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Original Research Article

Utility of Bone Marrow Aspiration and Bone Marrow Biopsy in Haematological Disorders

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Abstract

Background: Bone marrow aspiration (BMA) and Bone marrow biopsy (BMB) are very useful procedures for the diagnosis of haematological and non haematological malignancies, typing of anemia, pyrexia of unknown origin and infective diseases.

Objectives: To evaluate and compare the BMA and BMB findings in various haematological disorders.

Subjects: A total of 180 cases diagnosed with various haematological disorders in which bone marrow examination was done by using both the methods i.e. bone marrow aspiration and bone marrow biopsy were taken.

Results: Out of 180 cases, 158 cases were diagnosed on BMA and 168 cases on BMB. Rests of the 22 cases were dry tap on BMA and 12 cases were inadequate on BMB. Age ranged from 1.6 years to 80 years with the mean age of 36.30 years. Diagnostic accuracy of BMA was 100% in megaloblastic anaemia, acute leukaemia, metastatic marrow and ITP. BMB provided diagnosis in additional 6 cases of granulomatous lesion, 3 cases of MPD and 2 cases of LPD. Positive correlation between BMA and BMB was found to be 74.44%. The highest correlation was seen in reactive/leukemoid reaction (100%) and metastatic marrow (100%), correlation was least with aplastic anaemia (30.77%). No positive correlation was found in ITP and granulomatous lesion on BMA and BMB. Dry tap/ haemodilution on BMA were inconclusive in 22 cases (12.22%) maximum being for aplastic anaemia (8/13) cases. In all these cases BMB was diagnostic.

Conclusion: The utility and efficacy of BMB as compared to BMA have been discussed and debated. The answer, though complicated remains essentially the same. Both procedures complement each other.

Study Design: It was a cross sectional study conducted after approval from institutional ethical committee in the Department of Pathology, Sri Aurobindo Medical College and PG Institute, Indore.

Keywords: Bone Marrow Aspiration & Bone Marrow Biopsy.

Introduction

The technique of bone marrow aspiration (BMA) has been universally accepted and widely used. However, bone marrow biopsy (BMB) as a diagnostic procedure is being increasingly used in recent years.[1] BMA and BMB are very useful procedures for the diagnosis of haematological and non haematological malignancies, typing of anemia,

pyrexia of unknown origin and infective diseases [2]. BMB is essential for diagnosis of inadequate marrow aspirate, bone marrow fibrosis, granulomatous lesions, myeloproliferative disorders, myelodysplastic syndromes, aplastic anaemia, metastatic tumor and plasma cell dyscrasias [3,4]. The combined procedures of aspiration and biopsy give a higher yield and are essential in patients suspected with metastasis to the marrow, staging of Non-Hodgkin's lymphoma and Hodgkins'lymphoma [5]. In present study we evaluated and compared the BMA and BMB findings in various haematological disorders.

Material and Methods

The present cross-sectional study was conducted in the Department of Pathology of our institute. A total of 180 cases where both BMA and BMB were done simultaneously were included in the study. Only the first time diagnosed and clinically suspected hematological disorders or first time undergoing BMA & BMB procedure at our institute were included in study group. Known and already diagnosed cases of haematological disorders were exclusion criteria.

BMA were stained with Field, Geimsa stain, Perl's & cytochemical stains as needed. Biopsy specimen received were fixed in 10% formalin overnight and decalcified subsequently with decalcifying agent (50ml-Formaldehyde+30ml-distilled water+40ml-Formic acid). After routine processing and paraffin embedding, Haematoxylin and Eosin stained sections were studied. Special stains like Periodic acid-Schiff (PAS), Reticulin, Perl's stain, Zeil Nelson stain were used wherever required.

