ORIGINAL ARTICLE

DIAGNOSTIC SIGNIFICANCE OF BONE MARROW EXAMINATION AMONGST THE PATIENTS WITH ABNORMAL HAEMATOLOGICAL PARAMETERS

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Background: Bone Marrow examination is considered to be the most indispensable diagnostic tool for the evaluation of many neoplastic and non-neoplastic haematological disorders. After an initial assessment of suspicious cases on abnormal laboratory parameters along with the clinical presentation of the patient marrow examination is finally required for diagnosis as well as management of many haematological malignancies as it offers a clear cytological as well as histological picture of Bone Marrow aspirate and biopsy respectively. The Objective was to evaluate the significance of Bone Marrow examination in patients with abnormal haematological parameters. **Methods:** A retrospective study conducted at the Pathology Department of Pak Emirates Military Hospital from (Jan–June 2022) On data from150 patients who were advised to undergo bone marrow examination due to abnormal lab parameters and peripheral smear findings after informed consent and approval from the ethics review committee, to find out the correlation of abnormal haematological parameters and aspirate findings which have led to a definitive diagnosis. Data comprising basic demographic variables (age, gender etc.), Abnormal Haematological Parameters (CBC), peripheral smear findings and Aspirate findings were analyzed using SPSS version 23.0.**Results:** Out of 150 studied participants with abnormal haematological parameters 24 (16%) were diagnosed on bone marrow examination as acute leukaemia / Hodgkin's and Non-Hodgkin's lymphoma respectively, 13 (9%) cases of aplastic anaemia and Autoimmune HaemolyticAnaemia, 33 (22%)cases of hypersplenism, CML and multiple myeloma. While 22 (15%) cases were diagnosed with BME as CKD and reactive changes. Moreover, 22(15%) cases were found to have Iron Deficiency anaemia respectively. **Conclusion:** The study revealed that patients with abnormal haematological parameters should undergo bone marrow examination to ascertain the diagnosis for malignant as well as non-malignant conditions that could cause abnormal lab parameters.

Keywords: Bone Marrow Biopsy; Cytology; Morphology

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INTRODUCTION

Bone marrow as a large organ is considered to be prone not only to several infections, a site of metastatic infiltration, but also a primary source of origin of various metabolic disorders as well as non-neoplastic diseases.[1]

The Bone marrow involvement is manifested as abnormal laboratory findings, physical examination and peripheral smear morphology respectively.[2] So, it necessitates to evaluate such patients by bone marrow aspiration as well as biopsy consecutively. Therefore, bone marrow aspirate allows not only cytomorphological examination of marrow but also samples taken simultaneously for C/S, flow cytometry, cytogenetics and immunophenotyping.[3] So, certain malignant and non-malignant disorders are diagnosed within a few hours by just going through the cytomorphological picture on the aspirate and waiting for the bone marrow biopsy report which takes nearly 10 days.[3,4]

Therefore, life-threatening malignant conditions and those that require immediate medical intervention such as acute and chronic Leukemias should be taken into immediate consideration.[1,4,5] WHO has classified haematological disorders into myeloid, lymphoid or histiocytic types depending upon the cell line which has undergone a neoplastic transformation.[1,5,6] Whenever immature haemopoietic cells commonly known as blasts exceed a certain percentage in the bone marrow, i.e., more than 20% as well as their spillage into the peripheral circulation with concurrent infiltration to solid organs and lymphatic system are essential parameters to diagnose Acute Leukemias. According to French American British (FAB) classification as well as WHO revised criteria a minimum of 20% blasts are required to diagnose acute leukemias.[1,6,7]

Furthermore, Immunohistochemistry and cytogenetics and ultimately trephine reports are required to confirm the diagnosis.[8] Also, acute leukaemia is further classified as AML representing the proliferation of immature precursors of the myeloid lineage, i.e., monoblastic, megakaryoblast and erythroblast respectively. The spillage of these immature precursors into the blood will be manifested as abnormal lab parameters on CBC. Acute lymphoblastic leukaemia is characterized by uncontrolled production of immature lymphocytes of B and T Type.[1,7,910]

Consequently, chronic myeloid leukaemia and chronic lymphocytic leukaemia will be presented on CBC as increased total leucocyte count and the presence of the abnormal number of mature cells on peripheral smears that will necessitate the bone marrow intervention to make a final diagnosis. Apart from leukaemia several other haematological disorders like MDS, and multiple myeloma manifest initially as abnormal haematological parameters that necessitate bone marrow examination.[10,11] Also, MDS can lead to bone marrow fibrosis with subsequent transformation to acute myeloid leukaemia and ultimately bone marrow failure.[10–12]

