

HAEMATOLOGICAL DISORDERS DIAGNOSED IN ONE HUNDRED AND ONE SUCCESSIVE BONE MARROW EXAMINATION AT A TERTIARY CARE CENTRE IN QUETTA, BALOCHISTAN

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ABSTRACT

Objective: To determine the frequency of haematological disorders diagnosed by bone marrow examination at a tertiary care centre in Quetta, Balochistan.

Study Design: Prospective observational study.

Place and Duration of Study: Department of Pathology, Combined Military Hospital Quetta, from Jan 2018 to May 2019.

Methodology: A total of 101 one patients, who underwent bone marrow examination, were included in the study. Brief history, clinical examination and indication of procedure were also endorsed in a questionnaire designed for the study.

Results: Bone marrow of one hundred and one patients, included in the study, were evaluated. Mean age of the patients was 32.3 ± 18.4 years. There were 68 males (67%), while 33 were females (33%) with 2:1 male to female ratio. Pyrexia of unknown origin (PUO) was the most common indication for bone marrow examination with frequency of 20.7%. Nutritional anaemia was the most prevalent benign disorder (17%), whereas Acute Lymphoblastic leukaemia (ALL) accounted about 6.8% which is highest in malignant disorders.

Conclusion: This study has concluded that bone marrow examination is a useful technique and findings of bone marrow can modify the treatment. Thus procedure has a great diagnostic value. Both bone marrow aspiration (BMA) and bone marrow biopsy (BMB) are the complimentary techniques and supremacy of one method on other depends on the disorder.

Keywords: Aspiration, Bone marrow, Trepine biopsy.

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INTRODUCTION

Bone marrow examination is an extremely useful diagnostic tool for evaluation and diagnosis of not only hematological disorders but also numerous non-hematological diseases. Bone marrow examination is a relatively safe and invasive procedure, and leads to early diagnosis and specific management of the case^{1,2}. There is no contraindication of bone marrow technique. It provides the opportunity of directly examining the tissue which forms blood cells³.

During first decade of twentieth century bone marrow was obtained from a patient as investigative procedure and as a diagnostic tool. Sternal aspiration was commenced in 1920. Arinkin introduced the use of needle aspiration of bone marrow in 1929. Since 1950s core needle biopsy has also been widely used as a diagnostic technique⁴.

Bone marrow aspiration (BMA) and bone marrow biopsy (BMB) are the two basic and important methods for bone marrow examination. BMA involves suction of liquid bone marrow and trephine biopsy provides solid core of bone. BMA provides cytological details of developing cells whereas BMB is a histopathological

study which helps in assessment of cellularity and infiltration⁵. Both techniques provide distinct information which is complimentary and supportive to each other in reaching a conclusive diagnosis^{6,7}. Bone marrow involvement can be seen in both haematological and non-haematological disorders. Bone marrow disease can present with clinical symptom along with peripheral blood involvement as cytopenias, leucocytosis, leukoerythroblastic picture and many more. However peripheral blood picture cannot depict the exact stage and nature of disease⁸.

BMA is a simple and safe test that may either verify clinically expected diseases or may provide the previously unsuspected diagnosis⁹. Present study was designed to statistically analyse the data of patients who underwent bone marrow examination and to determine the prevalence and frequency of haematological and non haematological disorders diagnosed in this part of the country. It also evaluated the common indications of this technique, age distribution, male to female ratio, comparison of both techniques and ultimately the conclusions drawn.

METHODOLOGY

This prospective observational study was conducted in department of Pathology, Combined Military Hospital Quetta, from January 2018 to May 2019. A

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total of 101 patients, whom underwent bone marrow examination during study period through universal sampling method, were included. Patients were selected by non-probability consecutive sampling. Cases in which both BMA and BMB were done included in the study and comparative evaluation was carried out whereas cases in which only BMA was done were excluded from this study. Brief history, clinical examination and indication of procedure was also endorsed in a questionnaire designed for the study.