Results

The total numbers of cases studied were 180 where BMA and BMB were done together. All the smears and sections were reviewed for morphological details and findings of aspirate and biopsy were compared to each other. The age of the subjects ranged from 1.6 years to 80 years with the mean age of 36.30 years. There was male preponderance with male to female ratio of 1.27:1.Out of 180 cases, 158 cases was diagnosed on BMA with diagnostic accuracy of 87.77% and 168 cases were diagnosed on BMB with diagnostic accuracy of 93.33% (Table1).

Diagnostic accuracy of BMA was 100% in megaloblastic anaemia, acute leukaemia, metastatic marrow and ITP. BMB provided diagnosis in additional 6 cases of granulomatous lesion, 3 cases of MPDs and 2 cases of LPDs (Table 1). Dry tap/ haemodilution on BMA was inconclusive in 22 cases (12.22%), maximum being for aplastic anaemia (8/13) cases. In all these cases BMB was diagnostic. BMB was inadequate in 12 cases (6.66%) which were mainly observed in anaemia. All these cases were diagnosed on BMA (Table 3).

Out of total 180 cases studied a positive correlation between BMA and BMB was found to be 74.44%. The highest positive correlation was seen in reactive/ leukemoid reaction (100%) and metastatic marrow (100%) followed by acute leukaemia (91.30%) and megaloblastic anaemia (90.48%). Correlation was found to be least with aplastic anaemia (30.77%) followed by plasma cell dyscrasias (50%) and MPD's (66.67%) (Table 2). In present study no correlation was found in ITP and granulomatous lesion on BMA and BMB.

Table 1: Comparative evaluation of BMA and BMB diagnosis and diagnostic accuracy of BMA

Disorders	No. of Cases	BMA	BMB	Diagnostic Accuracy of BMA (%)
Aplastic/Hypoplastic anaemia	13	5	12	41.66%
Megaloblastic anaemia	21	20	20	100%
Micronormoblastic anaemia	22	23	19	-
Dimorphic anaemia	30	30	26	-
Normoblastic maturation	5	6	4	-
Acute leukemia	23	22	22	100%
LPDs	13	11	13	85%
MPDs	9	6	9	66.66%
Plasma cell dyscrasias	2	2	1	-
MDS	8	7	8	87.50%
ITP	4	2	2	100%
Reactive/Leukomoid reaction	6	6	7	85.70%
Granulomatous lesion	7	1	6	16.60%
Metastaitic marrow	2	2	2	100%
Normal marrow	15	15	17	88.23%
Dry tap		18	_	_
Hemodiluted		4	_	_
Inadequate		_	12	_

Table 2: Distribution of cases as per diagnosis with a positive correlation between BMA and BMB

Disorders	No. of cases	Positive correlation between BMA and BMB cases	Percentage (%)
Aplastic/Hypoplastic anaemia	13	4	30.77%
Megaloblastic anaemia	21	19	90.48%
Micronormoblastic anaemia	22	18	86.36%
Dimorphic anaemia	30	24	80.00%
Normoblastic maturation	5	3	60.00%
Acute leukemia	23	21	91.30%
LPDs	13	10	76.92%
MPDs	9	6	66.67%
Plasma cell dyscrasias	2	1	50.00%
MDS	8	7	87.50%
ITP	4	0	0.00%
Reactive/Leukomoid reaction	6	6	100.00%
Granulomatous lesion	7	0	0.00%
Metastatic marrow	2	2	100.00%
Normal marrow	15	13	86.67%
TOTAL	**180**	**134**	**74.44%**

