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Original Article

Pathology Section

Utility of Bone Marrow Cell Block in the Diagnosis of Haematological Disorders: A Cross-sectional Study

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ABSTRACT

Introduction: The examination of Bone Marrow Aspirate (BMA) smears and Biopsies (BMBx) are well established in the diagnosis of various haematological and non-haematological disorders. While both techniques have unique advantages over the other, they also have limitations that warrant the need for a method that integrates the benefits of both approaches but maximises sample utility. The examination of Bone Marrow Cell blocks (BMCB), akin to cell blocks from fine needle aspirates, may fulfil this need.

Aim: To evaluate the utility of the bone marrow cell block technique in various haematological disorders and to compare it with BMA smears and BMBx sections.

Materials and Methods: The present cross sectional study was conducted over a period of one year and six months (December 2017 and June 2019) in the Department of Pathology at Kempegowda Institute of Medical Sciences, Bangalore, Karnataka, India. There were 60 study subjects for whom bone marrow examination was advised by the clinicians. Bone marrow samples were procured from these 60 patients from whom 60 BMA smears, 51 BMCBs and 31 biopsies were obtained. Results from comparison of BMCB against BMA was divided into four categories based on the contribution of BMCB to the final diagnosis. With BMBx being the gold standard, BMCB was also evaluated against BMBx primarily based on Morphology with special stains for iron, reticulin as well as immunohistochemistry (CD3, CD20 and CD138). Data was tabulated and descriptive statistics, including means and percentages, were calculated. Cohen's kappa was employed to assess the strength of agreement between BMA/BMCB and BMCB/BMBx. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) software (version 23.0).

Results: A male to female ratio of 1:1 with a mean age of 47.3 years. A majority of the cases were non-neoplastic (46/51, 90.19%) of which 26/51 (50.98%) were anaemia of varying etiology; neoplastic disorders comprised of 9.8% (5/51), and a diagnosis could not be made in ten cases due to specimen inadequacy. BMCBs were comparable with BMA in 39.21%, improved the diagnosis in 27.45%, non-contributory in 33.33%. Overall, the BMCB was in agreement with 50% of the BMA smears ($p<0.001$), and with 54.8% of the BMBx ($p<0.001$). It was noted that utilising part of the first pull and adjusting the volume of the fixative improved the quality of BMCB.

Conclusion: The BMCB combines the morphologic clarity of an aspirate with the architectural details of a biopsy thereby maximising corroborative and diagnostic information. It is a resource effective, time-conscious technique that does not require special expertise and would be an invaluable addition to the examination of the bone marrow.

Keywords: Bone marrow studies, Bone marrow biopsy, Bone marrow aspiration, Clot section

INTRODUCTION

The examination of bone marrow(BM) is a time-tested method to diagnose various haematologic and non-haematologic disorders. Typically performed in the workup for unexplained fever, anaemia, Pancytopaenia, malignant haematological disorders, suspected bone marrow metastases and storage disorders [1].

As the procedure to obtain BM sample causes significant patient discomfort, the material procured is precious. Utilisation of the sample in the most efficient way possible is of paramount importance, not only to prevent repetition of the procedure but also to arrive at the most conclusive diagnosis.

Across literature, the bone marrow clot has been extensively examined [2,3,4] with studies by Ong MG et al [2] demonstrating its diagnostic value by integrating the benefits of aspirate and biopsy, which is in agreeance with various other studies [3-6]. However, amid numerous studies on clot sections, a dearth of research on BMCBs prompted the investigation of this technique and evaluation of its utility and efficacy.

BM aspirate (BMA) and BM biopsy (BMBx) are the common methods to study the BM. While both techniques offer unique advantages that improve diagnostic accuracy, they also have limitations [1] - the bone/stroma relationship is best observed on biopsy, while the BMA smear is the superior specimen to assess iron stores.Thus there is a need for a method that integrates the benefits of both approaches but maximises sample utility. The examination of BMCB, akin to cell blocks from fine needle aspirates, may fulfil this need.

MATERIALS AND METHODS

The present cross sectional study was conducted over a period of one year and six months (December 2017 and June 2019) in the Department of Pathology at Kempegowda Institute of Medical Sciences, Bangalore,Karnataka, India after obtaining the approval of Institutional Ethics Committee (KIMS/IEC/D-12/2017) There were 60 study subjects for whom bone marrow examination was advised by the clinicians. Bone marrow samples were procured from all 60 patients from whom 60 BMA smears, 51 BMCBs and 31 biopsies were obtained.

Study Procedure

With written consent, BMA and BMBx, using a Jamshidi biopsy needle (13G×3.5"),were obtained from the posterior superior iliac spine of all patients according to protocol. Imprint smears were made, and the remaining aspirate (1-2 mL) was collected in a K3-EDTA vacutainer (BD Vacutainer®) to create the BMCB.

