A DESCRIPTIVE STUDY OF THE USE OF BONE MARROW BIOPSIES IN A PAEDIATRIC AND YOUNG ADULT POPULATION: A TERTIARY HOSPITAL EXPERIENCE

**ABSTRACT**

**Introduction**: Bone marrow biopsy is important in the management of both primary haematological disorders and non-haematological disorders of the bone marrow. These disorders could be non-neoplastic, bone marrow infiltrative lesions or primary neoplastic disorders of the bone marrow.

**Aim:**To establish the role of bone marrow biopsy in the management of haematological and non–haematological disorders in paediatric population.

**Materials and Methods:**This is a descriptive cross sectional study, spanning from January 2017 to November 2023. All consecutive bone marrow biopsy samples of children within the study period were included in this study.

**Results:**During the study period, January 2020 to December 2023, a total of 40 bone marrow biopsies were done in paediatric patients 18years and below. Suspected acute leukaemiawas the most common indication. The commonest histological diagnosis was acute lymphoblastic leukaemia followed by aplastic anaemia.All the bone marrow biopsies submitted for histology had pathological diagnoses. There was 90% concordance between bone marrow biopsy and bone marrow aspirate. The diagnostic utility was 100%.

**Conclusion:** Bone marrow biopsy is safe in children and the uptake should be encouraged among physicians to aid patient management.

**Key words**: Anaemia, bone marrow, biopsy, haematological, neoplastic, paediatrics,

**INTRODUCTION**

The bone marrow occupies the interstices within bone.1 It is the site of myeloid, erythroid and megakaryocytic as well as lymphoid cell development.2,3,4It is one of the largest organs in the human body.Involvement of bone marrow in disease processes can lead to reduction or excess production of different blood cell lines. This can manifest as anaemia, thrombocytopenia, leucopenia, polycythemia, thrombocythaemia, leucocytosis or various combinations of these. This requires that physicians should in the course of patientmanagement thoroughly evaluate patients with a view to ensuring that bone marrow biopsy is taken when necessary.

Bone marrow cellularity and site of haemopoietic cell production changes throughout life. At birth, haemopoiesis is distributed throughout the human skeleton but it gradually recedes with time so that in normal adult life haemopoiesis found mainly in the sternum and pelvis.5,6. There is in fact an inverse relationship between cellularity and age. The rule of thumb to give the expected normal percentage cellularity for an individual is 100 minus age (100-age).6In the neonate, the marrows of all bones are involved in blood cell production with a cellularity of about 100% while in older children, most bones are still involved but with a lower cellularity of about 70%.5

Bone marrow biopsy is important in evaluating both primary haematological disorders and non-haematological disorders of the bone marrow. These disorders could be non-neoplastic such as anaemia, pancytopenia, and bone marrow infiltrative lesions or neoplastic disorders. The posterior superior iliac spine is the most commonly used site for bone marrow biopsy though the medial surface of the tibia can be used in infants.7

Bone marrow biopsy (BMB) and Bone marrow aspirate are complementary to each other and should be performed together for better evaluation of the bone marrow.8.9The final interpretation requires the integration of the full blood count profile assessment, peripheral blood film findings, bone marrow aspirate and trephine biopsy findings

**AIM**

To establish the role of bone marrow biopsy in the management of haematological and non–haematological disorders in paediatric population.

**OBJECTIVES**

1. To itemize the specific indications for bone marrow biopsies in paediatric population
2. To describe the range of diagnoses made from bone marrow biopsies and BMAs and to correlate these diagnoses where both were carried out at the same instance in the same patient.
3. To determine the diagnostic utility of the bone marrow biopsy procedure in patient management in paediatric population

**MATERIALS AND METHODS**

**Study design**

This is a descriptive cross sectional study, spanning from January 2020 to November 2023. All consecutive bone marrow biopsy samples submitted to the department of Anatomical Pathology Department University of PortHarcourt Teaching Hospital (UPTH) within the study period were included in this study. The age range of the patients was 0-18years. These bone marrow samples were obtained from patients attending the clinics of the Haemotology and Blood Transfusion Department UPTH and in whom bone marrow biopsies were indicated as part of their management. As a standard institutional requirement, informed consent had been obtained by the operatinghaematologists when the biopsies were taken. Both bone marrow aspiration and biopsies weretaken by the haematologistat the same instance, in those cases where BMAs were done in addition to the BMB.