Table 3: Distribution of cases diagnosed on BMA

Disorders	No. of cases	Percentage(%)
Cases with dry taps/ haemodilution on BMA diagnosed on BMB (no. of cases=22)		
Aplastic/ hypoplastic anaemia	8/13	69.23%
Dimorphic anaemia	1/30	3.33%
Micronormoblasticanaemia	1/22	4.55%
Megaloblastic anaemia	1/21	4.76%
Acute leukemia	1/23	4.35%
LPDs	2/13	15.38%
Myelofibrosis	1/2	50.00%
ITP	1/4	25.00%
Chronic granulomatous lesion	4/7	57.14%
Normal marrow	2/15	13.33%
Cases diagnosed by BMA alone where BMB was inadequate (no. of cases=12)		
Diamorphic anaemia	4/30	13.33%
Megaloblastic anaemia	1/21	4.76%
Micronormoblastic anaemia	2/22	9.09%
Normoblastic maturation	2/5	40.00%
Aplastic anaemia	1/13	7.69%
ITP	1/4	25.00%
AML	1/12	8.33%

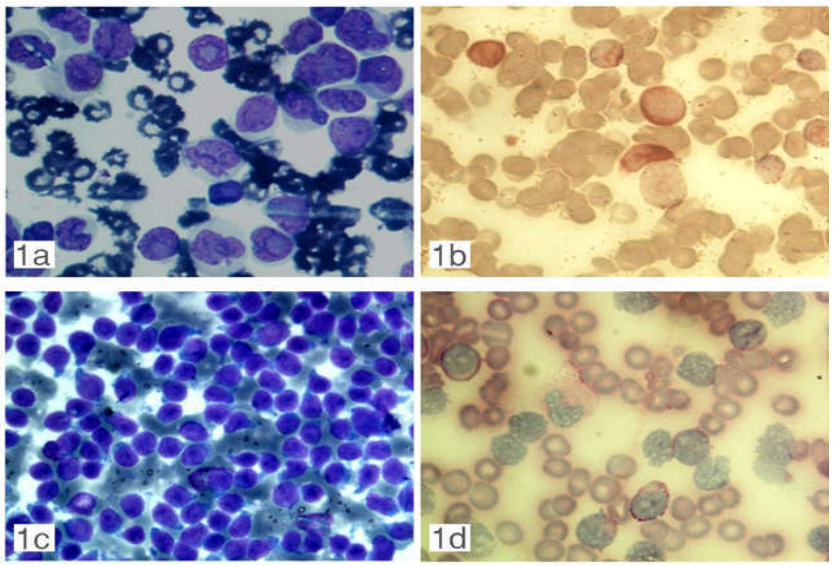

Fig. 1a: BMA showing large blasts with fine nuclear chromatin and pale blue cytoplasm. (Giemsa stain 10 x 100X). **b:** Peripheral smear showing Monoblasts with fine granular red brown staining of cytoplasm. (NSE stain, 10 x 100X). **c:** ALL: BMA showing large blasts with clumped nuclear chromatin and scanty cytoplasm with inconspicuous nucleoli. (Giemsa stain, 10x100X). **d:** BMA showing lymphoblasts with typical block positivity by periodic acid schiff stain. (PAS stain, 10 x 100X)

