

## Spectrum of Haematological & Non Haematological Disorder Diagnosed by Bone Marrow Examination: A Study of 115 Cases

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### Abstract

**Introduction:** Haematological and nonhaematological diseases affecting the bone marrow may be primarily or a secondarily spread to the marrow. In most of the cases, diagnosis can be arrived at by a detailed history, physical examination and few simple investigations. Bone marrow examination is a very useful tool in the diagnosis of hematological and non-hematological diseases. **Materials and Methods:** This retrospective study was done in the department of haematology, in a specialized diagnostic centre from July 2018 to July 2021. A total of 115 cases were included in this study. Clinical parameters were assessed, peripheral blood smear along with necessary haematological investigations were done. **Results:** Majority patient were male (70%). In total cases 44.4% patients were under 30 years of age. Among them 23(20%) were under 10 years. The most common indication for bone marrow examination was diagnosis & management of Acute Leukaemia 27(23.48%), Major presenting complaints were fever 49(42.61%), fatigue 46(40.0%) & bleeding manifestation 22(19.13%). On systemic examination, pallor was found in majority of the cases. Hematological malignancies were found in 77(66.96%) cases, non-malignant haematological disorders were found in 33(28.70%) cases. Acute leukaemic condition (ALL, AML) were the most common malignant conditions, 22(19.13%) & 17(14.78%) respectively. Most common nonmalignant haematological conditions were hypocellular marrow 17(14.78%). **Conclusion:** Acute Leukemia is a major indication of BME. Among the pathological condition malignant condition are commonly seen. And male are predominantly suffering more from haematological disorders than female. In majority cases acute leukaemic condition are seen in BME.

**Keywords:** Haematological, Non haematological disorders, Bone marrow examination.

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### Introduction:

Bone marrow examination (BME) plays an important role in diagnosis of hematological as well as non-hematological disorders. It is a simple and safe procedure and the particularly useful in the investigation of pyrexia of unknown origin as it leads to an etiological diagnosis in most of the cases<sup>1</sup>.

Haematological and nonhaematological diseases affecting the bone marrow may be primarily or a secondarily spread to the marrow. In both cases the normal marrow cellular architecture is damaged or displaced. The pattern of disorders affecting the marrow is quite different in developing countries than from developed countries<sup>2</sup>. In most of the cases, diagnosis can be arrived at by a detailed history, physical examination and few simple investigations. But in certain cases bone marrow examination is required for the confirmation of diagnosis.

Bone marrow is involved in variety of hematological and non-hematological disorders. The hematological disorders include acute leukemia, myeloproliferative neoplasm (MPN), hemato-lymphoid neoplasm, nutritional deficiency diseases. On the other hand nonhematological disorders include infectious diseases infiltrating the bone marrow such as tuberculosis, parasitic infections and metastatic deposits<sup>3</sup>.

Haematological disorders usually presents with anemia in any age group. Anemia is common worldwide and particularly so in developing countries<sup>4</sup>. The spectrum of haematological disorders is relatively different in developing world than the developed countries<sup>5</sup>. There is a wide spectrum of diseases revealing bone marrow changes. Majority of these disorders present with vague clinical symptoms and poses difficulty for clinicians in the diagnosis based on complete

blood picture and peripheral film only; necessitating the use of bone marrow aspiration and examination for diagnosis<sup>6</sup>.

BME evaluation may either confirm clinically suspected diseases or may provide the previously unsuspected diagnosis<sup>7</sup>. It is usually sufficient individually to diagnosed nutritional anemia, Acute leukemia's, myelodysplasia, myeloma and parasitic infections<sup>8</sup>. It allows excellent morphologic evaluation of cells, differential count and myeloid to erythroid ratio. It gives an assessment of hematological activity; deviation from the normal may be qualitative with abnormal cellular morphology or quantitative with presence or absence of iron stores as evaluated by Prussian blue staining<sup>9</sup>.

