

# DIAGNOSTIC ROLE OF BONE MARROW ASPIRATION AND TREPHINE BIOPSY IN HAEMATOLOGICAL PRACTICE

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Date Received:

September 09, 2013

Date Revised:

March 06, 2014

Date Accepted:

March 21, 2014

## ABSTRACT

**Objective:** To determine the usefulness of bone marrow aspiration and trephine biopsy in evaluation of the bone marrow in routine haematological practice.

**Methodology:** This study included 443 cases of bone marrow examination, referred to Pathology Department, Lady Reading Hospital Peshawar during the period extending from January 2012 till July 2013. All the bone marrow smears and bone biopsy sections were examined in detail. The diagnosis and findings on aspirate and biopsy were evaluated and compared with each other.

**Results:** In 73.8% of the cases the bone marrow aspiration and trephine biopsy showed same diagnosis i.e., bone marrow aspiration alone was sufficient for diagnosis in these cases. In the remaining 116 (26.2%) cases trephine biopsy sections or touch imprints were found to be necessary in for making final diagnosis. These cases were those of the hypoplastic / aplastic marrows, Myelofibrosis, lymphomatous infiltration and chronic granulomatous inflammation.

**Conclusion:** The study results suggest that both the aspirate and trephine biopsy complement each other. Nutritional anaemias, Haematological Malignancies and Immune Thrombocytopenia can be readily diagnosed by bone marrow aspiration alone. Trephine biopsy is necessary for diagnosing Granulomatous Inflammation and Hypoplastic/Aplastic Anaemia. Also trephine biopsy is required to diagnose Myelofibrosis and Lymphomatous infiltration.

**Key Words:** Bone marrow aspirate, Trephine Biopsy, Diagnostic usefulness.

This article may be cited as: Khan TA, Khan IA, Mahmood K. Diagnostic role of bone marrow aspiration and trephine biopsy in haematological practice. *J Postgrad Med Inst* 2014; 28(2):217-21.

## INTRODUCTION

Bone marrow examination is a useful and cost effective diagnostic procedure in haematological practice for the diagnosis of both neoplastic and non-neoplastic haematological diseases. These procedures are also employed for typing of anaemias, evaluation of cytopenias and pyrexia of unknown origin. The bone marrow examination may either confirm the clinically suspected disease or may provide the previously unsuspected diagnosis<sup>1-3</sup>. Bone marrow aspiration alone is usually sufficient to diagnose nutritional anaemias, most of the acute leukaemias and Immune Thrombocytopenias because of ease of the applying pearl iron stain and other cytochemical stains on aspirate smears but it does not provide important diagnostic information in patients with granulomatous disease, myelofibrosis and bone marrow infiltration<sup>4</sup>. Beside this the bone marrow examination is a commonly employed tool for staging

and prognosis of various solid tumors<sup>5</sup>. The presence of metastasis in the bone marrow is usually incurable but not necessarily fatal. It is therefore considered imperative to rule out marrow involvement in any malignancy where curative treatment is considered<sup>6</sup>. When both the procedures are performed simultaneously, they complement each other. Bone marrow aspirate smear are more useful to study morphology and applying pearl iron stain whereas trephine biopsy sections are used to study the architecture and pattern of distribution of the cells in the bone marrow. This study was conducted to determine and compare the diagnostic efficacy of bone marrow aspiration and trephine biopsy done simultaneously.

## METHODOLOGY

This study was conducted at haematology section of the Pathology department, Lady Reading Hospital,

Peshawar from January 2012 to July 2013. All patients who underwent simultaneous bone marrow aspiration and trephine biopsy (n=443) were included in this study.

After taking ethical approval and written informed consent about 0.5 to 1.0 cc bone marrow aspirates was taken from posterior superior iliac spine by using Salah's needle and employing standard technique. Bone trephine biopsy was taken using Jamshedi needle. The biopsy was fixed for 24 hours in 10 % buffered formalin and then decalcified overnight in a mixture of equal amounts of 8 % hydrochloric Acid and 10 % formic Acid. The fixation and decalcification of the biopsy was followed by automatic tissue processing, Paraffin embedding and sectioning. The bone marrow aspirate smears were stained by Geimsa stain while biopsy sections were stained by haemotoxyllin, eosin and reticulin. Pearl iron stain was performed for every case, while cytochemical stains were applied as and where required. All the bone marrow aspirate smear and trephine sections were reviewed for morphological details and compared for final diagnosis.

