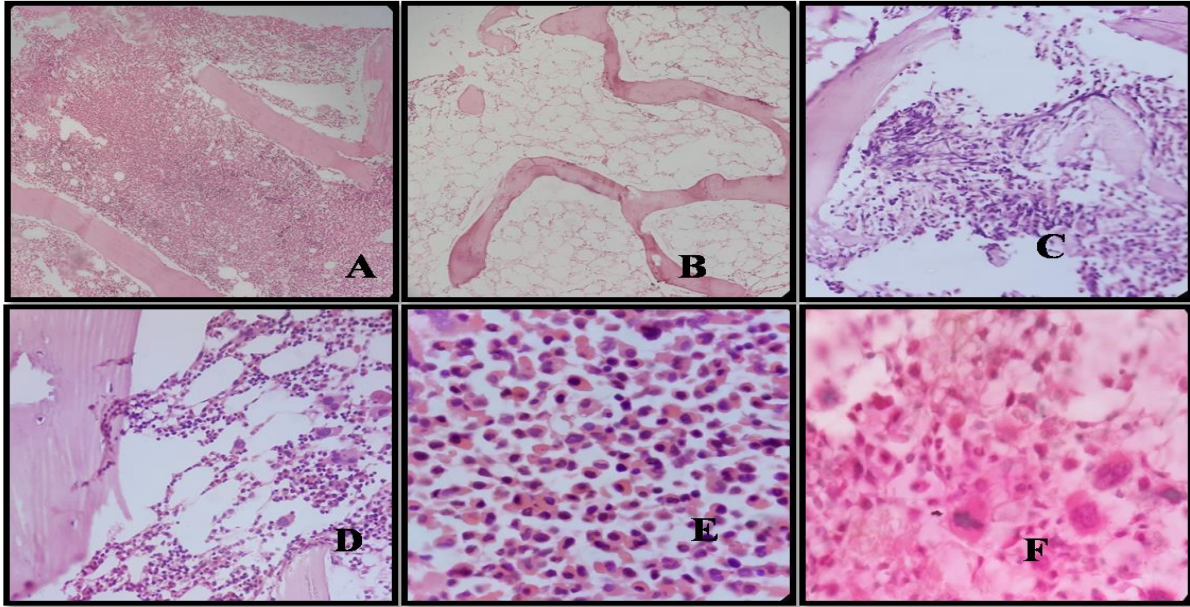


Figure 3 and 4 shows BMB findings in different conditions.

Figure 3-H & E stain-A)Hypercellular(40X) B)Hypoplastic(40X) C)Fibrosis(40X) D)ITPE(40X)Plasma cell dyscrasia(100X) F)Hodgkins lymphoma infiltration(100X).

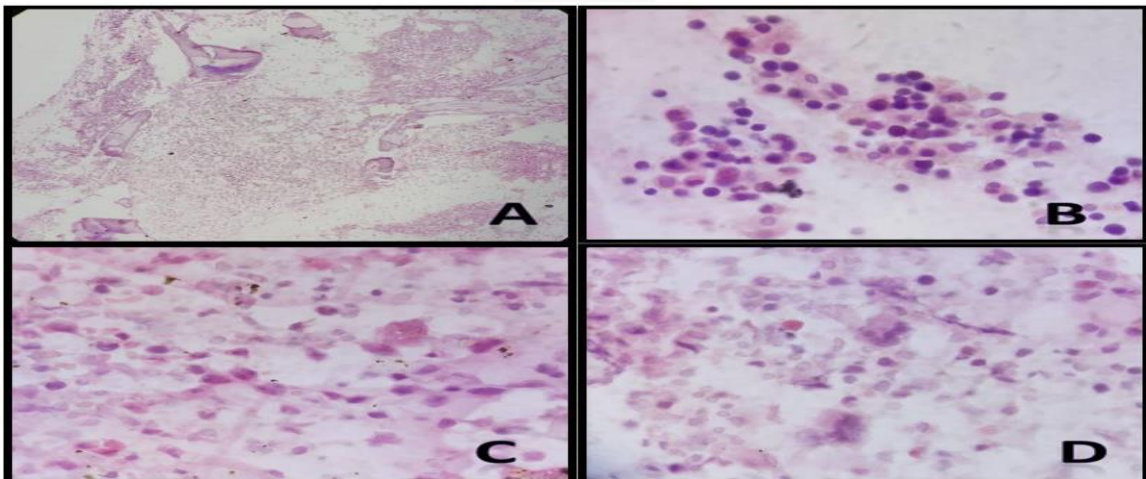


Figure 4-Myelodysplastic syndrome-Bone marrow biopsy H & E- A) Architectural distortion(40X) B) Erythroid dysplasia(100X) c)Abnormal myeloid precursors(100X) E)Megakaryocytic dysplasia(100X)