BMCB sample was fixed in 10% neutral buffered formalin (NBF) (1:3-5 mL aspirate to formalin) and filtered using Whatman filter paper (No. 16). The aspirate particles were scraped off, collected into a small button, and transferred to a labelled filter paper for routine processing and paraffin embedding. The BMA smears were air-dried and stained with Leishman and May Grunwald-Giemsa stains. BMBx were decalcified in 10% EDTA (for two days with two changes), followed by routine processing for paraffin embedding. Sections from both, BMBx and BMCB, were cut at approximately 3-4 microns thick and stained with haematoxylin and eosin.

BMCB findings were compared with BMA smears and BMBx sections seperately, with BMBx being the gold standard. Since cell blocks are typically processed in cytology, categories were referenced from studies [7] on cell block techniques in fluid cytology to facilitate this comparison. The BMCB findings were organised into four categories for comparison with the BMA smears:

I.	Comparable	Provides similar information as BMA smear.
II.	Improves	Provides additional information.
III.	Non-contributory	Block could be made but no information could be obtained, (for e.g., only blood without particles.)
IV.	Inadequate	No block could be made.

BMCB and BMBx were assessed based on comparable parameters, including overall diagnostic value, cellularity, and cellular morphology. Additionally, various special stains (Perl's, reticulin) and relevant immunohistochemistry such as CD3, CD20 and CD138 were performed on BMCB to evaluate their feasibility.

STATISTICAL ANALYSIS

Data analysis was conducted using SPSS software (version 23.0). Descriptive statistics, including means and percentages, were calculated. Cohen's kappa was employed to assess the strength of agreement between BMA/BMCB and BMCB/BMBx. A p-value of <0.05 was deemed statistically significant.

RESULTS

The study group consisted of 60 patients for whom bone marrow studies were advised by their physicians. Sixty aspirates, 51 cell blocks, and 31 biopsies were obtained. Nine aspirates did not yield a cell block, these cases, while not included in the final analysis, have been mentioned in this study to understand certain technicalities, such as what factors prevented a cell block from being procured and how best to obtain an optimal cell block.

Easy fatigability was the primary presenting feature, which was noted in 34/51 patients (66.67%) as shown in [Table/Fig-1], and unexplained anaemia is the most common indication for bone marrow examination, accounting for 50.98% (26/51)as depicted in [Table/Fig-2]. Ages ranged from four to 78 years, with a mean age of 47.31 years and no gender preponderance.

Presenting complaint	Number of cases	Percentage
Easy fatiguability	34	66.67
Fever	23	45.09
Headache	1	1.9
Backache	8	15.6
Breathlessness	3	5.8
Joint pain	2	3.9
Ecchymoses/Petechiae	2	3.9
Pain abdomen	3	5.8
Generalised lymphadenopathy	1	1.9

[Table/Fig-1]: Distribution of cases according to presenting features (n=51).

Indications	Number of cases	Percentage
Anaemia	26	50.98
Pancytopaenia	10	19.6
Suspected myeloma	6	11.7
Thrombocytopenia	2	3.9
Lymphoma staging	1	1.9
PUO	4	7.8
Polycythaemia	1	1.9
Hypereosinophilia	1	1.9

[Table/Fig-2]: Distribution of cases according to indications for bone marrow study (n=51).

Analyses of BMCB versus BMA

Category I: Of the 51/60 cases in which a BMCB could be obtained, 20/51 (39.21%) were assigned to Category I as listed in [Table/Fig-3]. Megaloblastic anaemia accounted for 10 of the 20 cases, with both BMA and BMCB being diagnostic in all cases.

