#### Bone marrow aspiration in north Sudan: the procedure, indications and the diagnostic value

# Wadie M Elmadhoun, <sup>(1)\*</sup> Sufian K Noor, <sup>(2)</sup> Sarra O Bushara, <sup>(2)</sup> Ahmed O Almobarak, <sup>(3)</sup> Nazik Elmalaika Husain, <sup>(4)</sup> Mohamed H Ahmed <sup>(5)</sup>

Department of of Pathology, Nile Valley University – Sudan <sup>(1)</sup> Department of Medicine, Nile Valley University – Sudan <sup>(2)</sup> Department of Pathology, University of Medical Sciences and Technology – Sudan <sup>(3)</sup> Department of Pathology, Omdurman Islamic University – Sudan <sup>(4)</sup> Department of Medicine, Milton Keynes University Hospital NHS Foundation Trust, Eaglestone, Milton Keynes, Buckinghamshire, UK <sup>(5)</sup>

#### Abstract

**Introduction:** Bone marrow aspiration (BMA) is a common and useful investigation tool in clinical practice to obtain information about both hematological and non-hematological disorders. The aim of the work was to identify the main indications for BMA in Atbara city, north Sudan and to determine the common diagnoses encountered.

**Methods:** All reports of BMA carried out during a 6-year period from 2009 to 2014, in the Modern Specialized Laboratory (the only site where BMA is conducted in Atbara) were reviewed. The information extracted included the main indications for performing this procedure, age groups involved, and the most common diagnoses established. A specially designed form was used for this purpose and the data were analyzed using SPSS computer program.

**Results:** A total number of 112 cases were subjected to bone marrow aspiration. The most frequent indications were: pancytopenia 43(38.4%), anemia 39 (34.8%), and suspected leukemia 13 (11.6%). In 86(76.8%) cases, BMA provided either the diagnosis or diagnostic clues to the disease process, while 26 (23.2%) of the aspirates revealed a normally functioning marrow.

**Conclusion:** Bone marrow aspiration is an important investigation for establishing the diagnosis in many medical conditions. The most common indication for this procedure in our study was pancytopenia and the most common finding was aplastic anemia.

Key words: Bone marrow aspiration, Atbara, Sudan.

Corresponding author:

Mohamed H Ahmed Department of Medicine, Milton Keynes University Hospital NHS Foundation Trust, Eaglestone, Milton Keynes, Buckinghamshire, UK Email: elziber@yahoo.com

# Introduction

Bone marrow aspiration is a useful investigation tool to help diagnose hematological non-hematological and disorders. <sup>(1,2)</sup> Hematological indications for this procedure include diagnosis, staging and follow-up of anemia, pancytopenia, lymphoproliferative disorders, lymphomas and many other conditions (Table 1). (3) Nonhematological disorders include pyrexia of unknown origin, granulomatous diseases, metastatic tumors and some inborn errors of metabolism. More sophisticated and ancillary techniques in which bone marrow aspiration is used include flow cytometry, genetic and chromosomal studies. (3) The procedure of bone marrow aspiration is cost-effective. technically simple for the experienced and is associated with minimal hazards when precautions are considered. (3)

We aimed by this work to describe our experience in Atbara, north Sudan with special emphasis on indications and findings of bone marrow examination.

# Material and methods

This was a descriptive retrospective laboratory-based study in which records of all patients underwent bone marrow aspiration in Atbara, during the period from 2009 to 2014 were retrieved and data extracted. The information obtained included the demographic data, the main indications for performing bone marrow examination and the most common diagnoses established. A special form was designed for this purpose in which data was displayed.

# The procedure of bone marrow aspiration and examination

In brief, the procedure consists of inserting a special needle into a bone and withdrawing the red marrow by suction or coring out a sample of the marrow to be examined microscopically. The steps of the procedure can be practically divided into:

## Pre-aspiration

Revised CBC and indication, check general condition of the patient (including examination of liver, spleen and lymph node groups), take patient consent, and ensure his/her comfort; patient lying of left side flexing right knee joint and extending left leg. Take universal infection precautions. Check that everything is ready and functioning: disinfectants, local anesthesia, well-fitting plastic syringe. Check the most prominent flat bone, the posterior superior iliac crest is most commonly chosen, but the anterior superior iliac crest may be easier in obese individuals or those with sacral edema.