BME is an invasive procedures performed by trained individuals using standard techniques and allow cytologic, immunophenotypic, cytogenic, molecular assessment and other specialized investigations. It should be done with great care in infants and neonates<sup>10</sup>. Before performing bone marrow aspiration full thorough study of tests already performed should be made<sup>11,12</sup>. For proper diagnosis along with BME complete clinical history, careful physical examination for clinical findings, complete haemogram (complete blood count, peripheral blood picture), and other laboratory investigations are required<sup>13,14</sup>. These results might be helpful for clinicians in selecting cases of bone marrow biopsy as numbers of patients are referred by them in a tertiary care hospital<sup>15</sup>.

Rationale of the study was to find out the common indications, in addition ascertain the etiological spectrum of disorders on bone marrow examination which will guide the clinicians about the frequency of hematological and non-hematological disorders and their management in a clinical setup.

#### Materials and Methods:

This retrospective study was done in the department of haematology, in a specialized diagnostic centre from July 2018 to July 2021 at Chattogram. A total of 115 cases were included in this study. Clinical parameters were assessed, peripheral blood smear along with necessary haematological investigations were done. Bone marrow aspiration was done thereafter. Patient's age, sex, clinical details including history, physical examination findings & investigation findings were taken from report sheet.

#### Peripheral Smear Preparation and Staining

Peripheral Smear was prepared and stained according to the guidelines in Practical Hematology, Dacie and Lewis, 10th Edition<sup>16</sup>.

#### Bone Marrow aspiration<sup>17</sup>

Under aseptic measures aspiration was done through posterior iliac crest. The patient was placed in a prone position, a pillow under their head. Lidocaine was used as the anaesthetic, providing the patient has no history of an allergic reaction to this medication. During this process, local anaesthetic is first infiltrated into the skin and subcutaneous tissue to anaesthetize an area approximately 1 cm. in diameter. After the skin is numb, lidocaine is infiltrated directly over the periosteum to numb an area approximately 2-3 cm in diameter. Salah needle is

advanced with steady pressure and a slight twisting motion to the center of the posterior iliac prominence. The needle was rotated back and forth (90o-180o) and careful pressure was applied to advance the needle through the cortical bone. A decreased resistance indicated penetration of cortex and entry into the marrow cavity. Needle was advanced about 1 cm into the marrow cavity. The obturator was unlocked and slowly removed 0.3 ml of marrow fluid was aspirated into a 10 ml syringe and specimen slides were prepared. A folded piece of gauze was placed over the site with a pressure bandage. The patient was asked to lie supine for at least 30 minutes.

#### Steps of preparing aspirated smear and staining methods<sup>16</sup>

Aspirate slides were stained with leishman stain. Perls stain for iron stores was done in all cases. Complete blood count (CBC), peripheral smear examination (PBF) was done in all cases.

#### Inclusion & Exclusion Criteria

All the cases that were referred for bone marrow examination and also for staging of haematological malignances and staging were included in this study. Children below 1 year of age were excluded.

#### Method of data processing & statistical analysis

Statistical analysis using descriptive statistic was done. All quantitative values were presented as mean  $\pm$  SD for continuous data and as percentages for categorical data. Qualitative data were presented as frequency and percentage. Quantitative data was analyzed by student's t-test. All tests were two-tailed and statistically significant results will be considered when p value  $<$  0.05. All statistical operations were analyzed by SPSS version 20 and Micro-soft Excel 10.

#### Results:

A total of 115 patients, aged between 2 to 80 years. Majority patient were male 80(70%) with M:F ratio of 2.3:1 (figure 1).

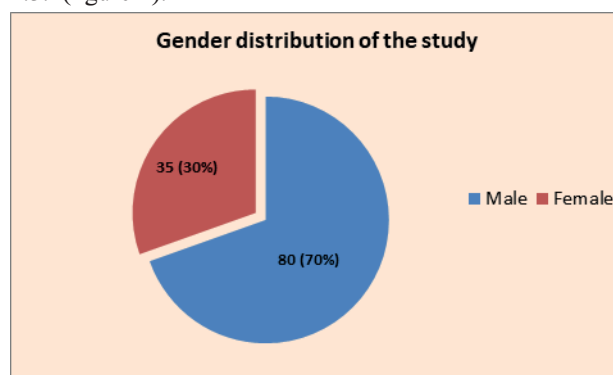


Figure 1: Gender Distribution of the study.