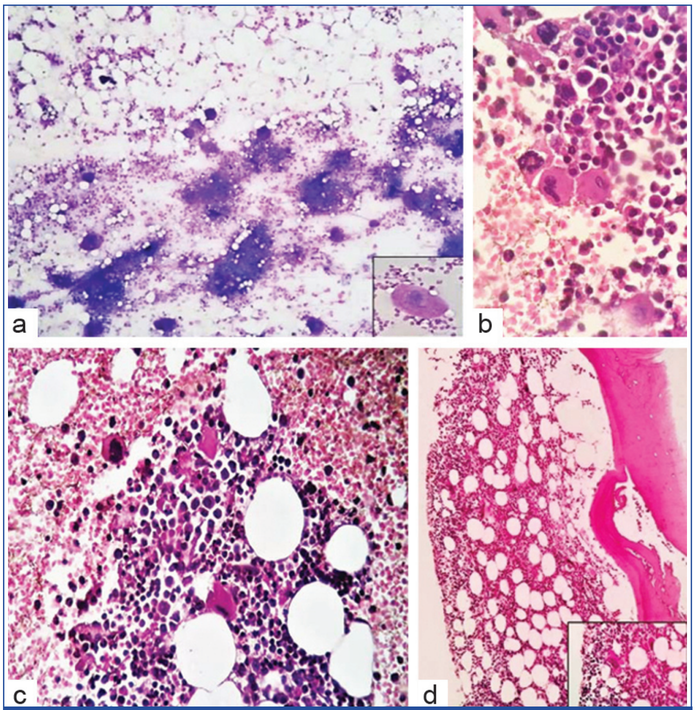
S. No.	Impression	Category I	Category II	Category III	Category IV	Total
1.	Normal marrow	0	3	2	2	7
2.	IDA	3	0	2	1	6
3.	Megaloblastic anaemia	10	2	0	0	12
4.	Dual deficiency	0	0	4	0	4
5.	Hypercellular marrow	1	0	0	0	1
6.	Hypoplastic marrow	0	2	2	1	5
7.	Myeloid hyperplasia	0	0	1	0	1
8.	Lymphoid hyperplasia	0	0	1	0	1
9.	Megakaryocytic hyperplasia	2	0	1	0	3
10.	Marrow Eosinophilia	1	1	0	0	2
11.	Reactive plasmacytosis	1	0	1	0	2
12.	TB-Marrow	0	0	1	0	1
13.	Hodgkins Lymphoma	1	0	0	0	1
14.	MDS	1	1	0	0	2
15.	Plasma cell dyscrasia	0	1	0	0	1
16.	Metastases to marrow	0	0	1	0	1
17.	Non-diagnostic	0	4	1	5	10
	Total	20	14	17	9	60

[Table/Fig-3]: Distribution of cases in their assigned categories in the analysis of BMCB vs BMA (n=60).
IDA: Iron deficiency anaemia

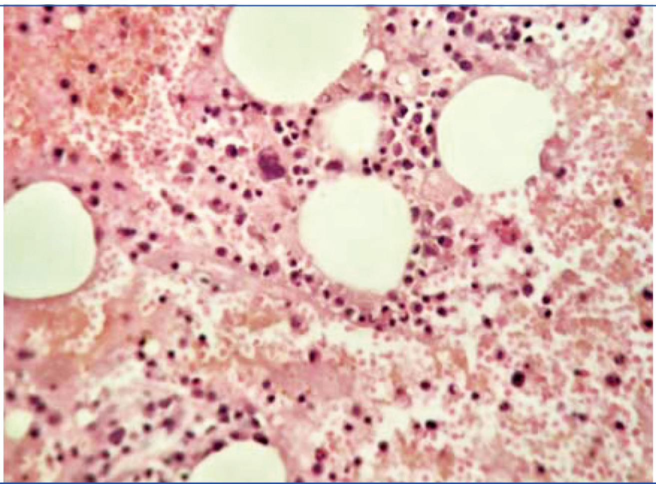
BMA smears were sufficient to make a diagnosis in all 6 cases of IDA, all of which showed decreased iron stores (1+). BMCB was comparable in 3/6 cases, non-contributory in two and inadequate in one case. Perls' stain revealed decreased iron stores (1+) on both BMA smears and BMCB sections.

Megakaryocyte hyperplasia was clearly observed in BMA smears, BMCB and BMBx, however megakaryocyte morphology was best appreciated in BMCBas seen in [Table/Fig-4a-d]. In one case of myelodysplastic syndrome, features of dysmegakaryopoiesis were observed in BMA smears, BMCB sections, and biopsy.

Reed-sternberg cells in a case of Hodgkin's lymphoma were more easily located in the BMCB due to the concentration of material in smaller areas, as depicted in [Table/Fig-5], in contrast to the BMA smears where they were occasional and often crushed during the smearing process.



[Table/Fig-4]: a) BMA in a case of megakaryocyte hyperplasia (MGG, 40x)(Inset: megakaryocyte, MGG, 400x); b) BMCB in megakaryocyte hyperplasia (H&E, 400x); c) BMCB showing clusters of immature megakaryocytes (H&E, 400x); d) BMBx (H&E, 100x) (Inset: Clusters of megakaryocytes, H&E, 400x).