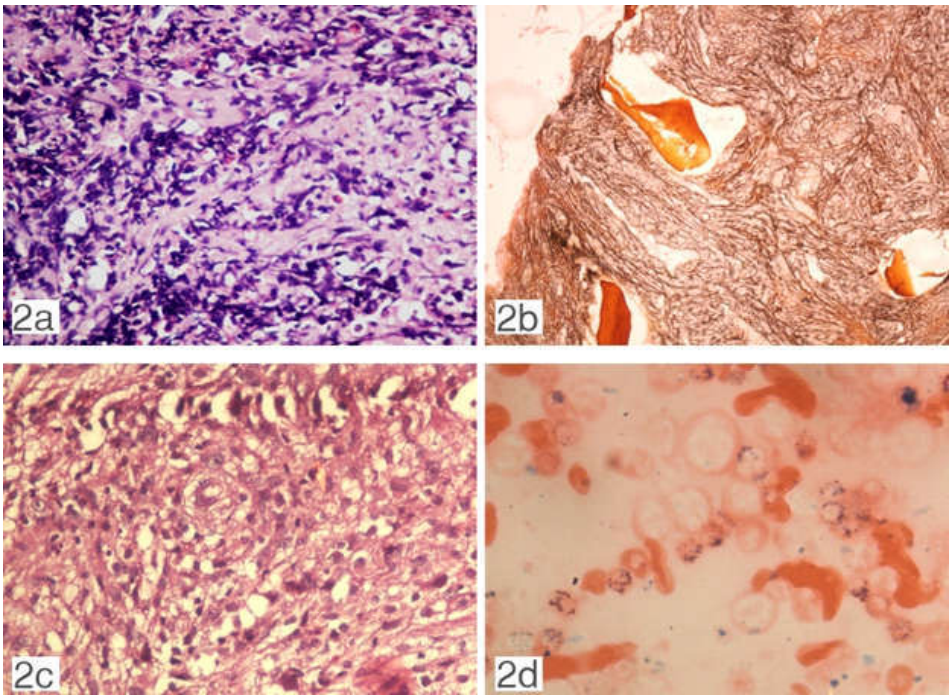

Fig. 2 a: *Myelofibrosis* BMB showing marked stromal fibrosis with decreased cellularity. (H & E 10 x 40X) **b:** BMB showing markedly increased coarse reticulin fibres forming diffuse network. (Reticulin stain, 10 x 10X). **c:** *Chronic granulomatous lesion:* BMB showing decreased cellularity, increase fibrous tissue with ill formed epitheloid cells granuloma. (H&E stain, 10 x 40X). **d:** *MDS-RARS-* BMA showing ring sideroblasts on perl staining. (Perl stain, 10 x 100X).

Discussion

BMA and BMB are important diagnostic procedures for the diagnosis of haematological, non haematological malignancies and other diseases. These procedures are also valuable for follow up of patients undergoing chemotherapy, bone marrow transplantation and other forms of medical treatment. It is a well known fact that bone marrow aspiration and bone marrow biopsy complement each other. Nowadays both specimens are routinely obtained at the same time and usually from same site. In our study, we did a comparative evaluation of all such BMA and BMB, to see the complementary role of both the procedures, to study the advantages and disadvantages of both the procedures done simultaneously.

In our study we did a comparative evaluation of BMA and BMB to see the complimentary role of both the procedure. There was 74.44% positive correlation between BMA and BMB in our study, which is higher than most of studies and slightly lower than Patel et. al. [6], Manju et. al. [7] and Chandra et. al. [8] studies. Higher positive correlation was found in reactive marrow followed by acute leukaemia and megaloblastic anaemia similar to findings in other studies. There was no positive correlation between BMA and BMB in cases of chronic granulomatous disease and ITP. Goyal S et. al. [9] and Chandra S et. al.[8] had similar finding in their study. Out of 9 cases of MPDs, 2 cases of Myelofibrosis showed no correlation between BMA and BMB. Khan TA et. al. [10] had similar finding in their study.

Present study observed that the diagnostic accuracy of BMB was higher (93.33%) in comparison to BMA (87.77%) in diagnosing various haematological disorders similar finding is seen in other studies which concluded that BMB has better diagnostic accuracy then BMA in various haematological disorders. Diagnosis of various haematological disorders on BMB and BMA in present study on comparing with other studies majority of cases diagnosed on bone marrow examination was of anaemia (91 cases). Out of 91 cases 84 cases were diagnosed on BMA and 81 cases were diagnosed on BMB. Highest diagnostic accuracy of BMA was found in Dimorphic, micronormoblastic and megaloblastic anaemia. It is well known fact that aspiration is better in making out individual cell morphology whereas biopsy is useful in study of architectural pattern of cell distribution. Parajuli S et. al.[11] also had similar findings. Out of 21 cases of megaloblastic anaemia, BMA and BMB had 100% diagnostic accuracy but usually BMA is performed alone in cases of clinically suspected megaloblastic anaemia and bone marrow biopsy is not considered useful for diagnosis [4]. Patel K et. al.[6] and Goyal S et. al.[9] got similar findings in their studies. Out of 13 cases of aplastic/