DISCUSSION

Bone marrow examination is an important investigation in hematology practice. BMA and BMB aid in the diagnosis of hematological and nonhematological conditions as well for follow-up of patients undergoing chemotherapy. The age range in our study was from 6 years to 80 years which was in concordance with other studies.⁵⁻⁸ The male to female ratio is 1.06:1 which is similar to other studies.^{5,9} The most common indication for BMA in our study was anaemia and malignancy followed by thrombocytopenia and pancytopenia. M Gohil et al⁵, D Dapus et al¹⁰ and S Tripathy et al¹¹ also reported anemia as the most common indication for BMA cytology in their studies contrasts to studies by S Pudasaini et al⁶ and L Bashawri et al¹² which showed pancytopenia and leukemia as the two most common diagnosis. Most of the cases had hypercellular marrow 97 cases(64.2%) followed by normocellular 43(28.4%) and hypocellular marrow 11 cases(7.2%) similar to other studies^{5,13}. Out of 100 cases(79.01%) of anaemia, 54 cases were of Iron deficiency anaemia(35.7%), 25 cases were of Megaloblastic anaemia (16.55%) and 21 cases were of Mixed deficiency anaemia(13.9%). 100% diagnoses were made on BMA with Leishman and pearls prussian blue stain. Erythroid hyperplasia was noted in BMB for iron deficiency and mixed deficiency anaemia cases. Megaloblastic anemia showed characteristic megaloblastic erythroid hyperplasia on BMA as well as BMB. These findings are in concordance with findings by M Kaur et al¹⁴ and Ch Toi P et al¹⁵.

Of 151 cases 7.2% cases were diagnosed as idiopathic thrombocytopenic purpura (ITP) on BMA and BMB which showed increased megakaryocytes. Indhudhara PB et al¹⁶ and LY Patil et al¹⁷ also reported the same findings. The cases of Aplastic anaemia 3 (1.98%) were hypocellular on BMA and were confirmed on BMB which showed hypocellularity with increased fat spaces.

Bone marrow examination is done as a part of the staging procedure in patients with a known diagnosis of lymphoma. NHL infiltration was seen on BMA and BMB in one case. One case of Hodgkin's lymphoma was referred to us for staging, aspiration of which showed no abnormality except for reactive changes whereas biopsy showed infiltration by Reed Sternberg cells. Bone marrow infiltration in Hodgkin's lymphoma is seen in 5 to 15% cases.¹⁸ Due to focal infiltration by lymphoma cells aspiration did not show findings and was diagnosed on biopsy. We found 12 cases of leukemia(7.94%) which is consistent to study done by M Gohil et al⁵. 3 cases of ALL and 6 cases of AML were diagnosed on aspiration and biopsy. Immunophenotyping and

cytogenetics was advised for these patients for further management. AML was reported more frequently than ALL in studies done by GayathriBN et al⁸,Egesie OJ et al¹⁹ and Kibria S et al²⁰.The case of myelofibrosis showed a leucoerythroblastic peripheral smear,aspiration showed dry tap and biopsy confirmed the diagnosis as it showed fibrosis by reticulin stain.

2 cases of multiple myeloma and one case of plasma cell leukemia were diagnosed on BMA. Biopsy should be done as sometimes plasma cell infiltration can be focal and can be missed on aspiration²¹. Biopsy showed increased plasmacytoid cells, Immunohistochemistry and serum electrophoresis was advised for confirmation and treatment of these cases. A case of CLL with diffuse involvement of marrow observed on biopsy was encountered which indicated poor prognosis and was consistent to study findings by M Kaur et al¹⁴. For CLL cases biopsy is mandatory as it give an accurate assessment of marrow infiltration as well as helps in prognosis. 4cases of lymphoproliferative disorder were diagnosed on BMA & BMB. The indications here were hepatosplenomegaly & anemia. One case of metastasis (adenocarcinoma) in marrow was diagnosed from a case of carcinoma prostate similar to Rathod KB et al.³

Dry tap was seen in 6 cases on bone marrow aspiration which were diagnosed on biopsy.3 cases of ALL, 2cases of CML and one case of Myelofibrosis were diagnosed on trephine biopsy. This shows that BMA and BMB are complementary and help in the final diagnosis. The diagnostic accuracy in this study of BMA is 96.02% in comparison to BMB which is 100% which correlates with other studies.^{16,22}

From the above discussion, it is very clear that bone marrow aspiration and bone marrow biopsy are complementary procedures for confirmatory diagnoses of hematological and non-hematological disorders. The BMA gives excellent cytomorphological details whereas BMB gives a topographic arrangement of cells in marrow framework which helps in diagnosis. Ancillary tests like Immunophenotyping, cytogenetics, and IHC can be done on aspiration and biopsy which helps in the prognosis of the patients.

CONCLUSION

Bone marrow aspiration and trephine bone biopsy are complementary procedures for bone marrow evaluation. Both these procedures can be done simultaneously, are easy, rapid and cost-

effective. These help in diagnosis, prognosis and therapeutic response of different types of hematological and non-hematological diseases.

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