

Evaluation of the Indications and Diagnostic Value of Bone Marrow Examination in Haematological Disorders in Ilorin Nigeria: A Review of 496 Cases.

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Abstract

Bone Marrow Examination (BME), either in the form of aspiration or biopsy, is an invasive procedure which is relatively safe and is still being performed routinely in the investigation and diagnosis of various malignant and non-malignant haematological disorders. The aims of this study were to evaluate the role of BME in the investigation and diagnosis of haematological disorders, and the pattern of disorders diagnosed by bone marrow examination in our centre.

This study was a retrospective review of all cases of BME, carried out at the Haematology Department of U.I.T.H Ilorin between 1st January 2005 and 31st December 2018. Case folders of all patients who had BME done during the study period, Bone Marrow aspiration and biopsy registers from Haematology Department, Bone Marrow Reports and Full Blood Counts (FBC) results were retrieved and analyzed. Relevant clinical information retrieved included: age, gender, clinical features at presentation, laboratory investigations, treatment regimen, and survival outcome among others.

A total of 496 cases had BME performed during the study period. The patients comprised 276 (55.8%) males and 220 (44.2%) females with a M:F ratio of 1.3:1. Their median age was 38.5 years and age range was 16 months to 85 years. Pathological marrow with diagnosis on BME was found in 441 (88.9%) while normal marrow (negative for any pathologic condition) was seen in 55 (11.1%) of patients. The leukemias (acute and chronic) were the commonest haematological disorders found on bone marrow examination, constituting 37.8% of cases. Unexplained anaemia was the commonest clinical feature at presentation necessitating bone marrow examination. Bone marrow examination is still very useful as a diagnostic tool in the hand of Haematologists in the investigation and diagnosis of various haematological disorders, and is relatively safe to perform even with presence of thrombocytopenia.

Key words: Indications, Diagnostic value, Bone marrow examination, Haematological, Ilorin

Introduction

The bone marrow is the spongy fatty tissue which is found in the hollow parts of long and flat bones in humans and other primates. It contains haemopoietic stem cells, endothelial cells, fibroblasts, adipocytes, reticular cells, osteoblasts and macrophages. The bone marrow is the most important site of haemopoiesis, where the various blood cells i.e. red blood cells, white blood cells and platelets are produced¹.

Haematological disorders often arise from abnormality in one of the three cell lineages in the bone marrow; hence examination of the bone marrow is important in determining the actual cause of these diseases.

Bone marrow was first obtained from patients for diagnostic purposes in early 20th century, and it became an important procedure with the introduction of sternal aspiration in the late 1920s².

Examination of the bone marrow either in the form of aspiration, biopsy or both has become an established investigative procedure in the diagnosis of several haematological and non-haematological disorders. The procedure is one of the routine and relatively safe invasive procedures which is carried out in hospitals and can be performed even in the presence of severe thrombocytopenia with minimal or no risk of bleeding^{2,3,4}. Bone marrow examination, despite being an invasive procedure, remains a popular and veritable tool in the armamentarium of Haematologists for evaluation and diagnosis of several haematological and non-haematological diseases⁵.

The bone marrow examination (BME) is performed by trained Haematologists during the initial evaluation of patients with blood and blood related disorders^{4,5}. Being an invasive procedure, patients for BME must be properly evaluated and educated about the procedure, and informed consent obtained. Various indications for which BME had been performed include unexplained cytopenias (anaemia, leucopenia and thrombocytopenia), unexplained splenomegaly, diagnosis of haematological malignancies such as leukemia, lymphomas and multiple myeloma, megaloblastic anaemias, staging for lymphomas and other solid tumors, monitoring of response to chemotherapy, staining for bone marrow iron stores, cytogenetics and molecular analysis^{5,6}.

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" a previous study by Al-ghazaly *et al* in Yemen, haematological malignancies was reported as the commonest indication for bone marrow aspiration (BMA)⁷. " Benin City, Nigeria, unexplained anaemias of 46.6% were reported by Adewoyin *et al*⁵ as the commonest indication while Damulak *et al*⁸ in Jos, Nigeria reported nutrient deficiency anaemias as the commonest indication (33.3%) for BMA in their study. " India, Khan SP *et al* reported megaloblastic anaemia(25.6%) as the commonest disorder diagnosed by bone marrow aspiration in their study⁹.