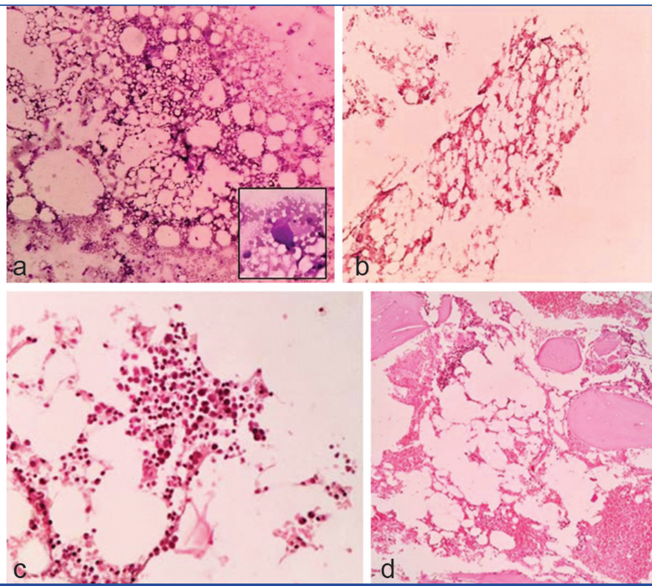


[Table/Fig-5]: BMCB in a case of Hodgkin's lymphoma with popcorn variant of Reed-Sternberg cell (H&E, 400x).

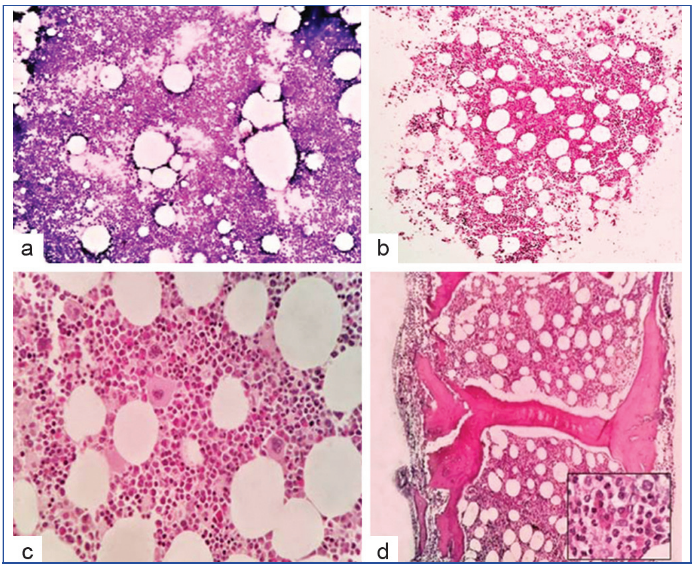
Category II: The BMCB improved the diagnosis in 14/51 cases (27.45%)– these cases are shown in [Table/Fig-3].

There were five cases with hypoplastic marrow of which two cases had enough particles to obtain BMCBs which showed hypocellular marrow as seen in [Table/Fig-6a-d], one was a dilute marrow with very few particles only hinting at a hypocellular marrow, and two aspirates were inadequate for evaluation. BMCB improved the diagnosis in two cases showing a hypocellular marrow and suppression of all lineages. A biopsy was done in four cases which confirmed the diagnosis.

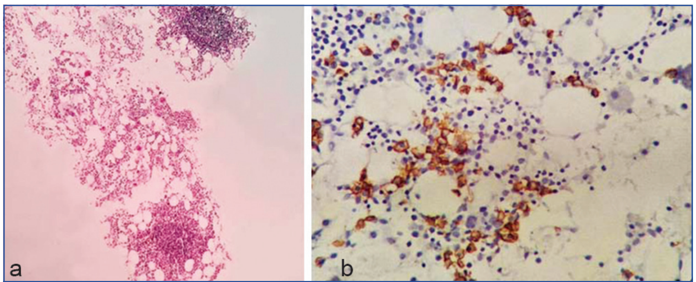
A case of marrow eosinophilia was diagnosed through BMCB, while the BMA smear did not reflect these findings, shown in [Table/Fig-7a-d]. In another case,as depicted in [Table/Fig-8a-b], the BMCB showed increased plasma cells and with immunohistochemistry (CD138) facilitated a diagnosis of plasma cell dyscrasia, when a BMBx could not be procured. Atypical megakaryocytes were also more easily detected in the BMCB, raising suspicion of MDS, which was confirmed by BMBx.



[Table/Fig-6]: a) Hypocellular BMA in a case of MDS (MGG, 40x) (Inset: Dysplastic megakaryocyte, MGG, 400x); b) Hypoplastic BMCB in a case of MDS (H&E, 100x); c) BMCB showing groups of megaloblasts (H&E, 400x); d) BMBx in a case of MDS (H&E, 100x).



[Table/Fig-7]: a) Hypercellular marrow with normoblastic maturation on BMA (MGG, 40x); b) Hypercellular marrow with eosinophilia on BMCB (H&E, 100x); c) Groups of eosinophils on BMCB (H&E, 400x); d) BMBx showing marrow eosinophilia (H&E, 40x) [Inset: Groups of eosinophils (H&E, 400x)].