Mean age of the study population was  $38.23 \pm 25.18$ , and there was no statistically significant difference of ages between male & female ( $p=0.442$ ). In this present study, the age group of the patients was from 2 to 80 years. The Maximum numbers of the cases (20%) were in the age group of 1-10 years. In total cases 44.4% patients were under 30 years of age (Table I).

**Table-I: Distribution of the cases according to age & sex.**

Age	Male	Female	Total	%
1-10	17	6	23	20.0
11-20	11	3	14	12.2
21-30	10	4	14	12.2
31-40	4	3	7	6.1
41-50	7	5	12	10.4
51-60	11	5	16	13.9
61-70	12	5	17	14.8
71-80	8	4	12	10.4
<b>Total</b>	<b>80</b>	<b>35</b>	<b>115</b>	<b>100.0</b>
Mean±SD	37.03±25.46	40.97±24.66	38.23±25.18	P= 0.442
Min-Max	2-80	3-80	2-80	

The most common indication (according to PBF findings) for bone marrow examination was diagnosis & management of Acute Leukaemia 29(25.22%). Other findings were anaemia for evaluation 24(20.87%) & Pancytopenia 21(18.26%) cases, Bicytopenia 14(12.17). Haematological findings are summarized in table II.

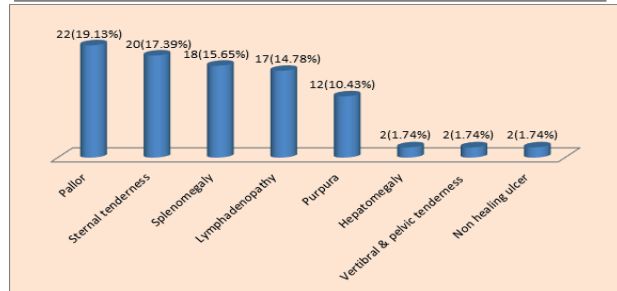
**Table-II: Indication of bone marrow study (according to PBF findings).**

Indication for Bone Marrow Examination	n	%
Diagnosis & management of Acute Leukaemia	29	25.22
Anaemia for evaluation	24	20.87
Pancytopenia	21	18.26
Bicytopenia	14	12.17
Diagnosis & management of CML	9	7.83
Leuko erythroblastic blood picture	7	6.09
Diagnosed Leukaemia with remission status	3	2.61
Thrombocytopenia	2	1.74
Leukocytosis	1	0.87
Multiple Myeloma	1	0.87
Myeloproliferative disorders	1	0.87
Rouleaux formation	1	0.87
Eosinophilia	1	0.87
Cutaneous T-cell lymphoma	1	0.87
<b>Total</b>	<b>115</b>	<b>100.00</b>

The clinical presentation of the cases varied from fever, fatigue and bleeding manifestation to non-specific symptom like neck swelling (Table III).

**Table-III: Clinical presentation of the cases including in the study.**

Indication for Bone Marrow Examination	n	%
Fever	49	42.61
Fatigue	46	40.00
Bleeding manifestation	22	19.13
Body ache/Bone pain	20	17.39
Generalized weakness	18	15.65
Back pain	14	12.17
Abdominal pain/Distention/Discomfort	11	9.57
Weight loss	7	6.09
Cough/Breathless	4	3.48
Vomiting/diarrhea	2	1.74
Lower limb pain	2	1.74
Neck swelling	1	0.87



**Figure 2: Clinical findings of the cases including in the study.**

Major presenting complaints were fever 49(42.61%), fatigue 46(40.0%), Bleeding manifestation 22(19.13%), Body ache/Bone pain 20(17.39%), Generalized weakness 18(15.65%). Other minor presenting complaints included back pain, abdominal pain/distention/discomfort, weight loss, Cough/Breathless. On systemic clinical examination, pallor was the commonest finding, seen in 22(19.13%). Other significant findings were sterna tenderness in 20(17.39%), splenomegaly in 18(15.65%), lymphadenopathy in 17(14.78%) (Figure 2).