## RESULTS

A total of 443 cases underwent simultaneous bone marrow aspiration and trephine biopsy. Out of those bone marrow aspiration was sufficient in making diagnosis in 327 (73.8 %) cases as it matched with the final diagnosis made on trephine biopsy. Trephine Biopsy was diagnostic in 439 cases with diagnostic accuracy of 99 %. (Table 1) shows the cases diagnosed on bone marrow aspirate and trephine biopsy. It shows that none of the cases of Chronic Granulomatous Inflammation, Myelofibrosis and Aplastic Anaemia was diagnosed on bone marrow aspiration. All the cases of Anaemia of Chronic disorder were diagnosed on aspirate smear, while 04 out 30 cases were not diagnosed on trephine biopsy. 34 out 36 (94.4 %) cases of Nutritional Anaemias were diagnosed on aspirate. Table 2 shows cases showing matching between bone marrow aspiration and trephine biopsy. It shows that 73.8 % cases showed matching between bone marrow aspiration and trephine biopsy. Table 3 shows the cases where the final diagnosis was different on bone marrow aspirate or tre-

**Table 1: Cases diagnosed on bone marrow aspirate and trephine biopsy**

Diagnosis	No. of cases	Bone marrow aspirate	Bone marrow biopsy
Nutritional Anaemia	36	34 (94.4%)	36 (100%)
Granulomatous Inflammation	03	NIL (0%)	03 (100%)
Infections	08	06(75%)	08 (100%)
Malaria	04	04(100%)	04 (100%)
Leishmenia	04	04(100%)	04 (100%)
Immune Thrombocytopenia	24	20(83.3%)	24 (100%)
Anaemia of chronic Disorder	30	30(100%)	26 (86.6%)
Haematological Malignancy	99	89 (89.9%)	99 (100%)
Acute myeloblastic leukaemia	38	36 (94.7%)	38 (100%)
Acute myeloblastic leukaemia	31	29 (93.5%)	31 (100%)
Chronic myeloid leukaemia	16	11(68/7%)	16 (100%)
Chronic lymphocytic leukaemia	14	13(92.8%)	14 (100%)
Multiple. Myeloma	09	06 (66.6%)	09 (100%)
Lymphoma	18	03 (16.6%)	18 (100%)
Myelodysplastc syndrome	05	04 (80%)	05 (100%)
Metastatic Solid Tumors	10	09 (90%)	10 (100%)
Aplastic Anaemia	48	NIL (0%)	48 (100%)
Normal marrow	28	20 (71.4%)	28 (100%)
Myelofibrosis	07	NIL (0%)	07 (100%)
Miscellaneous	11	09 (81.8%)	11 (100%)
Total	443	327 (73.8%)	439 (99%)

**Table 2: Cases showing matching or otherwise of bone marrow aspirate cytology with trephine biopsy**

Diagnosis	Percentage
Nutritional Anaemia	94.4 %
Granulomatous inflammation	00 %
Infection	92 %
Idiopathic thrombocytopenic purpura	83.3 %
Anaemia of chronic Disorder	86.6 %
Haematological Malignancies	89.9 %
Multiple Myeloma	66.6 %
Lymphoma	16.6 %
Myelodysplastic syndrome	80 %
Metastatic Solid Tumors	90 %
Aplastic	00 %
Normal marrow	71.4 %
Myelofibrosis	00 %
Miscellaneous	81.8 %

**Table 3: Cases where diagnosis on bone marrow aspiration was different from the final diagnosis**

Diagnosis	Bone marrow cytology	No. of cases (%)
Nutrition Anaemia	Failed Aspirate	02 (5.6%)
Granulomatous inflammation	Normal marrow	03 (100%)
Idiopathic thrombocytopenic purpura	Dry tap	04 (16.6%)
Chronic myeloid leukaemia	Dry tap due to fibrosis	05(31.3%)
Acute myeloblastic leukaemia	Dry tap due to packed marrow	02 (5.3%)
Acute lymphoblastic leukaemia	Dry tap due to packed marrow	02(6.5%)
Multiple Myeloma	Dry tap	02(22.2%)
Lymphoma	Normal marrow	06 (33.3%)
	Hypercellular	03 (16.6%)
	Atypical cells	04 (22.2%)
	Dry Tap	02 (11.1%)
Myelodysplastic syndrome	Megaloblastic Anaemia	01 (20%)
Hypoplastic / Aplastic	Dry tap	08(16.6%)
	Hypocellular	34(70.8%)
	Normal marrow	06 (12.5%)
Normal marrow	Hypocellular	03(10.7%)
	Dry tap	04 (14.3%)
	Lymphocytosis	01(3.6%)
Metastatic solid tumour	Normal marrow	01(10%)
Miscellaneous	Normal marrow	01(9 %)
	Hypocellular	01(9 %)
Myelofibrosis	Dry tap	07 (100%)

phine biopsy. It shows 50% (9/18) cases of Lymphomatous infiltration and all the cases (3/3) of Chronic Granulomatous Inflammation were labeled as normal marrow on bone marrow aspiration. In some cases bone marrow aspirate was not successful in diagnosis mostly due to failed aspirate.

