

## Critical Analysis of Bone Marrow Studies: A 5 Year Experience

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### ABSTRACT

**Introduction:** Bone marrow Aspirate (BMA) and bone marrow trephine biopsy (BMB) are the two diagnostic procedures done to evaluate various hematologic and non-hematologic conditions. Though both the procedures done on the same day are complementary to each other, discrepancies do occur. In few instances aspirate alone is done without a biopsy. This study is aimed to statistically analyze the diagnostic value of both the procedures and the lacuna observed.

**Methods:** A retrospective laboratory record based analysis was done on the bone marrow investigations reported during a period of 5 years (Jan.2011 – Dec.2015). The bone marrow investigations with simultaneous BMA and BMB done during the period of study were included. Descriptive statistical analysis was done for correlation of BMA and BMB diagnosis.

**Results:** Aspirate and biopsy were done on 934 cases. The diagnostic sensitivity of BMB was 94.74% and BMA was 86.14%. BMB and BMA were complementary to each other in 53.21% cases. BMB alone was diagnostic in 33.61% cases and BMA alone was diagnostic in 9.31% cases. Inadequate material for diagnosis was noted in 8.35% of BMB cases and 27.41% of BMA cases. Good positive correlation was noted in cases of immune thrombocytopenic purpura, multiple myeloma, anemia, reactive marrow and chronic lymphocytic leukemia.

**Conclusion:** Though both the procedures were complimentary to each other, inadequate aspirates due to disease conditions and faulty techniques were major drawbacks. It is preferable to perform both the procedures simultaneously for a more conclusive diagnosis.

**Keywords:** Bone Marrow Studies, Bone Marrow Aspirate, Bone Marrow Biopsy, Trephine Biopsy

### Introduction

BM examination is a valuable diagnostic tool in various hematologic and non-hematologic conditions, though a good percentage of them are reflected in the peripheral blood. Bone marrow Aspirate(BMA) and bone marrow trephine biopsy (BMB) are the two diagnostic procedures done to evaluate the disease process. Though both the procedures done on the same day are complementary to each other, discrepancies do occur. The occurrence of a dry tap or blood tap in certain disease conditions and technical default, lead to faulty diagnosis of the BMA in certain disease conditions. The BMA procedure is relatively easier and provides better cellular morphology and cell count; therefore it is always done by the clinician. In view of the pain and a relatively complex procedure BMB is often neglected. This study is aimed to statistically analyze the diagnostic value of both the procedures and the lacuna observed when any one of the procedure alone is performed.

### Materials and Methods

A retrospective laboratory record based analysis was done in the Department of Pathology on the bone marrow specimens reported during a period of 5 years (Jan.2011 – Dec.2015).All the bone marrow investigations with simultaneous BMA and BMB done during the period

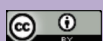
of study were included. Institution ethics committee approved the study. All the BMA has been stained with Leishman stain and May Grunwald Giemsa stain and Perl's stain for iron. All the BMB were fixed in 10% buffered formalin, decalcified in 10% formic acid and stained with hematoxylin and eosin after decalcification. Reticulin and iron stains are routinely done and other special stains and immunohistochemistry (IHC) were done whenever necessary. The reports had been released with the consensus of three pathologists.

The BMB reports were categorized into 12 categories as shown in Table 1. The numbers of BMA reports correlating with BMB were tabulated. The non concordant reports were also tabulated according to the categories in Table 2.

Descriptive statistical analysis was done using GNU PSPPO.8.4 for correlation of BMA and BMB diagnosis. The causes for poor correlation were discussed in comparison with previous studies.