On bone marrow examination, hematological malignancies were found in 77(66.96%) cases, non-malignant haematological disorders were found in 33(28.70%) cases. Acute leukaemic condition (ALL, AML) were the most common malignant conditions, 22(19.13%) & 17(14.78%) respectively. The next common malignancies in this study were Chronic myelogenous leukaemia (CML) and Plasma cell dyscrasia (PCD) both were 11(9.57%), there was 4(3.48%) cases of ALL under remission. Most common nonmalignant haematological conditions were hypocellular marrow 17(14.78%), Erythroid hypoplasia 6(5.22%) and myeloid hyperplasia 5(4.35%). All haematological findings are seen in table IV.

**Table-IV: Distribution (Bone marrow examination) of haematological disorders according to age & sex.**

Malignant Haematological Disorders											
	1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	M:F	Total Cases	%
ALL	8	6	5	3	-	-	-	-	13:9	22	19.13
AML	4	3	1	1	1	4	3	-	12:5	17	14.78
CML	2	-	3	-	3	2	1	-	8:3	11	9.57
PCD	-	-	-	-	1	4	3	3	8:3	11	9.57
MDS	1	1	-	-	2	-	2	1	6:1	7	6.09
AL	1	-	-	-	-	-	1	-	2:0	2	1.74
MPD	-	-	1	-	-	-	-	1	1:1	2	1.74
Cutaneous T-cell lymphoma	-	-	-	-	-	-	-	1	1:0	1	0.87
ALL in remission	4	-	-	-	-	-	-	-	4:0	4	3.48
<b>Total no. of cases</b>										<b>77</b>	<b>66.96</b>
Non-Malignant Haematological Disorders											
	1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	M:F	Total Cases	%
Hypocellular Marrow	1	3	1	1	2	4	3	2	12:5	17	14.78
Erythroid Hypoplasia	-	-	2	-	1	-	1	2	4:2	6	5.22
Myeloid Hyperplasia	-	-	1	1	1	1	-	1	2:3	5	4.35
Megaloblastic erythroid heperplasia	1	-	-	-	-	-	1	-	1:1	2	1.74
Megakaryocytic hyperplasia	-	1	-	-	-	-	-	-	1:0	1	0.87
ITP	1	-	-	-	-	-	-	-	1:0	1	0.87
Active marrow with dysplastic change	-	-	-	1	-	-	-	-	1:0	1	0.87
<b>Total no. of cases</b>										<b>33</b>	<b>28.70</b>



Total 3(2.61%) of non-haematological cases were seen in this study, all were Secondary metastatic deposition (Table V).