# During aspiration

Patient assurance, explain what you are doing to patient, check your assistance preparedness, administer adequate local anesthetic in skin, subcutaneous tissue and periosteum, wait for a few minutes (2-5 is enough) till patients tell you that there is no pain at insertion site. Insert needle with its trochar, remove trochar once inside marrow and aspirate 0.3 – 1.0 ml. May need to repeat aspirate if inadequate sample, or no bone fragments seen. Tell patient that you are finished with the aspiration process.

# Post aspiration

Assessing adequacy of the sample, make smears for staining and examination, part of the sample may be allowed to clot, preserved in a fixative solution and submitted for histopathology. Portions of the sample may be submitted to the microbiology laboratory for cultures or special stains e.g. ZN. Certain conditions may require other specialized studies such as genetic testing or cell marker studies. Patient care after aspiration: press firmly, then place adhesive plaster to site of needle insertion. Stop and manage bleeding in case it occurs. Reporting should be systematic: comment on cellularity, start with а RBCs megakaryoblasts/cytes, precursors, WBCs precursors, plasma cells, parasites and any other cells. Write your report and suggest further investigations if needed. (3)

## Complications of BMA

Are uncommon and include local pain, bleeding and infection in addition to complications of local anesthesia. <sup>(4)</sup>

## Contra-indications of BMA

These are relative and not absolute contraindications for BMA: the very ill/terminal patient, infection at site of aspirate (select another site).<sup>(4)</sup>

#### **Statistical analysis**

Data generated were coded, validated and analyzed using Statistical Package for Social Science (SPSS) version 20 (IBM Statistics, USA). Pearson chi squared test was used to test for significance between proportions; p value below 0.05 was considered statistically significant. The main variables analyzed were age, sex, indication of BMA and the final conclusion/diagnosis.

#### **Ethical Approval**

An ethical clearance of the research was obtained from the Ethical Committee of the Faculty of Medicine - Nile Valley University.

*General	indication/	Examples
use		
To find an	explanation	Anemia
for uncertair	n conditions	
		Pyrexia of unknown origin
		Pancytopenia
		Thrombocytopenia
		Leukomoid reaction
		Metastasis of tumors
		Leukoerythroblastic blood film
To confirm	a suspected	Myeloproliferative/myelodysplatic
diagnosis disorders	of certain	syndromes
		Lymphoma
		Metastatic cancer
		Leukemia
		Storage diseases
		Multiple myeloma
Follow-up	and	Leukemia
monitoring o	of therapy	
		Bone marrow transplantation
		Hairy cell leukemia
		Myeloproliferative disorder
tions is not e	xhaustive and	some indications are controversial.

# Table 1: General indications for and uses of bone marrow aspiration.

\*This list of indications is not exhaustive and some indications are controversial.

#### Results

A total of 112 cases were subjected to bone marrow aspiration in the period from 2009 up to 2014, with an increased frequency in the last two years (Table 2). The male to female ratio was 1:1. The age range was from one to 87 years (mean<u>+</u> SD=44.0 <u>+</u>22.1). Adults above 45 years were the majority (Table 2).

The most common clinical indications for bone marrow aspiration were pancytopenia 38.4%, anemia 34.8% and suspected leukemia 11.6%. (Table 3).

In 86(76.8%) cases BMA provided either the diagnosis or diagnostic clues to the disease process; while 26 (23.2%) of the aspirates revealed a normally functioning marrow.

The most frequent diagnoses made were bone marrow aplasia/hypoplasia 37.5%. normally functioning marrow 23.2%. myelodysplastic syndrome 7.1%, chronic myelocytic leukemia (CML) 7.1%, chronic myelocytic leukemia (CLL) 4.5% and visceral leishmaniasis 4.5%. While there were one case (0.9%) for each of the following conditions: acute lymphoblastic leukemia (ALL). idiopathic thrombocytopenic purpura(ITP), myelofibrosis, secondary cancer, Gaucher's disease and polycythemia. One case gave dry tap upon repeated aspirates. The most encountered conditions were displayed in Table 4.