The role of geographical location, climate, socioeconomic variables and pattern of infectious diseases have been shown to play an important role in the etiology and distribution of haematological disorders such as leukemia, megaloblastic anaemias and lymphomas^{7,10}. There have been reports of variations in the incidence of haematological diseases in developing countries compared with the pattern seen in the developed world¹⁰ and this could account for the variation in incidence and indications for BME reported in different climes.

" Nigeria, very few studies have documented the indications and the pattern of diseases which are diagnosed from BME in their centres. The aims of this study were to evaluate the diagnostic value, indications and the pattern of haematological disorders diagnosed by BME at the University of Ilorin Teaching Hospital, a tertiary health institution in the North central geo-political zone of Nigeria, and compare with reports from other centers within Nigeria and other parts of the world.

Materials and methods

This study is a hospital based retrospective review of all bone marrow examinations which were performed at the Haematology department of University of Ilorin teaching hospital(U.I.T.H),Ilorin between 1st January 2005 and 31st December 2018.U.I.T.H is a 650 bedded tertiary health institution located in Ilorin, North central geo-political zone of Nigeria. serves as a referral center for neighbouring states of Oyo, Osun, Ekiti, Kogi and Niger states of Nigeria.Ilorin, the capital city of Kwara state, Nigeria, is located on the latitude 8.50 North and longitude 4.550 East with a total population of 908,490 and an annual growth rate of 2.3%¹¹.

The Haematology department of U.I.T.H is involved in the investigations, clinical evaluation and management of blood and blood related disorders. also carries out laboratory services, interpretation of laboratory test results and receives consultations from other clinical departments of the hospital. Bone marrow examination is performed by the haematologists in the unit on primary patients of the unit as well as patients referred from other clinical departments for evaluation whenever it is considered

necessary to establish a diagnosis.

Bone marrow aspiration was done using either the Klima or Sallah aspiration needles, and bone marrow biopsy (BMB) was done using the Jamshidi marrow biopsy needle, which were re-used following sterilization by autoclaving in the earlier part of the study. However, with the availability of 18G disposable marrow needles, BM aspirations and biopsies were performed with the disposable needles in the latter part of this study. Bone marrow samples were obtained from either the right or left anterior and posterior superior iliac spines depending on ease of accessibility under local anaesthesia with full aseptic precautions. Bone marrow smears were made using standard procedure described by Dacie& Lewis¹².

Case folders of all patients who had bone marrow examination done during the study period, Bone marrow aspiration and biopsy registers from Haematology department, Bone marrow reports and Full blood counts (FBC) results were retrieved and analyzed. Relevant clinical information retrieved included age, gender, clinical features at presentation, laboratory investigations, treatment regimen, and survival outcome among others.

Final diagnosis of haematological diseases from bone marrow examination was arrived at by consensus among the Haematology Consultants and Residents in the department.

Data Analysis

The data obtained from the above sources were entered into Microsoft excel software and then analyzed using the Statistical Package for Social Sciences (SPSS) software version 21. The results were then presented in the form of frequency tables.

Results

There were a total number of 496 patients who had BME done within the study period. All the patients had BMA done while only 125 patients (25.2%) had BM biopsy in addition to aspiration. Two hundred and seventy six (55.8%) were males and 220 (44.2%) were females, giving a male to female ratio of 1.3:1. The median age of the patients at presentation was 38.5years, with their ages ranging between 16months and 85years.The largest number of patients who had BME done was in the age group 51-60years (n=82, 16.5%). Haematological disorders were found to occur more in adults (71.6%) than in the paediatric age group (28.4%). Table 1 shows the age and sex distribution of the patients who had BME during the study period. The site for BMA was the posterior superior iliac spine in 261 patients (52.6%) and anterior superior iliac spine in 235 (47.4%) of patients. The bone marrow cellularity was hypercellular in 403 (81.3%) patients, normocellular in 55 (11.1%) and hypocellular in 38 patients (7.7%). Table 3.

