

# Bone Marrow Procedures in Children Welfare Teaching Hospital/Medical City Complex Indications and results

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## Summary:

**Background:** Bone marrow aspiration (BMA) and biopsy is a procedure that is used to evaluate the cause of abnormal blood test results, to confirm a diagnosis or check the status of severe anemia of unknown cause, to evaluate abnormalities in the blood's ability to store iron and also to diagnose infection.

**Objectives:** To identify the main indications of bone marrow aspiration and the most common diagnoses encountered in children welfare teaching hospital.

**Patients and methods:** This was a prospective and retrospective descriptive study over 6- month period from 8th of February 2010 to 8th of August 2010 in children younger than 14 years. All bone marrow aspirate results were reviewed. The clinical data provided by clinicians were also noted. General Anesthesia was used in (439) patients, and local anesthesia was used in (321) patients. The procedure done under aseptic technique, aspiration sampling was generally performed before biopsy; the site of aspirate usually from the posterior iliac crest except for those less than 12 months where the tibia was the preferable site of aspiration

**Results:** There were a total of 757 performed bone marrow aspirations. The main indications for bone marrow examination were the following: 256 (34%) for diagnosis and follow up of leukemia, 154 (20%) for evaluation of fever of unknown origin, 95 (13%) for evaluation of hepatosplenomegaly, lymphadenopathy and or pallor, 54 (7%) for evaluation of solid tumors, 49 (6%) for evaluation of thrombocytopenia, 48 (6%) for evaluation of pancytopenia, 36 (5%) for evaluation of lymphoma, 29 (4%) for suspected storage or metabolic diseases, 21 (3%) for evaluation of undiagnosed masses in the abdomen, mediastinum, neck and jaw; 12 (1.6%) for evaluation of unexplained anemia, 3 (0.4%) for others. The most common results reported were: 312 (65%) normal BMA, 71 (14.5%) acute leukemia, 17 (3%) marrow involvement by malignancy (solid tumors, Non-Hodgkin Lymphoma), 8 (2%) megaloblastic anemia, 8 (2%) erythropoietic hyperplasia, 8 (2%) proliferation of reactive histiocytes with active hemophagocytosis, 4 (1%) kala azar.

**Conclusions:** The most common indication for this procedure in this hospital was to confirm diagnosis and follow up of acute leukemia. There is high rate of negative bone marrow examination which is unnecessarily done due to lack of further diagnostic facilities, also a high rate of non-informative results which might reflect inadequate experience of doctors performing the procedure. No complications were reported.

**Key words:** Bone Marrow Aspirate, Children, Welfare Teaching Hospital, indications

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## Introduction:

The procedure known as trepanning, or trephination, of bone is the oldest surgical practice that continues to have clinical relevance in modern times. The method dates as far back as the Neolithic period and initially entailed the drilling of cranial bones as a form of medical intervention for headaches and mental illnesses; however it was not until 1905, when the Italian physician Pianese reported bone marrow infiltration by the parasite *Leishmania*, that this procedure was applied toward clinical evaluation.(1)

In the present day, inspection of the bone marrow is considered one of the most valuable diagnostic tools to evaluate hematologic disorders.(2) Indications have included the diagnosis, staging, and therapeutic monitoring for lymphoproliferative and myeloproliferative disorders. Furthermore, evaluation of cytopenia, thrombocytosis, leukocytosis, anemia, and iron status can be performed.

The application of bone marrow analysis has grown to incorporate other non-hematologic conditions. For example, in the investigation for fever of unknown origin (FUO), specifically in those patients with acquired immune deficiency syndrome (AIDS), the marrow may reveal the presence of microorganisms, such as tuberculosis, *Mycobacterium avium* intracellular (MAI) infections, Histoplasmosis, Leishmaniasis,

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and other disseminated fungal infections, furthermore; the diagnosis of storage diseases (e.g. Niemann Pick disease and Gaucher disease), as well as the assessment for metastatic carcinoma and granulomatous diseases (e.g. Sarcoidosis) can be performed.