**RESULT**

During the study period, January 2020 to December 2023, a total of 40 bone marrow biopsies were done in paediatric patients 18years and below. The youngest age was 15months while the upper age limit adopted in this study was 18years. The mean age was 9.88years. Of these 40 patients, 21 were males and 19 females with a Male:Female ratio of 1.1:1. Twenty of these were between 0 to 9years and twenty between 10- 18 years (Table 1). The youngest were two patients of 15months of age.

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| --- |
| **Table 1- Age \* sex cross tabulation** |
| Count  |
|  | SEX | Total |
| Female | Male |
| AGE | 0-12months | 0 | 0 | 0 |
| >12months -4yrs | 6 | 4 | 10 |
| 5yrs-9yrs | 6 | 4 | 10 |
| 10yrs to 14yrs | 4 | 7 | 11 |
| ≥15y | 3 | 6 | 9 |
| Total | 19 | 21 | 40 |

Bone marrow aspiration and bone marrow biopsy were performed simultaneously for various indications (Table 2). Suspected acute leukaemia was the most common indication (14patients) followed by 9 patients each that presented with pancytopenia and chronic anaemia. A patient each was biopsied for suspected aplastic anaemia. Worthy of note were two girls aged 11 and 19 years being managed for chronic myeloid leukaemia who were now suspected to be in the accelerated and blast phase respectively.

|  |
| --- |
| **Table 2- Indication \* age Cross tabulation** |
| Count  |
|  | AGE | Total |
| 0-9 | 10-19y |
| INDICATION | AA | 0 | 1 | 1 |
| AL | 8 | 6 | 14 |
| CA | 4 | 5 | 9 |
| CML | 0 | 2 | 2 |
| LPN | 2 | 3 | 5 |
| PCT | 6 | 3 | 9 |
| Total | 20 | 20 | 40 |

Key AA- aplastic anaemia, AL- acute leukaemia, CA- chronic anaemia, CML- chronic myeloid leukaemia, LPN- lymphoproliferative neoplasm, PCT- Pancytopenia

Of the 40 patients biopsied, 16 had pancytopenia (Table 3). Eleven patients had derangement in two cell lines; 5 had isolated anaemia while a patient had normal full blood count. Seven patients had isolated leucocytosis. However 39 of the patients had anaemia alone or in combination with other cell line derangements (Table 4). Thirteen patients had leukocytosis, 17 had leucopenia while 10 patients had their white blood cell counts within the normal range (Table 5). Twenty-seven patients had reduced platelet count, two had thrombocytosis while 11 had their within normal expected values (Table 6).

|  |  |  |
| --- | --- | --- |
|  |  | **Table 3- AGE \* Full blood count \* agecross tabulation** |
|  |  | Count  |
|  |  |  | FBC |  |
| BCT | LCT | NOR | PCT | ANA | TOTAL |
| AGE | 0-9 | 4 | 5 | 1 | 9 | 1 | 20 |
| 10-19y | 7 | 2 | 0 | 7 | 4 | 20 |
| Total | 11 | 7 | 1 | 16 | 5 | 40 |
| BCT- bicytopenia, LCT- leucocytosis, NOR- normal full blood count, PCT- pancytopenia, ANA- anaemia**Table 4- Red blood cell \* SEX crosstabulation** |
| Count  |
|  | SEX | Total |
| Female | Male |
| RBC | Normal | 1 | 0 | 1 |
| Reduced | 18 | 21 | 39 |
| Total | 19 | 21 | 40 |

|  |
| --- |
| **Table 5- White blood cell \* SEX cross tabulation** |
| Count  |
|  | SEX | Total |
| Female | Male |
| WBC | Increased | 8 | 5 | 13 |
| Normal | 4 | 6 | 10 |
| Reduced | 7 | 10 | 17 |
| Total | 19 | 21 | 40 |

|  |
| --- |
| **Table 6- Platelets \* Sexcross tabulation** |
| Count  |
|  | SEX | Total |
| Female | Male |
| PLATELETS | Increased | 1 | 1 | 2 |
| Normal | 4 | 7 | 11 |
| Reduced | 14 | 13 | 27 |
| Total | 19 | 21 | 40 |

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| **Chi-Square Tests** |
|  | Value | df | Asymptotic Significance (2-sided) |
| Pearson Chi-Square | 10.526a | 11 | .484 |
| Likelihood Ratio | 13.681 | 11 | .251 |
| N of Valid Cases | 40 |  |  |
| a. 22 cells (91.7%) have expected count less than 5. The minimum expected count is .50. |