 Table 2. Frequency of sex and age group for patients, and year of bone marrow aspiration. Atbara,

 Sudan 2009 -2014. (n=112)

Variable	n	%
Sex		
Male	57	50.9%
Female	55	49.1%
Age group		
below 5 years	5	4.5%
5-15 years	11	9.8%
16 -30 years	22	19.6%
31 -45 years	19	17.0%
46 – 60 years	31	27.7%
above 60 years	24	21.4%
Year of aspiration		
2009	20	17.9%
2010	18	16.1%
2011	10	8.9%
2012	15	13.4%
2013	21	18.8%
2014	28	25.0%

 Table 3. Frequency of clinical indication of bone marrow aspiration in Atbara, Sudan 2009 -2014.

 (n=112)

Clinical indication	n	%
Pancytopenia	43	38.4%
Suspected leukemia	13	11.6%
Anemia	39	34.8%
Suspected Multiple	3	2.7%
Myeloma		
Pyrexia of Unknown	3	2.7%
Origin (PUO)		
Thrombocytosis	4	3.6%
Thrombocytopenia	3	2.7%
Polycythemia	1	0.9%
Unexplained	3	2.7%
splenomegally		

 Table 4. Frequency of the final diagnosis of bone marrow aspiration in Atbara, Sudan 2009-2014.

 (n=112)

Final Conclusion	Frequency	Percent
Hypoplastic bone	42	37.5%
marrow/Aplastic anemia		<u> </u>
Normally functioning	26	23.2%
marrow	•	7 404
Chronic myelocytic	8	7.1%
leukemia		
Myelodysplastic	8	7.1%
syndrome		
Chronic lymphocytic	5	4.5%
leukemia		

437

5	4.5%
3	2.7%
2	1.8%
2	1.8%
2	1.8%
2	1.8%
	3 2 2 2

#### Discussion

In this study we described, in brief, the basic concepts of bone marrow aspiration, along with our findings of the clinical indications and the final diagnoses in a 6-year period in Atbara city.

One hundred and twelve cases were involved in this study. The range of BMA requests per year was 10 to 28. This number is lesser than the expected to be seen in a population of 135,000 living in Atbara locality. But because BMA service was not available in this city before, the few number of requests is not unexpected, as physicians need time to be aware of the services available upon their request. Even after an initial increase in the rate of annual requests for BMA, there were drops in certain years. This finding may be attributed to the continuous immigration and replacement of physicians in our local community. However, there is noticeable increase in the rate of requests in recent years. Yet, some authors claim that BMA has deteriorated as a diagnostic tool in clinical practice. <sup>(5)</sup> This might be true in certain settings where other alternative diagnostic procedures exist. However; in most developing countries BMA is still essential and of great importance for establishing the diagnosis of many conditions.

There was no difference between males and females underwent BMA during study period. This can be explained by the fact that pancytopenia, anemia and hematological malignancies have no obvious sex predilection.

The most common age group underwent the procedure were adults above 45 years. This finding points to the age of bone marrow derangements such as myeloproliferative/myelodysplastic syndromes, myelofibrosis and aplastic anemia.

Aplastic anemia was the most common condition encountered. This is similar to that reported from India, <sup>(2)</sup> but higher than the rate

of anemia investigated in Saudi Arabia (8.3%). <sup>(6)</sup>The high "normally functioning marrow" (23.2%) results issued may be explained by the fact that many anemia's result from other causes rather than a bone marrow problem. Indications for platelet disorders may reflect the situation of infection (a common cause for platelets decrease/increase), or peripheral destruction rather than their synthesis in bone marrow.