Bone marrow analysis can also be performed in patients with idiopathic thrombocytopenia purpura (ITP), iron deficiency anemia, B12/folate deficiency, Polycythemia Vera, or infectious mononucleosis; but these conditions are more appropriately diagnosed by routine laboratory.(3)

Sampling of the marrow consists of either aspiration of the cellular component and/or acquirement of tissue fragments. Aspiration of the marrow has been primarily utilized for cytological assessment, with analysis directed toward morphology and obtainment of a differential cell count. Further sampling allows for material to be directed toward other ancillary test such as cytogenetics, molecular studies, microbiologic cultures, immunohistochemistry, and flow cytometry. Biopsies, on the other hand, allow for studies of the marrow's overall cellularity, detection of focal lesions, and extent of infiltration by various pathologic entities. (4, 5)

The objective of this study is to review the profile of bone marrow procedures done as part of clinical evaluation in children admitted to children welfare teaching hospital, its indications and the most common results that were obtained.

**Patients and Methods**

Over 6 months period, from 8th of February 2010 to 8th of August 2010 a prospective and retrospective descriptive study was done for (598) children younger than 14 years of age who were admitted to the pediatric oncology unit or general wards in Children Welfare Teaching Hospital and enrolled for the study, 4 patients were seen in the pediatric out-patients clinic. The information regarding the age, sex, clinical presentation, indications, type of anesthesia, volume of aspirated bone marrow, date of bone marrow aspiration & its result, were taken from the wards records and reports of bone marrow in the hematology department of the teaching laboratories.

Patient's age from 1 day-14 years; admitted to Children Welfare Teaching Hospital or seen at an outpatient clinic for whom bone marrow aspirate was done; were included in this study.

The non-informative bone marrow results and blood taps were excluded from the study.

General Anesthesia was used in (439) patients, and local anesthesia was used in (321) patients. The procedure done under aseptic technique, aspiration sampling was generally performed before biopsy; the site of aspirate usually from the posterior iliac crest except for those less than 12 months where the tibia was the preferable site of aspiration.

A 10 ml (or 20 ml) syringe was used to aspirate approximately

0.2 ml placed in an EDTA anticoagulant – containing tube.

Procedure usually done either, by the resident doctors or the most senior fellow in the unit for the difficult cases or first intrathecal therapy & CSF cytopsin in newly diagnosed cases of cancer Microsoft excel program was used for data analysis.

**Results**

The number of patients were (598), and number of BMA done were 757 , the BMA were repeated for 159 patients either because of inadequate results or for further follow up in patients with malignancies on chemotherapy.

From 598 cases included in the study, 372 cases were males (62%) and 226 were females (38%), male: female ratio was 1.6:1, as shown in table (1).

General anesthesia was used in 436 (58%), and local anesthesia was used in 321 (42%). Regarding information in the request form, from 757 BMA, 603 (80%) of requests were adequate and 154 (20%) inadequate information. From 757 BMA results, 479 (63%) BMA were informative cellular BM, 144 (19%) blood tap and not informative, 134 (18%) diluted with some details about cellularity as shown in table (2).

The main indications of BMA were distributed as follow: 256 (34%) BMA for diagnosis and follow up of leukemia ,154 (20%) for evaluation of fever of unknown origin,95 (13%) for evaluation of hepatosplenomegaly / lymphadenopathy and/or pallor, 54 (7%) for evaluation of solid tumors , 49 (6%) for evaluation of thrombocytopenia,48 (6%) for evaluation of pancytopenia,36 (5%) for evaluation of lymphoma, 29 (4%) for suspected storage or metabolic diseases, 21(3%) for evaluation of undiagnosed masses in the abdomen, mediastinum,neck, and jaw;12 (1.6%) for evaluation of unexplained anemia,3 (0.4%) for others as shown in table(3).

The common results obtained after exclusion of non-informative B.M and blood taps are : 312 (65%) normal BMA, 71 (14.5%) acute leukemia, 17 (3%) marrow involvement by malignancy (solid tumor, NHL) , 8 (2%) megaloblastic anemia, 8 (2%) erythropoietic hyperplasia , 8 (2%) proliferation of reactive histiocytes with active hemophagocytosis , 4 (1%) kala azar, 4 (1%) suspected metabolic or storage disease , 3 (0.5%) combined deficiency anemia, 44 (9%) others as shown in table (4).