[Table/Fig-8]: a) Hypocellular marrow with lymphoid follicles BMCB (Category II) (H&E, 100x); 8b) Immunohistochemistry for CD138 on BMCB showing strong membranous positivity (400x).

Category III: A total of 17/51 cases (33.34%) were deemed non-contributory and showed predominantly sinus blood and scattered cells that were insufficient for a conclusive diagnosis.The impressions drawn from the BMA and BMBx counterparts of these cases are elaborated in [Table/Fig-3].

Category IV: A total of 9/60 cases were classified as inadequate, meaning no block could be formed. These cases were included to explore the technical aspects and identify the causes that hindered adequate block formation.

The two methods (BMA and BMCB) showed agreement in 50% of the cases. There was moderate agreement between the two techniques, which was statistically significant (Cohen's Kappa=0.408, p<0.001).

Analyses of BMCB versus BMBx

Among the 31 cases with an accompanying biopsy, BMCB was diagnostic in 18 cases (58.06%) and non-diagnostic in 13 cases (41.93%) as depicted in [Table/Fig-9].

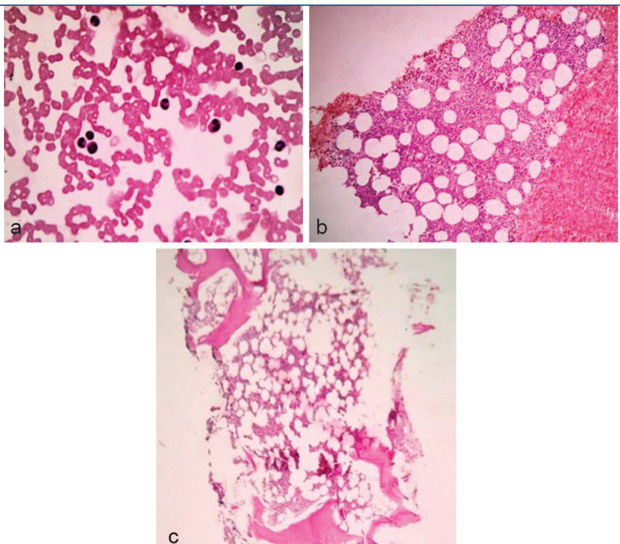
Sl. No.	Impression	Diagnostic category	Non-diagnostic category	Total
1.	Normal marrow	4	4	8
2.	Megaloblastic anaemia	6	0	6
3.	IDA	2	2	4
4.	Hypoplastic marrow	1	3	4
5.	Megakaryocytic hyperplasia	1	1	2
6.	Myeloid hyperplasia	0	1	1
7.	Lymphoid hyperplasia	0	1	1
8.	TB-Marrow	0	1	1
9.	Marrow Eosinophilia	1	0	1
10.	Hodgkin lymphoma	1	0	1
11.	MDS	2	0	2
	Total	18	13	31

[Table/Fig-9]: Distribution of cases in their assigned categories in the analysis of BMCB vs BMBx. (n=31).

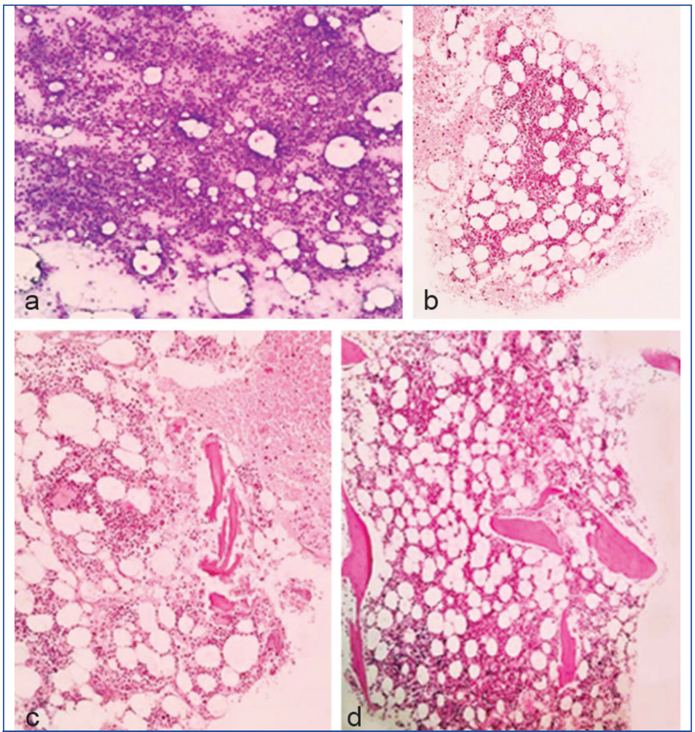
The cellularity of all BMCB specimens in the diagnostic category was comparable to that of their biopsy counterparts shown in [Table/Fig-10a-c] and [Table/Fig-11a-e]. Cytological details, such as the granules of eosinophils and nuclear details indicating dyserythropoiesis, were clearer and more discernible in the BMCB. Abnormal Localisation of Immature Precursors (ALIP) was observed in one case on the biopsy, underscoring the key advantage of biopsy in illustrating the bone/stroma relationship. Stains for reticulin fibres was performed on the BMBx and BMCB of one case and demonstrated excellent visualisation of reticulin fibres on the BMCB, as seen in [Table/Fig-12].