Whole procedure of bone marrow technique was explained to each patient. Informed consent was also obtained. Bone marrow examination was carried out using local anaesthetic technique under strict aseptic measures. BMA smears were stained by Leishman’s stain, Giemsa stain and Perl’s Prussian stain for iron. Positive control was also used to demonstrate iron. Cytochemical stains including Sudan Black B (SBB) and Leucocyte Alkaline Phosphatase (LAP) were also used wherever indicated. Each smear was assessed for cellularity, cytology and quantity of erythroid, myeloid, megakaryocytes and abnormal cells in bone marrow. Minimum of 500 nucleated cells (myelogram) were examined in bone marrow smear.

BMB were extracted from posterior iliac crest and fixed by using 10% neutral buffered formalin. Decalcification was done by 5-10% Nitric acid in 2-3 days. Later on biopsy was embedded in paraffin and 2-4 um thick sections were cut and stained using Haematoxylin and Eosin method. Furthermore, Reticulin stain was done to grade fibrosis.

Institutional ethical review board (IRB approval no. Ext-23-05/READ-IRB/007) approved this study. Statistical analysis was done using SPSS-22. Quantitative variables were presented by mean and SD whereas qualitative variables were expressed as frequency and percentage.

RESULTS

A total of 101 patients underwent bone marrow examination. Table-I shows age and gender distribution of the patients. Mean age of the patients was 32.3 ± 18.4 years and ranged from 4 months to 75 years and majority of the patients were in second decade of their life. Figure shows the clinical indications for bone marrow examination. Pyrexia of unknown origin (PUO) was the most common clinical indication with frequency of 21 (20.7%) followed by pancytopenia 19 (18.8%).

Table-II shows diagnosis drawn from bone marrow examination. Nutritional deficiency was the most

common diagnosis with 18 cases followed by Acute leukaemia and Idiopathic thrombocytopenic purpura with 11 cases each. Four cases showed diluted marrow on BMA and unfit for opinion however on BMB diagnosed with lymphoproliferative disorder, hypoplastic marrow, megaloblasticanaemia and normocellular respectively. Fourteen bone marrow cases were normocellular on both BMA and BMB.

Table-I: Age and gender distribution of study subjects.

Age (Years)	n (%)	Male, n (%)	Female, n (%)
0-10	10 (9.9)	6 (5.9)	4 (3.9)
11-20	14 (13.8)	7 (6.9)	7 (6.9)
21-30	33 (32.6)	25 (24.7)	8 (7.9)
31-40	18 (17.8)	15 (14.8)	3 (2.9)
41-50	8 (7.9)	6 (5.9)	2 (1.9)
51-60	6 (5.9)	4 (3.9)	2 (1.9)
61-70	10 (9.9)	3 (2.9)	7 (6.9)

Table-II: Diagnosis of bone marrow examination.

S. No	Diagnosis	n (%)
1	Nutritional Deficiency Anaemia	18 (17.8)
2	Acute Leukemia	11 (10.8)
3	Idiopathic Thrombocytopenic Purpura	11 (10.8)
4	Myeloproliferative Neoplasm	8 (7.9)
5	Hypersplenism	7 (6.9)
6	Dysplastic Marrow	5 (4.9)
7	Anaemia of Chronic Disorder	4 (3.9)
8	Hypocellular Marrow	4 (3.9)
9	Erythroid Hyperplasia	3 (2.9)
10	Myeloid Hyperplasia	3 (2.9)
11	Marrow Showing Reactive Changes	2 (1.9)
12	Chronic Granulomatous Infection	2 (1.9)
13	Myelodysplastic Syndrome	2 (1.9)
14	Lymphoproliferative disorder	2 (1.9)
15	Gaucher Disease	1 (0.9)
16	Diluted Marrow	4 (3.9)
17	Normal Study	14 (13.8)
Total		101 (100)

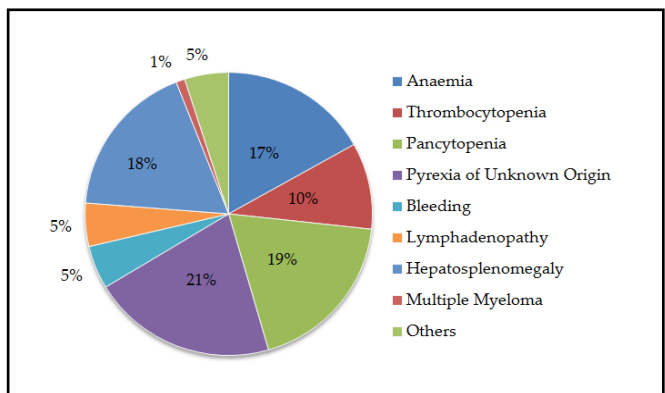


Figure: Clinical indications for bone marrow examination.