**Table (1): Sex distribution of 598 patients**

sex	Number	%
Male	372	62
Female	226	38
<b>Total</b>	<b>598</b>	<b>100</b>

Male: female 1.6:1

Table(2):BMA procedure data

Types of anesthesia		
	Number	%
General anesthesia	436	58
Local	321	42
Information in the request form		
Adequate	603	80
Inadequate	154	20
BMA cellularity		
Informative , cellular	479	63
Not informative, blood tap	144	19
Diluted with some details	134	18

Table (3): Indications of BMA

Indications	Number	%
Diagnosis and follow up of leukemia	256	34
Evaluation of fever of unknown origin	154	20
Evaluation of hepato-splenomegaly, lymphadenopathy, pallor	95	13
Evaluation of solid tumor	54	7
Evaluation of thrombocytopenia	49	6
Evaluation of pancytopenia	48	6
Evaluation of lymphoma	36	5
Suspected storage and metabolic diseases	29	4
Evaluation of undiagnosed masses(abdominal,mediastinal,cervical)	21	3
Evaluation of unexplained anemia	12	1.6
Others ( referred as per specialist request from endocrine, gastrointestinal, neurology and renal units)	3	0.4
Total	757	100

Table (4) Main results obtained from 479 informative BM

Results	Number	%
Normal bone marrow	312	65
Acute leukemia	71	14.5
Marrow involvement by malignancy (Non-Hodgkin Lymphoma,solid tumor)	17	3
Megaloblastic anemia	8	2
Erythropoitic hyperplasia	8	2
Proliferation of reactive histiocytes with active hemophagocytosis	8	2
Kala azar ( Leishman Donovan bodies)	4	1
Suspected metabolic or storage diseases	4	1
Combined deficiency anemia	3	0.5
Others ( referred as per specialist request from endocrine, gastrointestinal, neurology and renal units)	44	9
Total	479	100

### Discussion:

The spectrum of hematological disorders in children is very wide. Bone marrow examination is a useful test in reaching the final diagnosis.It is one of the most common and safe procedures in medical practice.Rarely infection, excessive bleeding or embolism has been reported after bone marrow procedures. (6)

In the current study, male: female ratio is 1.6:1, which is nearly similar to that mentioned in Githang study in Kenya 2001 in which the ratio was 1.5:1 (7), but it is different from that mentioned in Mukiibi JM study in Zimbabwe 1989, in which the ratio was 1.1:1(8).

In spite of the fact that general anesthesia was used in 58% of the patients, yet there was no fully adherence to the published guidelines on childhood sedation, this is in agreement with a study done by C. Barnes et al.(9)

From 757 BMA (63%) were informative aspirate and (37%) BMA were not informative and diluted marrow which is comparable to that mentioned in Naznin study in Kuantan 2002 in which (58%) of aspirate were informative and (42%) of aspirates were inadequate (10), this indicate the need for performance of the procedure by well experienced doctors for obtaining informative results and avoiding overburden of samples on laboratory personnel specially in setting with limited human and technical resources.

The most frequent indication of BMA in the current study is the diagnosis and follow up of leukemia which is similar to that mentioned in Bashawri LA study in Saudi Arabia 2002(11). The second indication is evaluation of fever of unknown origin which is different from that mentioned in Bashawri LA study in Saudi Arabia 2002 (11) in which it was the sixth indication, while in Githang study in Kenya 2001(7) it was the seventh indication, may be due to shortage of diagnostic facilities in our setting mandating bone marrow studies.

The third indication is evaluation of hepatosplenomegaly/ lymphadenopathy and/or pallor, which is different from that mentioned in Githang study in Kenya 2001(7), and Bashawri LA study in Saudi Arabia 2002(10) in which it was the sixth and seventh indications respectively.

The fourth indication is evaluation of solid tumors; which was similar to that mentioned in Githang study in Kenya 2001(7).

The fifth indication is evaluation of thrombocytopenia, which is similar to that mentioned in Githang study in Kenya 2001(7), while it is different from that mentioned in Bashawri LA study in Saudi Arabia 2002(11) in which it was the fourth indication. The sixth indication is evaluation of pancytopenia, which is different from that mentioned in Bashawri LA study in Saudi Arabia 2002(11) in which it was the third indication.

The seventh indication is evaluation of lymphoma, in which is different from that mentioned in Bashawri LA study Saudi Arabia 2002 (11) and Githang study in Kenya 2001(7), in

which it was the third indication.

The most common result obtained in this study was negative BM (65%), this high rate of negative results indicates that the procedure is unnecessarily done may be due to lack of further diagnostic facilities for various pediatric diseases.

The most common disorder obtained was acute leukemia, as agreed with Bashawri LA study in Saudi Arabia 2002(11).