### Results

During the five years 934 BMB and 1379 BMA were reported. All the BMB were preceded by BMA at the same time and usually the same site as suggested by Islam A.<sup>[1]</sup>



The age group of the patients ranged from 14 days of life to 82 years. The male: female ratio was 1.4:1. The diagnostic sensitivity of BMB was 94.74% (811 cases) and BMA was 86.14% (584 cases). BMB and BMA reports were complementary to each other in 497 (53.21%) cases. BMB alone was diagnostic in 314 (33.61%) cases and BMA alone was diagnostic in 87 (9.31%) cases. Inadequate material for diagnosis was noted in 78(8.35%) of BMB cases and 256 (27.41%) of BMA cases. Table 1. shows the number of cases in each category according to BMB reports and the sensitivity and false negativity with BMA. Table 2. shows the spectrum of BMA in comparison with BMB reports when there was negative correlation. Good positive correlation was noted in cases of immune thrombocytopenic purpura (75.68%), multiple myeloma (70.9%), anemia (69.37%), reactive marrow (67.57%) and chronic lymphocytic leukemia (60%). Poor correlation was seen in granulomatous inflammation (10%) myeloproliferative neoplasms (25%) metastasis (27.27%), lymphoma (29.41%) and myelodysplastic syndrome (32.43%).

BMA was the tool in diagnosis of 45 (4.82%) cases reported as normal in BMB and 41 (4.39%) cases where the BMB was inadequate for evaluation. A case of hypocellular MDS was diagnosed by BMA.

## Discussion

Bone marrow examination is a valuable investigation in hematologic and various non-hematologic disorders. This study was conducted to conclude whether BMA and BMB should be advocated at the same time which is still a controversy.

The diagnostic sensitivity of BMB was 86.83% including inadequate samples and 94.74% excluding them, which is almost similar to previous studies by Chandra et. al (99.2%) and Ayadayesh M.H. et. al (98.8%).<sup>[2,3]</sup> The BMA was diagnostic in 62.5% when inadequate smears were included and 86.14% excluding them. The diagnostic accuracy was slightly higher than the other studies. BMA and BMB were complementary to each other in 497(53.21%) cases. 27.41% inadequate aspirates were responsible for the lower percentage than previous studies.<sup>[4,5]</sup> Good positive correlation was observed with cases of immune thrombocytopenic purpura (ITP), anemia and reactive marrow among the non malignant conditions. The same observations were noted by Toi PC et. al. and Khan T.A. et al.<sup>[4,6]</sup> Though erythroid hyperplasia and increased megakaryocytes were observed in anemia and ITP in the BMB , morphologic assessment was possible with BMA .Hypocellular

**Table 1: No. of cases and correlation of BMA and BMB**

S. No.	Disease	BMB		BMA – Diagnostic sensitivity		BMA – False negative	
		Cases	%	Cases	%	Cases	%
1	Hypocellular marrow	170	18.2	60	35.3	110	64.7
2	ITP	37	39.6	28	75.68	9	24.32
3	Acute leukemia	147	15.7	83	56.46	64	43.53
4	MPN	52	5.57	13	25	39	74.91
5	MDS	37	3.96	12	32.43	25	67.58
6	MM	38	4.07	27	70.9	11	28.95
7	Metastasis	11	1.18	3	27.27	8	72.73
8	Anemia	36	3.85	25	69.37	11	30.56
9	Inflammatory	10	1.07	1	10	9	90
10	Lymphoma	17	1.82	5	29.41	12	70.59
11	Normal/Reactive	296	31.69	200	67.57	96	32.43
12	Inadequate	78	8.35	37	47.44	41	52.56
13	CLL	5	0.54	3	60	2	40