**Table-V: Distribution (Bone marrow examination) of non-haematological disorders according to age & sex.**

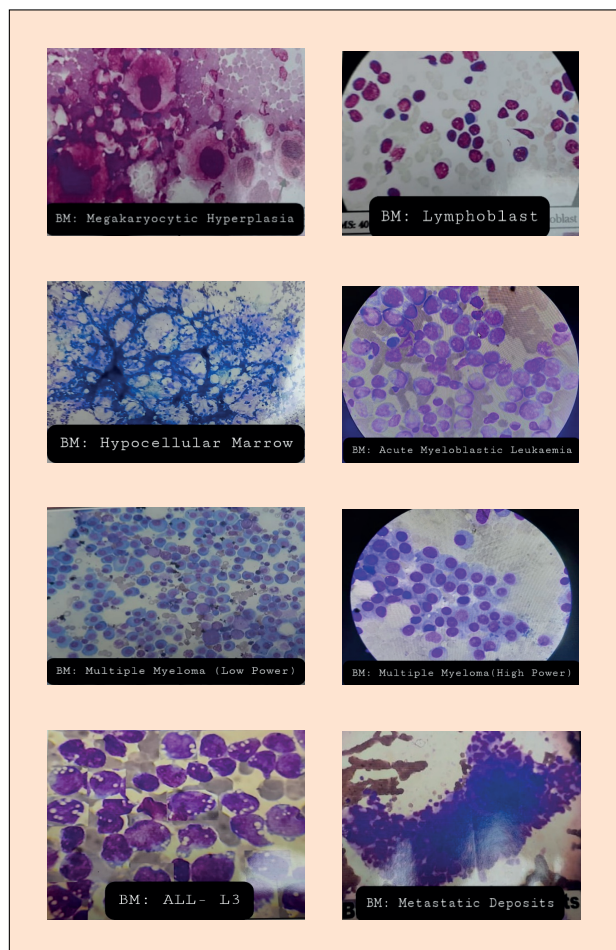
	Non Haematological Disorders								M:F	Total Cases	%
	1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80			
Secondary (Metastatic deposition)	-	-	-	-	1	1	1	-	3:0	3	2.61

The present study also encountered a single case of Normal study and inadequate sample respectively (Table VI).

**Table-VI: Distribution of other haematological conditions according to age & sex.**

	Distribution of other haematological conditions								M:F	Total Cases	%
	1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80			
Normal study	-	-	-	-	-	-	1	-	0:1	1	0.87
Inadequate Sample (Blood tap only)	-	-	-	-	-	-	-	1	0:1	1	0.87

Pictograms of different findings of bone marrow studies are shown in figure 3.



**Figure-3: Pictograms of different findings of Bone Marrow examination.**

## Discussion:

Bone marrow is one of the most widely distributed organs of the body. It is the principle site of haematopoiesis. BME is safe invasive procedure that can be done to arrive at a final diagnosis in certain haematological disorders. It helps to evaluate cytopenias, thrombocytosis, leukocytosis, anemia and iron status. It is also a diagnostic tool in nonhaematological disorders such as storage disorders and systemic infections. It is an ambulatory procedure performed under local anaesthesia with minimum morbidity.

In the present study, out of 115 cases there were 80(70%) males and 35(30%) females. Male: Female was 2.3:1. Which was almost similar to the study of Kumar V et al.<sup>1</sup> In most of the studies we found that, male are predominantly suffering more from haematological disorders than female<sup>1,8,13-15,18-20</sup>. But in the study of Munir AH et al. that was conducted in Peshawar- majority patients were female<sup>11</sup>. The age of the patients who underwent BME ranged from 2-80 years which is similar with the study of Chowdhury MRK<sup>2</sup>. The mean age of the study population was 38.23 years, almost similar with Atchya M et al.<sup>18</sup> In our study commonest group of patients were very young 1-10 years (20%), instead in other studies commonest patient were in above 30 years group (between 31-50)<sup>2,13,18</sup>.

In our study most common indications for BME examination were Diagnosis & Management of Acute Leukaemia (n-27, 23.48%), Anaemia (n-24, 20.87%) pancytopenia (n-21, 18.26%) and Bicytopenia (n14, 12.17%). This is also similar to that of the studies done by Chowdhury MRK et al.<sup>2</sup> Qahtani AS<sup>15</sup> Pudasaini S<sup>21</sup>. However pancytopenia was the first common indication in the study done by Sudhakar G<sup>13</sup>.

Major presenting complains of this study were fever 49(42.61%), fatigue 46(40.00), Bleeding manifestation 22(19.13), Body ache/Bone pain 20(17.39%), Generalized weakness 18(15.65%). Fever was also the prime symptom of the study of Kumar V<sup>1</sup>. On systemic clinical examination, pallor was the commonest finding seen in 22(19.13%) cases. Which is also similar with the study of Ali I<sup>9</sup>. Instead splenomegaly was the commonest finding in the study of Kumar V<sup>1</sup>.