hypoplastic anaemia, 38.46% cases were diagnosed on BMA while 92.3% cases were diagnosed on BMB. Khan TA et. al.[10] had similar finding i.e. BMB was more diagnostic for aplastic anaemia in their study. This shows that BMB remains the gold standard for diagnosing aplastic anaemia. Acute leukaemia diagnostic accuracy of BMA was 100%. Out of 23 cases of acute leukaemia, 22 cases were diagnosed on BMA which were distributed as 13 cases of AML (M3- 2cases, M6- 1 case, M1- 1 case), 6 cases of ALL (L2- 1case) and 3 cases were unclassified. To differentiate between myeloid and lymphoid leukaemia we performed MPO staining, myeloid blasts were positive with MPO staining, while PAS stain was done on ALL cases in which one case (L2) showed block positivity on it.

On Bone marrow biopsy out of 22 cases, 9 cases diagnosed as AML, 6 cases as ALL and 10 cases were of acute leukaemia which couldn't be differentiated. This concludes that BMA is better than BMB for the classification of the leukaemia because cellular morphology is better understood on aspiration. Parajuli S et. al.[11] and Ghodhasara J et. al. [12] also got similar findings in their studies. Out of 13 cases of LPDs, 11 cases were diagnosed on BMA and all the 13 cases were diagnosed on BMB. 5 cases of Lymphoma cell infiltration were diagnosed on BMA whereas 8 cases of lymphoid infiltration (NHL) were diagnosed on BMB. One case of Hairy Cell Leukaemia was also diagnosed both on BMA and BMB. One case of lymphoma was diagnosed on biopsy but aspiration was normal. It shows that BMB was better than BMA as biopsy renders information which cannot be determined from aspiration, such as spatial distribution, extent of infiltration, cellularity and fibrosis. Goyal S et. al.[9] and Mahajan V et. al.[13] also had similar findings in their study. Out of 9 cases of myeloproliferative disorders, 6 cases were diagnosed on BMA while all the 9 cases were diagnosed on BMB. Diagnostic accuracy of BMA was 66.60%. Out of 9 cases, 2 cases of Myelofibrosis were diagnosed on BMB while on BMA one case was dry tap and another showed micronormoblastic anaemia. Thus BMB was more accurate and sensitive in diagnosing MPDs compared to BMA. Studies by Goyal S et. al. [9], Mahajan V et. al.[13] and Kaur M et. al.[14] have findings in concordance with present study.

BMA does not have much role in diagnosis of primary myelofibrosis (PMF) because diffuse osteomyelosclerosis, intrasinusoidal hematopoiesis and vascular proliferation, which are characteristic of fibrotic PMF, can be confirmed and graded on biopsy sections only [4].

In the present study out of 8 cases of MDS, 7 cases were diagnosed on BMA and BMB diagnosed 8 cases. Diagnostic accuracy of BMA was 85%. Khan TA et. al. also had similar finding in their study whereas in Mahajan V et. al. [13] and Goyal S et. al.[9] diagnostic accuracy of BMA was 100%. In MDS, aspirate was 100% sensitive but trephine biopsy provided additional information such as detection of abnormal localization of immature precursors (ALIP) and aggregates of myeloblasts. Presence of fibrosis or fatty changes in marrow can make accurate disease characterization very difficult or impossible on aspirates [15].

In our study, out of 2 cases of plasma cell dyscrasias, both the cases were diagnosed on BMA but only one on BMB, therefore diagnostic accuracy of BMA is better than BMB. Mahajan V et. al. [13] also had similar findings whereas Goyal S et. al. [9] had better diagnostic accuracy for BMB.