Table 1: showing Age and Sex distribution of patients who had Bone marrow Examination performed during the study period

Age Range (Years)	Sex		Total number of patients (%)
	Male (%)	Female (%)	
0 - 10	40 (8.1)	30 (6.0)	70 (14.1)
10 – 20	42 (8.5)	29 (5.8)	71 (14.3)
21 – 30	28 (5.7)	26 (5.2)	54 (10.9)
31 – 40	22 (4.4)	24 (4.8)	46 (9.3)
41 – 50	32 (6.5)	20 (4.0)	52 (10.5)
51 – 60	43 (8.7)	39 (7.9)	82 (16.5)
61 – 70	46 (9.3)	34 (6.9)	80 (16.1)
>70	23 (4.6)	18 (3.6)	41 (8.3)
Total	276 (55.8)	220 (44.2)	496 (100)

Unexplained anaemia was found to be the commonest clinical feature at presentation in patients who had BMA, occurring in 456 (91.9%) patients. Fever was the next presenting feature in 392 (79.2%) patients and body weakness accounted for 74.2% of cases (Table 4).

A total of 441 (88.9%) patients had pathological outcome while 55 (11.1%) had normal marrow appearance. Haematological malignancies – leukemias, lymphomas, myelomas and other myeloproliferative disorders accounted for 65.1% of cases while the non-malignant haematological disorders – aplastic anaemia, megaloblastic anaemia, iron deficiency anaemia, idiopathic thrombocytopenic purpura, erythroid hyperplasia accounted for 22.2% of cases diagnosed by BME in this study. Normal marrow cellularity was recorded in 11.5% and secondary metastasis to bone marrow was seen in 1.6% of cases (Table 2 shows the distribution of the various haematological disorders which were diagnosed by BME during the study period.

The leukemias (acute and chronic leukemias) were the commonest malignant condition diagnosed by BMA in our study, constituting 37.8% of cases. The lymphoma cases (NHL, Hodgkins diseases and Burkitt's lymphoma) were 59 (11.9%) and multiple myeloma (11.5%). The non malignant haematological disorders which were diagnosed by BME include Megaloblastic anaemia (6.3%), Aplastic anaemia (5.8%), Idiopathic thrombocytopenic purpura (3.0%),

Table 2: showing the distribution and frequency of Haematological disorders which were diagnosed by Bone marrow examination during the study period.

Diagnosis	Sex distribution		Total number	%
	Male	Female		
Acute myeloid leukemia (AML)	24	22	46	9.3
Acute lymphoblasticleukemia (ALL)	32	21	53	10.7
Chronic myeloid leukemia (CML)	22	27	49	9.9
Chronic lymphocytic leukemia (CLL)	23	16	39	7.9
Multiple myeloma (MM)	30	27	57	11.5
Non Hodgkin's lymphoma (NHL)	27	24	51	10.3
Hodgkin's lymphoma (HL)	3	1	4	0.8
Burkitt's lymphoma (BL)	2	2	4	0.8
Myelodysplastic syndrome (MDS)	7	7	14	2.8
Essential thrombocythemia (ET)	1	1	2	0.4
Polycythemia vera (PV)	1	1	2	0.4
Myelofibrosis (MF)	1	0	1	0.2
Hairy cell leukemia (HCL)	1	0	1	0.2
Aplastic anaemia (AA)	19	10	29	5.8
Megaloblastic anaemia (MBA)	17	14	31	6.3
Iron deficiency anaemia (IDA)	4	2	6	1.2
Autoimmune haemolytic anaemia (AIHA)	5	2	7	1.4
Idiopathic Thrombocytopenic purpura (ITP)	5	10	15	3.0
Erythroid hyperplasia	12	10	22	4.4
Secondary metastasis to bone marrow	5	3	8	1.6
Normal marrow	35	20	55	11.1
Total	276	220	496	100

Table 3: Cellularity of Bone marrow aspirates in study patients who had Bone marrow examination during the study period.

Bone marrow cellularity	No. of cases	Percentage (%)
Normocellular	55	11.1
Hypocellular	38	7.7
Hypercellular	403	81.3
Total	496	100

Erythroid hyperplasia (3.0%) and iron deficiency anaemia (1.2%). Table 2.