**Table 2: BMA reports which differed from BMB**

S. No.	Category – BMB	BMA	No.	%	False negative
1	Hypo cellular marrow	Inadequate	65	38.23	64.7
		Normal	35	20.59	
		ITP	2	1.18	
		MDS	1	0.59	
		Anemia	6	3.53	
		Inflammation	1	0.59	
2	ITP	Inadequate	3	8.11	24.32
		Normal	4	10.8	
		Hypocellular	2	5.41	
3	Acute leukemia	Inadequate	55	37.41	43.53
		Normal	3	2.04	
		Hypocellular	3	2.04	
		Lymphoma	2	1.36	
		MDS	1	0.68	
4	MPN	Inadequate	26	49.91	74.91
		Normal	8	15.38	
		Anemia	5	9.62	
5	MDS	Inadequate	15	40.55	67.58
		Hypocellular	3	8.11	
		Anemia	7	18.92	
6	MM	Inadequate	11	28.95	28.95
7	Metastasis	Inadequate	8	72.73	72.73
8	Anemia	Inadequate	11	30.56	30.56
9	Granulomatous inflammation	Inadequate	3	30	90
		Normal	4	40	
		Hypocellular	1	10	
		Hemophagoatosis	1	10	
10	Lymphoma	Inadequate	8	47.06	70.59
		Normal	3	17.65	
		Acute Leukemia	1	5.88	
11	Normal/Reactive	Inadequate	51	17.23	32.43
		Inflammatory	2	0.66	
		Chediak-Higashi	1	0.33	
		Hemophagocytosis	2	0.66	
		Lympho Proliferative disorder	1	0.33	
		Hypocellular	14	44.73	
		ITP	5	1.69	
		Anemia	20	76.76	
12	Inadequate	Normal	26	33.33	52.56
		Acute Leukemia	8	10.26	
		Anemia	4	5.13	
		ITP	2	2.56	
		MDS	1	1.28	

marrow and chronic granulomatous inflammation were better diagnosed with BMB. This had been well stated by Bain BJ.<sup>7</sup>

Among the hematologic malignancies multiple myeloma (MM) had good positive correlation of 70.9% similar to earlier studies.<sup>8</sup> Also BMB provided a platform to perform IHC to assess the clonality. BMA was helpful in diagnosing 56.46% of acute leukemia diagnosed by BMB. The major cause for lack of confirmatory diagnosis was inadequate aspirate (37.41%). Though BMB was considered unnecessary for the diagnosis of acute leukemia if the aspirate is good, a dry tap is often noticed due to packed marrow which may not permit BMA diagnosis as well as adequate samples for flowcytometry also. BMB was the only conclusive diagnostic tool in those cases and categorization can be done with IHC. The diagnostic utility of BMA in myeloproliferative neoplasms (MPN) was low since all the cases were myelofibrosis which yielded a dry tap. BMB was superior to BMA in diagnosing lymphoma. Our observations were similar to Sitalakshmi et al and Nanda et al and are in contradiction to Mahajan et al.<sup>9,10,5</sup> Moderate positive correlation was noted in CLL. But 40% of cases were not diagnosed similar to Kaur et al.<sup>11</sup> Though morphological characters of MDS were observed well in BMA, the diagnostic accuracy of BMB was superior as abnormal localization of immature myeloid precursors can be identified and IHC can be performed as stated by Winfield DA in his review papers<sup>12</sup>. The diagnostic accuracy of lymphoid infiltration in the BMA was only 30% lower than the study by Musolino et al.<sup>13</sup> The non hematologic malignancies were diagnosed with better accuracy in BMB as observed by Mishra P et al.<sup>14</sup> In cases of unknown primary site or unsuspected malignancy, BMB had been a tool for diagnosis and IHC.

Though BMA and BMB are complementary to one another, the diagnostic accuracy of BMB is more in granulomatous and infiltrative diseases. In acute leukemia when there is a packed marrow, BMA is often inadequate. However in our study, a few cases of Chediak-Higashi syndrome, hemophagocytosis and myelodysplastic syndrome (MDS) could be diagnosed by BMA when there was inadequate BMB.

## Conclusion

The present study indicates that BMA and BMB are highly valuable diagnostic procedures in hematological and non hematologic disorders as well as in malignant and non malignant conditions. Though both the procedures were complimentary to each other, inadequate aspirates

due to disease conditions and faulty techniques are major drawbacks. BMB provided a histologic overview and was more accurate in diagnosing infiltrative conditions with an added advantage of performing IHC. Though painstaking, it is preferable to perform both the procedures simultaneously for a more conclusive diagnosis.

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