Thirteen cases were classified as non-diagnostic for the cell block. Among these, 10 showed only blood with scattered cells, while the aspirate in three cases did not yield a block at all.

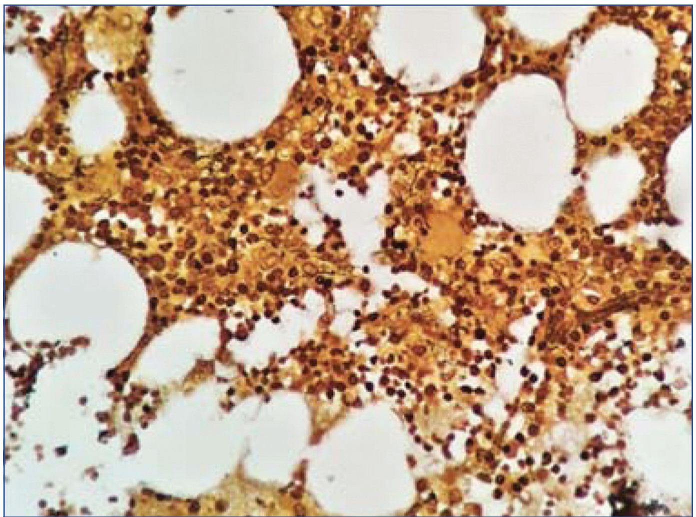
The two methods (BMBx and BMCB) showed agreement in 54.8% of the cases, with moderate agreement between them. This agreement was statistically significant (Cohen's Kappa=0.502, p<0.001).



[Table/Fig-10]: a) Dilute marrow on BMA (Leishman, 400x); b) Normocellular marrow on BMCB (Category II) (H&E, 100x); c) BMBx - Normal bone marrow study (H&E, 40x).



[Table/Fig-11]: a) Hypercellular marrow on BMA (MGG, 40x); 11b) Normocellular marrow particle on clot section (H&E, 100x); 11c) Normocellular marrow with bony spicule on BMCB (Category II) (H&E, 40x); 11d) Normal bone marrow study on BMBx (H&E,40x).



[Table/Fig-12]: Reticulin stain on BMCB (2+) (400x).

DISCUSSION

BMA and BMBx are established techniques with several advantages, but they also have specific disadvantages that highlight the need for a method that bridges the gap between them. This prompted investigation of the BMCB technique and its comparison with BMA smears and BMBx, allowing assessment of its utility in enhancing diagnostic yield. There appears to be a dearth of articles on BMCB in English literature, although "clot sections" of BM have been studied [2,4,8,9]. After evaluating various methods for preparing clot sections, [2,4,8,9] the modified "particle clot section" method (described in Wintrobe's Clinical Haematology [8] was chosen due to its minimal turnaround time and maximum particle concentration. This method does not utilize a fixative and so, the fixation method followed by Ong et al. [2] was adopted i.e., fixation in 10% NBF.

An extensive review of the English literature revealed a lack of articles focused on the bone marrow cell block and its role in diagnosing haematological disorders, making it difficult to compare the results of the current study with others. An attempt was then made to compare the findings with those published by authors [2-6,9,10] who studied the utility and role of bone marrow clot sections.

Consistent with the findings of Liao KT et al. [6] and Al-Diab JM al., [5] anaemia (50%) and pancytopaenia (20%) were the most common indications for BM examination.

Among the 60 cases, there were 45 non-neoplastic disorders, and five neoplastic disorders, that are described and compared with other studies[5,11,12] in [Table/Fig-13]. Ten cases could not be offered a diagnosis due to specimen inadequacy.