Discussion

A total of 496 bone marrow examinations were recorded in this study. There were 276 (58.5%) males and 220(44%) females with haematological disorders with a male:female ratio of 1.3:1. This observation was similar to those reported by Mangoch *et al*¹³ and Thiagarajan *et al*¹⁴ in their studies.

" this study the median age of the patients was 38.5years and the age at presentation ranged between 16 months to 85years. The mean age and age range of patients in our study was corroborated by the findings of Atchyuta *et al*¹⁵ which reported in their study a median age of 39.1 years and age range from 13 month to 83 years. Similar findings were also reported by Pudasani *et al*¹⁶ and Gayathri *et al*¹⁷.

The maximum number of patients who had BME was recorded in the age group 51-60years in our study. However, much lower age group at presentation was recorded by Mangoch *et al* and Anjum *et al* who reported 11-20 years and 21-30 years respectively^{13,18}.

In our study, the commonest clinical presentation necessitating bone marrow examination was unexplained anemia, occurring in 91.9% of cases, and was followed by fever of unknown origin which occurred in 79% of cases. Bone pains and back pains were found in 40.3% of patients while organ enlargement (lymph nodes, spleen and liver) occurred in 76.2% of patients. Similar observations were reported by Damulak OD *et al*⁸ in Jos, Nigeria, and Parajuli *et al*¹⁹ in Nepal. However, the finding in our study is at variance with the study of Bashawri in Saudi Arabia who reported peripheral pancytopenia as the commonest clinical indication for BMA in their study²⁰. The result of this study showed that acute leukemias were the most frequently encountered haematological disorder by bone marrow examination constituting 99 (20%) of cases studied. The number of acute lymphoblastic leukemia was 53(10.7%) while acute myeloid leukemia was 46(9.3%)s. The prevalence of acute leukemias was higher in males (n=59;59.6%) compared with females (n=40; 40.4%). Similar finding

Table 4: Presenting Clinical features in patients with Haematological diseases who had Bone marrow examination during the study period

Clinical Presentation	Frequency	Percentage(%)
Anaemia	456	91.9
Weakness	368	74.2
Fever	392	79.0
Bleeding	105	21.2
Bone pain	108	21.8
Back pain	46	9.3
Weight loss	154	31.0
Lymphadenopathy	106	21.4
Splenomegaly	187	37.7
Hepatomegaly	85	17.1
Intra abdominal masses	42	8.5
Jaw mass	8	1.6
High PCV	2	0.4

was reported by Shorsh *et al* in Iraq which found acute leukemias to be the most frequent diagnosis by bone marrow examination constituting 28.1% of patients in their study²¹. " another study by Ekwere *et al*²² in Uyo, Nigeria, acute leukemias were the commonest finding by bone marrow examination constituting 16.1% of the cases studied. However, our study was at variance with the report of Bedu-Addo *et al* in Ghana which reported acute leukemia as the fourth most common condition diagnosed by bone marrow examination in their study²³.

The second most common diagnosis in our study were the chronic leukemias made up of chronic myeloid leukemia (n=49, 9.9%) and chronic lymphocytic leukemia (n=39, 7.9%) and represented 17.7% of overall cases. Atchyuta *et al* also found chronic leukemias as the commonest malignant haematological disorder in their study¹⁵, CML being more common than CLL which is in agreement with the finding in our study but at variance with the study of Shorsh *et al*²¹ which reported CLL as the commonest chronic leukemia diagnosed by bone marrow examination in their study.

The incidence of haematological malignancies had been reported to be influenced by geographical location, socio-economic and nutritional factors as well as pattern of infections; and this could be a reason for the observed variation in the pattern of haematological malignancies diagnosed by BME in this study and other studies within Nigeria and elsewhere.^{10,24}

" our study, the malignant lymphomas (NHL, HL and BL) were the next in frequency, with NHL constituting the largest number (n=57, 86.4%) of the malignant lymphoma cases. Similar findings were reported by Mangoch *et al*¹³ from India and by Troussard *et al*²⁵ in France where NHL was reported as the most frequent malignant lymphoma encountered in

their studies. Other malignant haematological disorders which were diagnosed by bone marrow examination in our study, in descending order, were multiple myeloma (n=57; 11.5%), myelodysplastic syndrome (n=14; 2.8%), Essential thrombocytopenia (n=2; 0.4%), Polycythaemia vera (n=2; 0.4%) and Hairy cell leukaemia (n=1; 0.2%).