The rarity of cases of pyrexia of unknown origin diagnosed in this study may be explained by the fact that, Sudan is a tropical country and the list of differential diagnoses for PUO is long, so that BMA can hardly settle the diagnosis. The role of BMA in settling the diagnosis in PUO is well studied by some authors, <sup>(7)</sup> as in only 16.5% was BMA diagnostic.

The rate of hematological malignancies was considerable (15.2%). This is lower rate when compared to the study done in Saudi Arabia. <sup>(7)</sup> The most common hematological malignancy was chronic myelocytic leukemia 8 cases (7.1%) followed by chronic lymphocytic leukemia 5 cases (4.5%), acute myeloblastic leukemia 2 cases (1.8%) and multiple myeloma 2 cases (1.8%)

There were 5(4.5%) cases of visceral leishmaniasis (kalazar) encountered in our laboratory. However, all these cases when traced back were found to be from endemic areas of the disease in east, Sudan.

Trephine biopsy as an adjunct to BMA is reported to increase its rate of accuracy, and facilitates sophisticated studies to be performed. <sup>(8-10)</sup> Bone marrow aspiration under CT scan has recently been reported and claimed to increase the diagnostic value of the procedure. <sup>(11)</sup>

The need for collaboration between all stakeholders: physicians, hematologists, pathologists, oncologists and technicians are

very important in improving the diagnostic yield of bone marrow examination. <sup>(12)</sup>

Limitations of our study include the small sample size that may not allow generalization. Despite this limitation, however, this study is novel and is the first of its kind in north Sudan and is anticipated to constitute a database for future studies.

In conclusion, bone marrow aspiration is a useful investigation tool in clinical practice. It is a safe and cost-effective procedure under the hands of the experienced; and is of added value when clinical notes and a peripheral blood films are also obtained.

#### Acknowledgements

We thank the medical students Alimam Altayeb and Munzer M Sayed for their help in data collection.

#### Conflict of interest: none.

## Funding: none

#### **References:**

- 1. Trewhitt KG. Bone marrow aspiration and biopsy: collection and interpretation. OncolNurs Forum. 2001; 28(9):1409-15.
- Mahajan V, Kaushal V, Thakur S, Kaushik R. A comparative study of bone marrow aspiration and bone marrow biopsy in hematological and non-hematological disorders- an institutional experience. JIACM 2013; 14(2):133-5.
- 3. Bain B J. Bone marrow aspiration. J ClinPathol 2001; 45:657-63.
- Malempati S, Joshi S, Lai S, Braner DAV, Tegtmeyer K. Bone marrow aspiration and biopsy. N Engl J Med 2009; 361:e28.

- Remberger M, Ringdén O, Mattsson J. Bone marrow aspiration technique has deteriorated in recent years. Bone Marrow Transplant. 2015; 50(7):1007-9.
- Bashawri LA. Bone marrow examination: indications and diagnostic value. Saudi Med J 2002; 23(2):191-6.
- Gupta R, Setia N, Arora P, Singh S, Singh T. Hematological profile in pyrexia of unknown origin: role of bone marrow trephine biopsy vis-à-vis aspiration. Hematology. 2008; 13(5):307-12.
- Nanda A, Basu S, Marwaha N. Bone marrow trephine biopsy as an adjunct to bone marrow aspiration. J Assoc Physicians India 2002; 50:893-5.
- Fend F, Tzankov A, Bink K, Seidl S, Quintanilla-Martinez L, Kremer M, Dirnhofer S. Modern techniques for the diagnostic evaluation of the trephine bone marrow biopsy: methodological aspects and applications. ProgHistochemCytochem. 2008; 42(4):203-52.
- 10. Wilkins BS, Clark DM. Making the most of bone marrow trephine biopsy. Histopathology. 2009; 55(6):631-40.
- Pfeifer C, Ternes T, St. Clair S, Palko W, Dakhil C. Bone marrow aspiration under CT-guidance: technique and value. Oncology 2015; 29(4 Suppl 1).
- 12. Wilkins BS. Pitfalls in bone marrow pathology: avoiding errors in bone marrow trephine biopsy diagnosis. J ClinPathol. 2011; 64(5):380-6.