Diagnosis	Al-Diab JM et al[5] 2016, (n=114)	Atla B et al[11], 2015, (n=105)	Mahajan V et al[12], 2013, (n=460)	Present study (n=51)
Normal marrow	56.14	3.8	22	11.67
Hypoplastic marrow	7.9	-	5	8.34
Anaemia	0.88	49.5	33.26	36.67
Hypercellular marrow	-		8.9	1.67
Myeloid hyperplasia	-	-	-	1.67
Megakaryocyte hyperplasia	2.64	6.7	0.2	5
Marrow eosinophilia	-	-	-	3.34
Reactive plasmacytosis	-	-	-	3.34
Tuberculosis - marrow	-	-	2.3	1.67
Lymphoid hyperplasia	1.76	-	-	1.67
Hodgkin’s lymphoma	-	2.9	-	1.67
Plasma cell dyscrasia	3.51	4.7	4.3	1.67
MDS	4.39	0.9	1.08	3.34
Metastases	0.88	-	0.6	1.67
Non-diagnostic	-	-	1.3	16.67

[Table/Fig-13]: Distribution of cases according to impression and comparison with other studies.

Analyses of BMCB versus BMA

Megaloblastic anaemia was the most prevalent type among anaemias. Both BMA and BMCB were diagnostic in all 12 cases. A diagnosis of Iron Deficiency Anaemia (IDA) can usually be made through peripheral blood findings and biochemical tests [13] and while the gold standard remains the analysis of iron stores on an aspirate smear[14] it was found that Perls’-stained BMCB sections and biopsies were comparable to the smears. Since BMBx can add to patient discomfort, iron stains on BMCB can be particularly useful, especially when aspirate smears are inadequate [15,16] as observed in this study.

BMBx is superior to aspirate smears for diagnosing aplastic or hypoplastic marrows [17]. However, some studies [6,9] noted that both BMA smears and clot sections were sufficient in themselves to accurately diagnose cases of hypoplastic marrow. Superior architectural details of an adequate BMCB as seen in this study demonstrated that it could be as valuable as a BMBx in cases of hypoplastic or aplastic marrows pictured in [Table/Fig-6b].

The BMCB showed similar success in the analysis of megakaryocyte number and morphology. A presumptive diagnosis of immune thrombocytopaenic purpura (ITP) was made in three cases with megakaryocyte hyperplasia, supported by relevant clinical and haematological findings. While BM studies are not required for managing ITP according to the American Society of Haematology, [18] they can be valuable in differentiating ITP from conditions such as essential thrombocythemia, chronic myeloid leukaemia, primary myelofibrosis, and AML-M7 [19] particularly when atypical features are present [8].

BMCB was also found to be useful in cases of marrow eosinophiliashown in [Table/Fig-7a-d]. The present study included two cases of eosinophilia-one with an absolute eosinophil count (AEC) of 1188/µL and another with an AEC of 8850/µL. The morphology of individual cells in BMCB was comparable to that in BMA smears, aiding in the exclusion of malignancies associated with eosinophilia, such as chronic myeloid leukaemia, chronic lymphocytic leukaemia, and chronic eosinophilic leukaemia [20-22].

BM examination can aid in distinguishing reactive plasmacytosis from neoplastic processes [5]. The BMCB of marrow plasmacytosis displayed clear morphology of plasma cells, along with the advantage of illustrating their distribution pattern. Two cases suspected of myeloma, presenting with easy fatigability and backache, showed increased plasma cells in BMA smears. One BMCB was diagnostic, while the other was non-contributory, with no atypical cells observed. Research indicates that clot sections outperform aspirate smears in diagnosing multiple myeloma [23,24].

Additionally, BMCB can serve as a reservoir for IHC. Several studies highlight the use of clot sections in IHC, due to the lack of decalcification resulting in better antigenic retrieval [2,9,24]. The BMCB proved valuable in one case, as it revealed increased plasma cells in the BMCB, and in the absence of a BMBx, it provided material for performing CD3, CD20 and CD138 staining, as demonstrated in [Table/Fig-8a-b].

Many studies[4,6,10,25] have highlighted the use of clot sections in cases of lymphoma, suggesting that BMCB could be equally useful. In a case of Hodgkin's lymphoma, Reed-Sternberg cells were more easily identified in the BMCB due to the concentration of material in smaller areas. The BMCB sections were stained for CD15 and CD30, however, extensive non-specific staining of background cells was noted. Sub-optimal quality of the block in this case could explain the background staining.

BMCB maintains antigenic fidelity and can aid in confirming the diagnosis probably without the need for antigen retrieval as there is minimal formalin exposure. However, increased red cells in the BMCB may give rise to background staining as was noted in the above case, highlighting the need for refinement of the technique.

Granulomas are more readily appreciated in biopsies and clot sections compared to aspirate smears. Other studies [2,3,6] have found the clot section to be superior to BMA smears. The present study included one case of pyrexia of unknown origin with suspected tuberculosis. The BMA showed a few epithelioid cells, while the BMBx revealed vague granulomas, which were confirmed to be tuberculosis by ZN stain for AFB. Due to dilute marrow, a good BMCB could not be prepared, highlighting some of the technical challenges.