Various histological diagnoses were made (Table 7). The commonest was acute lymphoblastic leukaemia (12patients) which had an equal sex distribution with 8 patients less than 10years (Table 8). Eight patients (the second commonest) were diagnosed histologically of aplastic anaemia (figure 1), of which five were less than 10years and five were females. Acute myeloid leukaemia (figures 2 and 3) was diagnosed in 4 patients of which 3 were males and three were 10 years and above. Erythroid hyperplasia was diagnosed in 3 patients. Two patients were diagnosed of chronic myeloid leukaemia with one in accelerated phase and the other in blast phase. Two patientswere also diagnosed of megaloblastic anaemia. Other sundry diagnoses with a patient each were chronic osteomyelitis, hypoproliferativeanaemia, lymphoproliferative neoplasm with bone marrow involvement, neutrophilic hyperplasia and megakaryocytic suppression.

Table 7- Bone marrow biopsy diagnoses

|  |
| --- |
| **Crosstab** |
| Count  |
|  | SEX | Total |
| Female | Male |
| BMB | AA | 5 | 3 | 8 |
| ALL | 6 | 6 | 12 |
| AML | 1 | 3 | 4 |
| CML | 2 | 0 | 2 |
| CO | 0 | 1 | 1 |
| ERH | 1 | 2 | 3 |
| HPA | 2 | 2 | 4 |
| LPN | 0 | 1 | 1 |
| MBD | 1 | 1 | 2 |
| MGA | 0 | 1 | 1 |
| MGS | 1 | 0 | 1 |
| NH | 0 | 1 | 1 |
| Total | 19 | 21 | 40 |

AA- aplastic anaemia, ALL- acute lymphoblastic leukaemia, AML- acute myeloblastic leukaemia, CML- chronic myelocytic leukaemia, ERH- erythroid hyperplasia, HPA- hypoproliferativeanaemia, LPN- lymphoproliferative neoplasm infiltration of the marrow, MBD- metastatic bone marrow disease, MGA- megaloblastic anaemia, MGS- megakaryocytic suppression, NH- neutrophilic hyperplasia

Table 8- Bone marrow biopsy diagnoses by age

|  |
| --- |
|  |
| Count  |
|  | AGE | Total |
| 0-9 | 10-19y |
| BMB | AA | 5 | 3 | 8 |
| ALL | 8 | 4 | 12 |
| AML | 1 | 3 | 4 |
| CML | 0 | 2 | 2 |
| CO | 1 | 0 | 1 |
| ERH | 2 | 1 | 3 |
| HPA | 2 | 2 | 4 |
| LDB | 0 | 1 | 1 |
| MBD | 0 | 2 | 2 |
| MGA | 0 | 1 | 1 |
| MGS | 1 | 0 | 1 |
| NH | 0 | 1 | 1 |
| Total | 20 | 20 | 40 |

AA- aplastic anaemia, ALL- acute lymphoblastic leukaemia, AML- acute myeloblastic leukaemia, CML- chronic myelocytic leukaemia, ERH- erythroid hyperplasia, HPA- hypoproliferativeanaemia, LPN- lymphoproliferative neoplasm infiltration of the marrow, MBD- metastatic bone marrow disease, MGA- megaloblastic anaemia, MGS- megakaryocytic suppression, NH- neutrophilic hyperplasia

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Figure 1: Photomicrograph of low power haematoxylin and eosin stained bone marrow diagnosis of aplastic anaemia (X40)

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Figure 2: Photomicrograph of haematoxylin and eosin stained sections of acute myeloid leukaemia showing numerous dysplastic myeloblasts replacing the marrow spaces (X100).



Figure 3: Photomicrograph of Giemsa stained sections of acute myeloid leukaemia showing numerous dysplastic myeloblasts replacing the marrow spaces (X400).