Second result is marrow involvement by malignancy (NHL, solid tumors) as agreed with Githang study in Kenya 2001(7).

Third result is megaloblastic anemia, which is different from that mentioned in Mukiibi JM study in Zimbabwe 1989(8) &Fazlur et al study in Pakistan 2005 in which it was the commonest finding (12), may be due to higher rate of nutritional deficiency in these areas and also different from that mentioned in Bashawri LA study in Saudi Arabia 2002(11) in which it was the seventh common finding.

In the current study, kala azar is detected only in 4(1%) aspirates, which is similar to that mentioned in Naveen et al study in Karachi 2007 (13). A study done by Fayzi et al (14) showed that bone marrow examination appeared to be valuable as a diagnostic procedure in 36.7% of cases, although it cannot be used for assessment of asymptomatic Kala azar.

The procedure was relatively safe as the study didn't report any complication which was comparable to Bain BJ study (4).

#### **Conclusions:**

Bone marrow examination is a very important investigation for establishing the diagnosis of many conditions, especially hematological neoplasms. The most common indication for this procedure in Children Welfare Teaching Hospital was to confirm and follow-up of acute leukemia which is the most common diagnosis. There is a high rate of negative bone marrow examination which is unnecessarily done due to lack of further diagnostic facilities, also high rate of non-informative results which might reflect inadequate experience of doctors performing the procedure. No complications were reported.

#### **Author's Contribution:**

Study Conception & design: Dr. Salma AL-Hadad & Dr. Mazin Al-jadiry

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#### **References:**

1. Parapia LA. Trepanning or trephines: a history of bone marrow biopsy. *Br J Haematol.* Oct 2007; 139(1):14-9.
2. Fend F, Tzankov A, Bink K, et al. Modern techniques for the diagnostic evaluation of the trephine bone marrow biopsy:

*methodological aspects and applications. Prog Histochem Cytochem.* 2008; 42(4):203-52.

3. Mazzella FM, Perrotta G. Peripheral blood and bone marrow. In: Schumacher HR, Rock WA, Stass SA, (eds). *Handbook of Hematologic Pathology.* New York, NY: Marcel Dekker, Inc.; 2000:1-26.

4. Bain BJ. Bone marrow trephine biopsy. *J Clin Pathol.* Oct 2001; 54(10):737-42.

5. Trewhitt KG. Bone marrow aspiration and biopsy: collection and interpretation. *Oncol Nurs Forum.* Oct 2001; 28(9):1409-15; quiz 1416-7.

6. Omal IK, Sumer H, Tufan A, Shorbagi A. Bone marrow embolism after marrow aspiration and biopsy. *Am J Hematol.* 2005;78(2):158.

7. Githang ' a JN, Dave P. Bone marrow examination at a pediatric hospital in Kenya. *East Afr Med J.* 2001; 78: S37-9.

8. Mukiibi JM, Paul B, Gordeuk VR. A prospective analysis of 620 bone marrow examinations in Zimbabwe: preliminary observations. *Cent Afr J Med.* 1989 June; 35(6): 416-9.

9. C. Barnes, P. Downie, G. Chakiadis, S. Camilleri, P. Monagle, K. Waters. Sedation practices for Australian and New Zealand Paediatric oncology patients. *Journal of Paediatrics and Child Health; Volume 38, Issue 2. April 2002; pages 170-172. (IVSL)*

10. Naznin M, Wahab AJ, Kalavathy R. A review of bone marrow examinations in Tengku Ampuan Afzan hospital. *Kuantan.* 2002; 4(1):1-8.

11. Bashawry LA, Bone marrow examination, Indications and diagnostic value. *Saudi Med J* 2002; 23:191-6.

12. Fazlur Rahim, Irshad ahmed, Saiful Islam, Muhammad Hussain, Taj Ali Khan, Qudsia Bano. Spectrum of hematological disorders in children observed in 424 consecutive bone marrow aspirations/ biopsies. *Pak J Med Sci.* 2005; 21(4):433-6.

13. Naveen Naz Syed, Bushra Moiz, Salman Naseem Adil, Mohammad Khurshid. Diagnostic importance of bone marrow examination in non-hematological disorders. *JPMA* 2007; 57:123-5.

14. Mohammad Ali Hosseinpour Fayzi, Leila Mehdizadeh Fanid, Abbass Ali Hosseinpour Fayzi, et al.: *Journal Biotechnology.* 2008; 7(2):175-181. (IVSL).