The use of BMCB in Myelodysplastic Syndromes (MDS) can be complex. In this study, a 62-year-old male exhibited dysmegakaryopoiesis on BMCB, findings which were confirmed on BMBx. The architectural layout of the BMCB resembled that of the BMBx, and the clustering of megakaryocytes in small areas facilitated the identification of dysmegakaryopoiesis, aligning with observations by Uniya U et al. [9] However, in another case the BMBx revealed paratrabecular localisation of megakaryocytes suggestive of abnormal localisation of immature precursors (ALIP), which was not visible in the BMCB. This case highlights a significant limitation of the BMCB: its inability to demonstrate the parenchymal/bone relationship.

BMCB versus BMBx

In this study, 31 cases had an accompanying biopsy, BMCB was diagnostic in 18 cases (58.06%) and non-diagnostic in 13 cases (41.93%).

Among the cases where BMCB was obtained, seven marrows were normocellular, nine were hypercellular, and two were hypocellular. The cellularity observed in the BMCB was comparable to that in the biopsy across all cases, aligning with findings from various studies.[2,9,10,15] BMCB is particularly useful in cases of hypocellular marrows as shown in [Table/Fig-6a-d], consistent with studies by Uniya U et al.[9] Conversely, Cotelingam JD et al.[3] view the clot section to be less reliable unless multiple clot sections with several marrow particles are evaluated. Thus, BMCB combined with BMA can serve as an effective complementary tool for assessing bone marrow cellularity, particularly when BMBx is not feasible.

Cellular morphology is better appreciated in BMCB than in BMBx, but it does not reach the gold standard set by aspirate and touch preparations [2,3]. This may be due to the fact that BMCB does not require prolonged formalin fixation or decalcification, which can cause shrinkage artifacts and adversely affect nuclear proteinsleading to decreased dye uptake by nuclear chromatin and suboptimal staining [26,27]. However, this issue primarily arises with acid decalcifiers rather than chelating agents, whose slow, gentle process does not appear to affect tissue staining properties, as observed inthisstudy.

Stains for reticulin fibers can be conducted on BMCBs, but less reliably so than on biopsies, which are the preferred specimens [2,3] due to the challenges in aspirating collagen fibers [3]. In one case, reticulin staining on both BMBx and BMCB were performed,and it was found that the BMCB exhibited well-discernible reticulin fibers demonstrated in [Table/Fig-12].

Analyses of BMCB technique

The quality of the aspirate significantly impacts the cell block preparation. In this study, material from the first pull was used for aspirate smears, while the second pull was used for the BMCB. The second pull was likely to have been contaminated by sinus blood resulting in the 'non-contributory' and 'inadequate' cases that were observed. Splitting the aspirate pulls is recommended, using half for smear preparation and the other half for the cell block.

The volume of fixative also influenced the quality of the resulting block. Following the protocol by Ong MG et al. [2], initially 5mL of fixative was used, which seemed to dilute the marrow and caused the entire specimen to filter through the paper. It is recommended that the fixative volume should be adjusted based on the volume and quality of the aspirate and it appears that 2-5mL of 10% NBF is ideal.

The BMCB proves to be particularly valuable in non-neoplastic disorders where biopsies are typically not performed, such as megaloblastic anaemia, IDA, and ITP [9]. However, it has limitations and should be used complementary to BMA smears and biopsy sections. In certain cases-such as when a biopsy is immediately unavailable [10], technical difficulties arise, or in hematological malignancies requiring multiple follow-up examinations [10,28]-the BMCB may serve as a suitable substitute for a biopsy.

Liao KT et al. [6] emphasized the ease of preparing a clot section and its advantage in assessing the distribution pattern of cells-information not obtainable from an aspirate smear.

Many studies [4,29] suggest that BMBx remains the superior specimen, with Barekman CL et al. [29] noting that the clot section's primary value lies in its corroborative role.

Anner RM et al. [30] and other studies [2,3,9,10,24] stress the utility of clot sections for storing material for ancillary tests that enhance histological diagnosis. Additionally, clot sections and cell blocks offer advantages like eliminating the need for extra analgesia, improving patient comfort, [5,10] and reducing turnaround time [10]. These advantages play a role particularly in cases that require frequent sampling of bone marrow.

At present, literature on BMCB is limited, with most studies focusing on clot sections. Both techniques share similar advantages and disadvantages: they are easy to obtain, storable, and suitable for various tests. It appears that the main difference is that clot sections have lower particle concentration and higher sinus blood contamination. While neither can truly replace an aspirate smear or a trephine biopsy, their value as a complementary test lies in their ability to provide corroborative information and augment diagnostic yield.

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