Of the 16 patients with pancytopenia, 7 were diagnosed of aplastic anaemia, 5 were diagnosed of acute lymphocytic leukaemia, 3 of acute myeloid leukaemia and one of megaloblastic anaemia (Table 9). Of the 10 with derangement in two cell lines, 4 were diagnosed of acute lymphocytic leukaemia, two of hypoproliferativeanaemia and a patient each was diagnosed of neutrophilic hyperplasia, megakaryocytic suppression, metastatic bone disease, lymphoproliferative neoplasm with bone marrow involvement, and aplastic anaemia. Seven patients had isolated leukocytosis of which the bone marrow diagnoses of 4 were acute lymphocytic leukaemia, two were chronic myeloid lymphocytic, and one was chronic osteomyelitis. The full blood count values statistically affect bone marrow biopsy histological diagnoses (Table 10)

Table 9- Bone marrow biopsy diagnoses cross tabulated with the full blood count

|  |  |  |
| --- | --- | --- |
|  | FBC |  |
| BCT | LCT | NOR | PCT | ANA | TOTAL |
| BMB | AA | 1 | 0 | 0 | 7 | 0 | 8 |
| ALL | 4 | 4 | 0 | 5 | 0 | 12 |
| AML | 0 | 0 | 0 | 3 | 1 | 4 |
| CML | 0 | 2 | 0 | 0 | 0 | 2 |
| CO | 0 | 1 | 0 | 0 | 0 | 1 |
| ERH | 0 | 0 | 1 | 0 | 2 | 3 |
| HPA | 2 | 0 | 0 | 0 | 2 | 4 |
| LPN | 1 | 0 | 0 | 0 | 0 | 1 |
| MBD | 1 | 0 | 0 | 0 | 1 | 2 |
| MGA | 0 | 0 | 0 | 1 | 0 | 1 |
| MGS | 1 | 0 | 0 | 0 | 0 | 1 |
| NH | 1 | 0 | 0 | 0 | 0 | 1 |
| Total | 10 | 7 | 1 | 16 | 6 | 40 |
| AA- aplastic anaemia, ALL- acute lymphoblastic leukaemia, AML- acute myeloblastic leukaemia, CML- chronic myelocytic leukaemia, ERH- erythroid hyperplasia, HPA- hypoproliferativeanaemia, LPN- lymphoproliferative neoplasm infiltration of the marrow, MBD- metastatic bone marrow disease, MGA- megaloblastic anaemia, MGS- megakaryocytic suppression, NH- neutrophilic hyperplasia  |
| **Chi-Square Tests** |
|  | Value | df | Asymptotic Significance (2-sided) |
| Pearson Chi-Square | 109.030a | 77 | .010 |
| Likelihood Ratio | 81.653 | 77 | .337 |
| N of Valid Cases | 40 |  |  |
| a. 96 cells (100.0%) have expected count less than 5. The minimum expected count is .03. |

The 40 bone marrow biopsies were done concurrently with bone marrow aspirates. There was 92% concordance in the diagnoses of acute lymphocytic leukaemia with zero concordance in chronic osteomyelitis and metastatic bone marrow disease. Other diagnoses had concordance of 100%.

|  |  |
| --- | --- |
| **Table 10 :BMB/BMA concordance** |  |
|  |  |
|  | **BMA** | Total |  |
|  | AA | ALL | AML | CML | ERH | HPA | LDB | MGA | MGS | NH | CR (%) |
| **BMB** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| AA |  | 8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 100 |
| ALL |  | 0 | 11 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 12 | 92 |
| AML |  | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 100 |
| CML |  | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 100 |
| CO |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| ERH |  | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 3 | 100 |
| HPA |  | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 4 | 100 |
| LDB |  | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 100 |
| MBD |  | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 2 | 0 |
| MGA |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 100 |
| MGS |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 100 |
| NH |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 100 |
| Total |  | 8 | 13 | 3 | 2 | 3 | 6 | 1 | 1 | 1 | 2 | 40 |  |

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|  |
|  | **INDICATION \* BMB crosstabulation**BMB | Total |
| AA | ALL | AML | CML | CO | ERH | HPA | LDB | MBD | MGA | MGS | NH |
| INDICATION | AA | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| AL | 0 | 10 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 13 |
| BCT | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| CA | 0 | 0 | 1 | 0 | 0 | 1 | 4 | 0 | 0 | 1 | 1 | 0 | 8 |
| CML | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| LD | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 0 | 1 | 6 |
| PCT | 7 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 10 |
| Total | 8 | 13 | 4 | 2 | 1 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 40 |

The areas of discordance between bone marrow biopsy and bone marrow aspiration diagnoses were in the two cases metastatic bone marrow disease in which BMA did not see the foreign cells and so reported it as hypoproliferativeanaemia. There was a case of acute myeloid leukaemia in an 8 year old female that was wrongly diagnosed as acute lymphocytic leukaemia in the bone marrow biopsy.