In present study out of 7 cases of granulomatous lesion one case was diagnosed on BMA and 6 cases were diagnosed on BMB. BMB had a higher yield in detecting granuloma as compared to BMA. These findings were consistent with Tripathy S et. al. [16] and Mahajan V et. al.[13] This is mainly because of focal involvement of marrow by granuloma which is difficult to detect on aspiration smear.

Two cases of non haematopoietic metastatic deposits (primarily diagnosed as prostatic adenocarcinoma) were seen in present study by both BMA and BMB. Toi PC et. al.[2] and Mahajan V et. al.[13] had less diagnostic accuracy as compared to our study due to focal involvement of bone marrow and increased fibrosis associated with metastasis. Hence, both aspiration and biopsy are complementary to each other.

Marrow aspirates has been primarily utilized for cytological assessment. It is an important step to arrive at the confirmatory diagnosis of wide varieties of haematological disorders. Bone marrow examination also gives explanation of unexplained cytopenias and leukaemia. It gives a more complete picture of the reaction of the haemopoietic tissue to anaemia than can be gained from the peripheral blood smear alone. Trephine biopsy; on the other hand, allow studying marrow's overall cellularity, detection of focal lesion, and extent of infiltration by various pathologic entities [17].

In present study out of 180 cases 22 cases were dry tap/ haemodiluted on BMA which were diagnosed on BMB which is comparable to various other studies Patel S et. al. [18] and Atla BL et. el. [19] which had similar findings.We also found 2 cases which were dry tap on aspiration and reported normal marrow on biopsy. Most of the dry taps were found to be of aplastic anaemia (69.23%), chronic granulomatous lesion (57.14%) and Myelofibrosis (50%). All these cases were diagnosed on BMB. Various causes of dry tap are fibrosis, hypercellularity and faulty technique. Fibrosis is better diagnosed with reticulin stain on BMB. Dry tap in most of the cases, is like a diagnostic alert for underlying bone marrow pathology. Instead of dismissing it as an outcome of faulty technique, dry tap must be

followed by BMB. Inadequacy of BMB (6.6%) was slightly higher than other studies by Tripaty et. al.[16] and Dambhare PT et. al.[20]. We feel this is due to the aspiration done prior to core biopsy from the same site leading to drained out effect and hypo cellular picture on BMB. When both the procedures are to be done simultaneously, it is preferable to use the two needle technique. Change the position of the needle after one procedure in order to get maximum marrow material.

Conclusion

The utility and efficacy of BMB as compared to BMA have been discussed and debated. The answer, though complicated remains essentially the same. Both procedures complement each other. Bone marrow aspiration is easy to perform and is important for cytological assessment with analysis directed towards morphology. Dry tap, in most of the cases is like a diagnostic alert for underlying bone marrow pathology. Bone marrow biopsy is the diagnostic investigation in dry tap cases like Aplastic Anaemia, Myelofibrosis, MDS and metastatic tumors. The cellular architecture is well preserved when compared to bone marrow aspiration.

The advantages in correct diagnosis of a case by bone marrow biopsy in conjunction with the clinical, haematological and aspiration study, far outweighs the minor disadvantages with biopsy. Despite the growing complexity and dependence on newer methodologies and ancillary assays including immunochemistry, cytogenetic analysis, flow cytometry and molecular assays, which may have augmented and refined the diagnostic criteria formerly obtained by light microscopy, the traditional role of examination of BMA and histopathological evaluation of BMB remains as important as it has been in the past.

Conflict of Interests

There was no conflict of interests with respect to all authors.