DISCUSSION

Bone marrow examination is a significant investigation tool that can diagnose both haematological and non-haematological disorders in a short time. Bone marrow examination has many advantages as it provides diagnosis in significant number of cases¹⁰. This diagnostic tool is very specific and a sensitive procedure and has a great clinical significance. It shortens patient's hospital stay as this diagnostic tool is rapid and less time consuming and definite treatment starts early¹¹. Bone marrow aspiration and biopsy are essential techniques that not only complement each other but also enhance diagnostic accuracy in focal involvement of bone marrow.

Principle observation of our study was that nutritional anaemia was the most occurring haematological disorder identified in these patients i.e. 18 (17.8%). Nutritional anaemia was identified most common disorder in other similar studies with a frequency ranging from 19% to 68%. Our findings matched with study of Meenu, *et al* in which nutritional anaemia was 19%¹⁰. Second most common disorder diagnosed was Immune thrombocytopenic purpura with a frequency of 11 (10.8%).

Most common haematological malignancy in our study was Acute leukaemia 11 (10.8%) and further distribution showed ALL being 7 (6.8%) and AML 4 (3.9%) which is contradictory to other similar studies such as Rahim *et al* and Srikanth *et al* in which AML had high frequency among haematological malignancies^{11,12}. Second most common haematological malignancy was Myeloproliferative Neoplasm constituting about 8 (7.8%) and half of them were cases of Chronic Myeloid Leukemia in chronic phase¹³.

In our study most of the cases were diagnosed on bone marrow aspiration were consistent with trephine findings which is documented in other previous studies as by Ghodasara *et al* and Mahajan *et al*^{14,15}. However chronic granulomatous inflammation was detected only on trephine biopsy in two of our cases¹⁶. Both of these cases presented with PUO and were diagnosed only on BMB. Similar results were exhibited in study by Daleep *et al* that all cases of granulomatous inflammation were diagnosed on bone marrow biopsy¹⁷. From this observations it is obvious that due to patchy involvement of bone marrow, BMB is necessary in diagnosis of granulomatous inflammation.

There were four diluted marrows which on trephine biopsy reported of having lymphoproliferative disorder, hypoplastic marrow, megaloblastic anaemia

and normocellular marrow respectively. The main reason for diluted marrow was either due to packed marrow or fibrosis¹⁸. In case of dry tap or diluted marrow bone marrow biopsy should always accompany bone marrow aspiration before considering it as a result of faulty technique.

Most common clinical condition leading to bone marrow examination was PUO in twenty-one cases. These patients were diagnosed with Chronic granulomatous inflammation, ALL, Myelofibrosis, Gaucher's Disease, Anaemia of chronic disorders, Hypersplenism and with Reactive changes in marrow. Gupta *et al* study showed granulomas the most frequent finding (76%) in BMB¹⁹. BMB increases etiological diagnosis in the presence of fibrosis and granulomas²⁰.

There were few limitations of our study. Number of cases were less in sub groups so increase number of cases would have provided better correlation between BMA and BMB.

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RECOMMENDATION

In future study touch imprint should be included as an evaluating tool in bone marrow examination to further increase diagnostic accuracy and efficiency of procedure.

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CONCLUSION

This study has documented that bone marrow examination is a useful technique and although it is a confining procedure but should be performed when there is a distinct indication. Findings of bone marrow can modify the course of treatment. Thus procedure has a great diagnostic value. Both BMA and BMB are the complimentary techniques and supremacy of one method on other depends on the underlying disorder.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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