In the present study 113(98.261%) of the marrow was pathological and 2(1.793%) were normal. Among the pathological condition malignant condition was more common 80(69.57%) than non-malignant 33(28.70%). Malignant haematological conditions were 77(66.96%). In the study of Chowdhury MRK<sup>2</sup> 33.55% of their patients had non-malignant haematological conditions while 47.37% had haematological malignancies. From our study we found that in comparison with non malignant haematological disorders, malignant haematological conditions are more common, among these Acute leukaemia is predominant<sup>8,10,11,15,18,21-22</sup>. But in the study of Sudhakar G<sup>13</sup> malignant haematological disorders were present in 20.05% cases and non-malignant haematological disorders were present in 70.18% cases. Erythroid hyperplasia was the

commonest diagnosis in the study of Bashir N et al<sup>14</sup>. Out of 77 malignant haematological conditions acute leukaemia was 41(35.65%). Among the acute leukemia, acute lymphoblastic leukaemia (ALL) was 22(19.135) and acute lymphoblastic (AML) was 17(14.78%). Chowdhury MRK et al<sup>2</sup> also reported 14.47% of AML, that is almost similar with our study. The common age group among AML group were 1-10 years and 51-6- years with M:F ratio of 2.4:1. In ALL common group was 1-10 years with M:F ratio of 1.44:1. In CML common group was 21-30 years and 41-50 years with M:F ratio of 2.67:1. In the study of Atchyuta M et al.<sup>18</sup> the common age group in AML was 51-60 years with M:F ratio of 1.1:1; the common age group in ALL was 1-14 where all are male. In CML the common age group was 31-40 years with M:F ratio of 1:1.5. We also found 4(3.48%) cases of ALL in remission stage, all were male & under 1-10 years. Where in the study of Atchyuta M 2.67% were under remission with M:F ratio of 6:4.

Among the non malignant condition, Hypocellular marrow was seen in 17(14.78%) majority cases with the common age group between 51-60 years (M:F=2.4:1) in our study, similar with Chowdhury MRK<sup>2</sup>. When compared to other studies, megaloblastic anaemia was commonest (17.5%) in Sudhakar et al<sup>13</sup> and (26.5%) in Bashir N et al<sup>14</sup> studies. In the study of Atchyuta M<sup>18</sup> in megaloblastic anaemia commonest age group was 21-30 years with M:F ratio of 1.2:1. Hypocellular marrow was also reported as 5.3%, 19% and 29%<sup>21,22,23</sup>. In the present study ITP was seen in only one case (0.87%), a male patient under 10 years. In the study done by Pudasani et al.<sup>21</sup> ITP was seen in 10.5% cases and also reported as 6.21% and 14.5%<sup>5, 25</sup>. In this study Erythroid hypoplasia were seen in 6(5.22%) cases with M:F ratio of 2:1. Instead majority studies Erythroid hyperplasia were commonly seen. Erythroid hyperplasia were also reported as 34%(M:F 1.1:1), 21% and 19.6%<sup>18,21,24</sup>.

In our study metastatic depositions were in 3(2.61%) cases, and the entire patients were male. Where metastatic deposition were also reported as 3.1%, 1.75%, 3.6%, 1.2% and 0.8%<sup>8, 13-15,18</sup>. There was only one (0.87%) normal study & inadequate sample (0.87%) were in our study. Instead 10.4% and 12% normal study was reported by Atchyuta M<sup>18</sup> and Bashir N<sup>14</sup> respectively. Inadequate sample were moreover reported as 0.8% and 2.94%<sup>10,18</sup>. Like others study our inadequate sample case was female.

#### Conclusion

Bone marrow examination is a useful tool in the diagnosis of various hematological and non-hematological disorders. Acute Leukemia is a major indication of BME. Among the pathological condition malignant condition are commonly seen. And male are predominantly suffering more from haematological disorders than female. In majority cases acute leukaemic condition are seen in BME.

**Conflict of Interest:** None.

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