The incidence of multiple myeloma (MM) in our study (11.5%) was found to be higher than those reported in similar studies by Ekwere *et al* (8.1%) in Uyo, Nigeria²², Kibria *et al* (9.04%) in India³, and Shorsh *et al* (4.9%) in Iraq²¹. The higher percentage of MM diagnosed by bone marrow examination in our study may be explained by the larger number of multiple myeloma cases which were seen in our subjects compared to the other studies. However, the prevalence of MDS (2.8%) which was found in our study was much lower compared to 9.7% reported by Ekwere *et al*²².

" the evaluation for nutritional anaemias by bone marrow examination, megaloblastic anaemia was seen in 31(6.3%) of cases, while iron deficiency anaemia was recorded in only 6(1.2%) patients. This observation in our study is at variance with some studies which found iron deficiency anaemia to be most common nutritional anaemia in their studies^{22,26,27}.

" the present study, erythroid hyperplasia was found in 22 (4.4%) patients. This finding was much lower compared with studies done by Atchyuta *et al* (34%), Pudasani *et al* (21%) and Jha *et al* (19.6%) respectively^{15,16,28}.

Idiopathic thrombocytopenic purpura (ITP) was seen in 15 (3%) patients in our study. The diagnosis of ITP was made following exclusion of other causes of low platelet counts in the patients. The incidence of ITP in our study was found to be much lower when compared with the reports from other studies by Shorsh *et al* (8.6%)²¹, Pudasani *et al* (15.7%)¹⁶, Kibria *et al* (10.5%)³ and Khan TA *et al* (6.21%)²⁹. However, our finding was in agreement with the report of Atchyuta *et al*¹⁵ which found ITP in 17 (4.4%) of their subjects that had bone marrow examination done.

" our study, Aplastic anaemia was seen in 29 (5.8%) patients and corroborated the 3.7% which was reported by Awwalu *et al* in Zaria, Nigeria³⁰. However, this was much lower when compared with similar studies done by Kibria *et al*, Chowdhury *et al* and Sreedevi *et al* which reported 9.3%, 15.13 %, and 8% respectively^{3,31,32}.

Metastatic deposits from malignancies outside of the bone marrow were seen in 8 (1.6%) cases in the present study. Other authors which had reported cases of metastatic deposits in the bone marrow in their studies were Al- Ghazaly *et al* (0.96%)⁷, Kusum *et al* (1.4%)³³, Tasleem *et al* (2.5%)³⁴, and Mehdi *et al* (25%)³⁵.

Overall, in our study, bone marrow

examination was pathological in 441 (88.9%) patients while active normocellular marrow was seen in 55 (11.1%) patients. The findings from our study was comparable to the 9.8% of active bone marrow which was reported in Iraq by Shorsh *et al*²¹ but at variance with the report of Okinda *et al* in Kenya where a higher prevalence of 35.1% of active normal marrow was reported which was attributed to over induction of bone marrow examination even in cases with bicytopenia and mild anaemia³⁶.

Complications resulting from bone marrow examination such as haemorrhage and cellulitis at site of aspiration or biopsy were rarely encountered in our study and bone marrow examination was successfully carried out even in cases with low platelet counts without any serious bleeding. Similar observations were made by Shosh *et al*²¹ and Bain BJ³⁷ which were in support of bone marrow examination being a safe procedure even in the presence of thrombocytopenia.

Conclusion

" ne marrow examination, although, an invasive procedure is safe when performed by trained specialists, and remains an important tool in the armamentarium of Haematologists in the diagnosis of various malignant and non malignant haematological disorders. When a definitive diagnosis cannot be made from routine investigations such as complete blood counts and other peripheral blood indices, bone marrow studies can help to make a diagnosis, plan the treatment as well determine the prognosis and follow up of patients. " the present study, bone marrow examination was able to establish diagnosis in 88.9% of patients. This study has therefore shown that bone marrow examination is safe and still a useful tool which is important in the diagnosis and management of haematological malignancies as well as non- malignant haematological conditions.

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