All the bone marrow biopsies submitted for histology had pathological diagnoses. These gave a diagnostic utility of 100%

Table 11: Diagnostic discordance between BMB and BMA

|  |  |  |
| --- | --- | --- |
| **BMB DIAGNOSIS** | **BMA DIAGNOSIS** | **GOLD STANDARD** |
| MBD | HA | BMB |
| ALL | AML | BMA |

MBD = Metastatic bone marrow disease; AML = Acute myeloid leukemia; ALL = Acute lymphoblastic leukaemia; HA = Hypoprolifrativeanaemia;

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Table 12: The Diagnostic Utility of BMB (Children)

|  |  |  |
| --- | --- | --- |
|  | Frequency | Percept (%) |
| **NORMAL BONE MARROW** | **0** | **0** |
| **INADEQUATE BONE MARROW SAMPLE** | **0** | **0** |
| **PATHOLOGICAL DIAGNOSES** | **40** | **100** |
| Total | 40 | 100.0 |

**DISCUSSION AND CONCLUSION**

During the study period, January 2020 to December 2023, a total of 40 bone marrow biopsies were done in paediatric patients. This is due to the poor intake among clinicians on the importance of bone marrow biopsy in management of patients. The youngest age seen in this study was 15months in while the upper age limit adopted in this study was 19years. Other studies showed lower age limits in infancy 10,11,12. This shows that infants can tolerate BMB ifperformed by experienced and qualified doctors.

Suspected acute leukaemia was the most common indication (14patients) followed by 9 patients each that presented with pancytopenia and chronic anaemia. Lalita*et.al* had the commonest indication as chronic anaemia10 while Balasubramanian*et.al* had the commonest indication as cytopenias.12 All the patients suspected to have acute leukaemia were anaemic, 7 had increased leucocyte count, 5 had reduced leucocyte count and 1 had a normal leucocyte count. However, 6 patients had normal platelet count and 7 had thrombocytopenia. This indicated that not all patients with acute leukaemia will have leukocytosis and thrombocytopenia. The peripheral blood smear must be examined for abnormal or increased blasts although we know that cases of aleukemic leukaemia do exist.13 The 13 patients suspected of having acute leukaemia had a bone marrow diagnosis of acute leukaemia (lymphoblastic or myeloblastic). Marrow examination is thus important in aiding the diagnosis of acute leukaemia.

The commonest bone marrow biopsy histological diagnosis in this study was acute lymphoblastic leukaemia (12patients) which had an equal sex distribution with 8 patients less than 10years. The second commonest was aplastic anaemia. Acute myeloid leukaemia was diagnosed in 4 patients of which 3 were 10 years and above. This corresponds with other studies that observed the commonest bone marrow diagnosis in children to be acute lymphoblastic leukaemia.11,14,15

Chronic myeloid leukaemia (CML) is usually not a diagnosis that should be made on bone marrow but it can be used to examine CML patients suspected to have transformation9. Worthy of note were two girls aged 11 and 19 years being managed for chronic myeloid leukaemia who were now suspected to be in the accelerated and blast phase respectively. These suspicions were confirmed on bone marrow biopsy examination.

The 40 bone marrow biopsies were done concurrently with bone marrow aspirates. There was 90% concordance between BMA and BMB. Gilotra*et al*. had concordance rate of 87%.16 Lower rates were seen in other studies; Das et al had a concordance rate of 77.18%17,Aljadayeh*et al*. was 76.2%18, Khan *et al*. was of 73.8%.19There was 92% concordance in the diagnoses of acute lymphocytic leukaemia with zero concordance in chronic osteomyelitis and metastatic bone marrow disease. Other diagnoses had concordance of 100%.The areas of discordance between bone marrow biopsy and bone marrow aspiration diagnoses were in the two cases metastatic bone marrow disease in which BMA did not see the foreign cells and so reported it as hypoproliferativeanaemia. Metastatic deposits appear in foci in many cases, which could make the BMA unable to see the metastatic cells sometimes. There was a case of acute myeloid leukaemia in an 8 year old female that was wrongly diagnosed as acute lymphocytic leukaemia in the bone marrow biopsy. This is because BMA gives a better view of cellular morphology than BMB hence the need to correlate the two.

All the bone marrow biopsies submitted for histology had pathological diagnoses. These gave a diagnostic utility of 100%( Diagnostic utility reviews how many of the BMBs that came out with a definitive pathological diagnosis)20.The 100% diagnostic utility shows how important BMB is in the management of ill children.

Ethical Approval:

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent.

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