## DISCUSSION

Examination of the bone marrow is one of the diagnostic pillars of haematological practice. Bone marrow aspiration and trephine biopsy are the two procedures done for the diagnosis of haematological and non haematological disorders. These procedures are also employed for follow up of patients on chemotherapy, bone marrow transplantation and other forms of treatment<sup>1, 4, 5, 15</sup>.

Bone marrow aspiration and trephine biopsy complement each other and in many centers both the specimens are obtained at the same time and from the same site<sup>1, 11</sup>. In our study a comparative evaluation of bone marrow aspiration and trephine biopsy was done to determine the diagnostic usefulness of both the procedures. We observed 73.8% positive correlation between bone marrow aspiration and trephine biopsy. Chandra et al have reported 78% positive correlation between the two procedures whereas another study has reported 61.25% positive correlation<sup>2, 3</sup>. Good sensitivity of bone marrow aspiration (94.4 %) was found in diagnosing Nutritional Anaemia. Only 02 cases were not diagnosed on bone marrow aspirate smear due to failed aspirate. Cases of Anaemia of chronic disorder were easily diagnosed on bone marrow aspirate (100 %) as compared to trephine biopsy. The probable cause could be loss of iron during processing of biopsy sections. We found 92 % positive correlation in cases of infections and 83.3 % in cases of Idiopathic Thrombocytopenia (ITP). In 04 cases of immune thrombocytopenia the aspirate was dry. 89.9 % positive correlation was found in haematological malignancies as 89 out 99 cases were diagnosed on bone marrow aspirate. Out of 10 cases missed from diagnosis on aspirate, smear was dry tap due to fibrosis (05 cases of CML) and packed marrow (04 cases of Acute Leukaemia). We found bone marrow aspiration of comparable reliability to bone biopsy in diagnosing nutritional anaemia, ITP and haematological malignancies. The same finding was observed by Nauda et al<sup>3</sup> and Chandra et al<sup>4</sup>.

In our study we observed 90 % positive correlation in cases of metastatic tumors which is higher than the other studies<sup>3, 12</sup> who reported 70% and 33% positive correlation between the two. However trephine biopsy was found as gold standard for diagnosing the metastatic tumors as not only its diagnostic efficacy was 100%, but

it was also helpful in search for the primary tumor. In the present study poor correlation was observed in cases of lymphoma (16.6 %). All the cases of lymphoma were diagnosed on trephine biopsy but the lymphoma cells were observed only in 04 out of 18 (22.2%) cases on bone marrow aspirate smear. Our findings correlated with those of Bird et al<sup>1</sup> & Schmid et al. 16

In our study 100 % case (03/03) of Granulomatous inflammation in the bone marrow were diagnosed on trephine biopsy and none of the case was diagnosed on bone marrow aspirate. This is mainly because of focal involvement of the marrow by granuloma which is very difficult to detect on aspirate smear. Other studies have also observed detection of granulomas more on trephine biopsy than aspirate<sup>3, 4</sup>.

All the cases of Myelofibrosis (07/07) were diagnosed on trephine biopsy and the bone marrow aspirate was unsuccessful in all cases due to marked fibrosis. About sixty six percent (6/9) cases of multiple myeloma showed a positive correlation in aspirate smear and trephine biopsy. All these cases of multiple myeloma were diagnosed on trephine biopsy, but the aspirate was dry in 02 cases and one case was reported as Normal marrow on aspirate, but showed localized clusters of plasma cells on trephine biopsy. Similar observations were made by Stifter et al in his study<sup>9</sup>.

Bone marrow biopsy remained the gold standard for diagnosing Aplastic Anaemia. In our study 34/48 cases showed hypo cellular marrow on aspirate smear, 08/48 were dry tap and 06/48 were diagnosed as cellular marrow, probably due to accidental aspiration from normal marrow space. About 71 % (20/28) of the normal bone marrow showed matching in aspirate smear and bone biopsy in our study. This was due to the fact that 08/28 cases were either diagnosed as hypo cellular marrow, Dry tap or lymphocytosis on bone marrow aspirate.

## CONCLUSION

Bone marrow aspiration and trephine bone biopsy complement each for bone marrow evaluation. Both the procedures can be done simultaneously as bone marrow aspirate give better morphology of the cells and bone marrow biopsy give a good picture of the architecture and pattern of distribution of cells. Though bone marrow aspirate alone is usually sufficient in diagnosing nutritional anaemia most of the haematological malignancies and immune thrombocytopenia, we found bone marrow biopsy very useful in diagnosing Granulomatous inflammation, lymphomatous infiltrations, Myelofibrosis and Aplastic Anaemia.

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## CONTRIBUTORS

TAK participated in planning of study and manuscript writing. IAK helped in data analysis. KM supervised the study and helped in manuscript writing. All authors contributed significantly to the final manuscript.