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References

1. Bearden JD, Ratkin GA, Coltman. Comparison of the diagnostic value of bone marrow biopsy and bone marrow aspiration in neoplastic disease. J ClinPathol 1974; 27:738-40.
2. Toi PCh, Varghese RG, Rai R. Comparative evaluation of simultaneous bone marrow aspiration and bone marrow biopsy: an institutional experience. Indian J Hematol Blood Transfus 2010;26:41-4.
3. Bain BJ. Bone marrow aspiration. J ClinPathol 2001;54:657-63.
4. Bain BJ. Bone marrow trephine biopsy. J ClinPathol 2001; 54:737-42.
5. Fend F, TzankA, Bulk K. Modern technique for the diagnostic evalution of the trephine bone marrow biopsy: Methodological aspect and application. Prog Histochem Cytochem 2008;42:203-52.
6. Patel K, Savjiani N, Gharia B, F JJJ. Comparison of bone marrow aspiration, cytology, touch imprint cytology and bone marrow biopsy for bone marrow evaluation. Int Arch Integr Med 2015;2:1-10.
7. Manju, Kumar V, Gupta N, Kapoor A, Kumar HS. Role of bone marrow aspiration and biopsy in diagnosis of haematological disorders: A prospective study. J Pharma Biomed Sci 2016;6:150-4.
8. Chandra S, Chandra H. Comparison of bone marrow aspirate cytology, touch imprint cytology and trephine biopsy for bone marrow evaluation. Hematology Report 2011;3:22.
9. Goyal S, Singh UR, Rusia U. Comparative evaluation of bone marrow aspirate with trephine biopsy in haematological disorders and determination of optimum trephine length in lymphoma infiltration. Mediterr J Hematol Infect Dis. 2014 Jan 2;6(1):e2014002.
10. Daniel H, Harvey J. Bone marrow aspiration and morphology. In: Ronald Hoffman, editor. Hematology Basic Principles and Practice, 3ed ed. Philadelphia: Churchill Livingstone; 2000.p.2460.
11. Parajuli S, Tuladhar A. Correlation of bone marrow aspiration and biopsy findings in diagnosing haematological disorders- a study of 89 cases. J patholnapal 2014;4:534-8.
12. Ghodasara J, Gonsai RN. Comparative Evaluation of Simultaneous Bone Marrow Aspiration and Bone Marrow Trephine Biopsy-A Tertiary Care Hospital Based CrossSectional Study. Int J Sci Res 2014;3:358.
13. Mahajan V, Kaushal V, Thakur S, Kaushik R. A comparative study of bone marrow aspiration and bone marrow biopsyin haematological and non haematological disorders –An institutional experience. J Indian AcadClin Med 2013;14:133-5.
14. Kaur M, Rana APS, Kapoor S, Puri A. Diagnostic Value of Bone Marrow Aspiration and Biopsy in Routine Hematology Practice. J ClinDiagn Res 2014;8:13-6.
15. Buhr T, Büsche G, Choritz H, Langer F, Kreipe H. Evolution of Myelofibrosis in Chronic Idiopathic Myelofibrosis as Evidenced in Sequential Bone Marrow Biopsy Specimens. Am J ClinPathol 2003;119:152-8.
16. Tripathy A, Dudani S. Comparative Evaluation of Simultaneous Bone Marrow Aspiration and Trephine Biopsy – Experience From Routine Hematology Practice. Indian J ClinPract 2013;24:446-50.

17. Trewhitt KG. Bone marrow aspiration and biopsy: collection and interpretation. OncolNurs Forum 2001; 28:1409-15.
18. Patel S, Nathani P, Shah N, Shah CK. Diagnostic Role of Bone Marrow Aspiration and Trephine Biopsy in Haematological Practice. Guja Med J 2015;70:37-41.
19. Atla BL, Anem VL, Dasari A. Prospective study of bone marrow in haematological disorders. Int J Res Med Sci 2015; 3:1917-21.
20. Dambhare PT, Tote VD, Wasnik PN, Kumbhalkar DT. Role of Bone Marrow Trephine Biopsy in Diagnosing Hematological Disorders Which Shows Bone Marrow Aspiration Failure-Two Year Observational Study of 58 Cases. Int Inter discp Res J 2015;5:66-75.