Bone marrow fibrosis has been considered as an adverse histological feature amongst the patients of Myeloproliferative disorder and has a poor prognostic outcome. According to the revised new risk stratification system, i.e., cytogenetic scoring system and revised international prognostic scoring system respectively.[12,13] Also, non-malignant disorders comprise a diverse group of conditions including many inherited conditions as well as non-hereditary conditions such as anaemia (an aplastic, mixed deficiency, megaloblastic), peripheral destruction of platelets and fever of unknown origin.[1,7,14] Therefore, bone marrow examination has significant importance in the diagnosis and management of both neoplastic and non-neoplastic haematological disorders which represents initially in the form of abnormal lab parameters implicating the need for bone marrow examination.[2,3,15]

MATERIAL AND METHODS

A Prospective cross-sectional study was conducted at the Pathology Department Pak Emirates Military Hospital Rawalpindi from July–December 2022 on 150 admitted patients who were advised to have bone marrow examination due to abnormal haematological parameters after taking informed consent and approval from the Ethics Review Committee. The sample size was calculated using the WHO calculator by taking the prevalence of similar cases in a tertiary care hospital in Southern Pakistan of 2.6% as a reference, keeping a confidence level of 95% and requiring absolute precision of 5% and an anticipated population of 2.4%. Non-probability consecutive sampling technique was used. Data was analyzed using SPSS Version 23.0 For quantitative data mean (Standard Deviation) was determined. In addition, the frequency in percentages of qualitative variables was calculated. The Chi-square test was applied to assess the frequency differences. Patient demographic variables, detailed history and general physical examination were performed. All haematological parameters including CBC, and peripheral smear findings along with indication for bone marrow examination were noted on a proforma. All patients underwent bone marrow aspiration and biopsy simultaneously. Samples were taken from the Posterior Superior iliac Spine using a Jamshidi needle (regular / adult, 11 gauge) after applying local anaesthesia. 0.5ml of bone marrow blood was aspirated and used for assessing red cell morphology, and marrow cellularity (erythropoiesis, myelopoiesis as well as megakaryocytes) with abnormal cell evaluation. Samples were also sent for C/S where required. In addition, bone marrow biopsy material was taken and sent for histopathological evaluation to make a definite diagnosis.

RESULTS

Results found that the majority of studied participants were male with 41–60 years of age group comprising (43%). However, the mean age of studied participants was 54.3±15.2 TLC was 30.3±67.9 and platelets were 157.5±181.8, and haemoglobin levels were 23.2±139.6 respectively.

On general physical examination, it was found that 58 studied participants had no visceromegaly, 37 had massive splenomegaly and 42 had mild splenomegaly. However, 13 cases have shown hepatosplenomegaly respectively. It was found that 79 non-suspicious cases had thrombocytopenia, 76 had anaemia, and 37 had normal TLC. Similarly, 20 suspicious cases had thrombocytopenia, 52 had anaemia, and 23 had normal TLC. Out of 150 patients who underwent bone marrow examination 24 (16%) cases presented with Anaemia, Thrombocytopenia, and Leucocytosis were diagnosed as cases of acute leukaemia / Hodgkin's and non-Hodgkin's lymphoma. Thirteen (9%) cases presented with pancytopenia had autoimmune haemolytic anaemia, plastic anaemia and megaloblastic anaemia. While 33 (22%) patients with anaemia and thrombocytosis have been diagnosed on aspirate as cases of hypersplenism, CML and multiple myeloma respectively. Moreover, 22 (15%) cases with cytopenia were later diagnosed to have CKD and reactive changes. Furthermore, 22 (15%) cases presented with severe anaemia had shown iron deficiency respectively.

Table-1: Demographic profile and Descriptive variables of studied participants.

Demographic profile		Frequency n(%)
Gender	Female	64 (43)
	Male	86 (57)
Age Group	<20	3 (2)
	21-40	21 (14)
	41-60	64 (43)
	<60	62 (41)
Descriptive variables		**Mean± SD.**
Age (years)		54.3 ± 15.2
Total leukocyte Count (10^9/L)		30.3 ± 67.9
Platelets Level (10^9/L)		157.5 ± 181.8
Haemoglobin Level (g/dl)		23.2 ± 139.6

Table-2: Frequencies of general physical examination of studied participants.

General Physical Examination	Frequency n (%)
Pallor	75 (50)
Mild Splenomegaly with cervical lymphadenopathy	42 (28)
Massive splenomegaly with Generalized Lymphadenopathy	37 (25)
Hepatosplenomegaly / Enlarged Inguinal Lymph Nodes	13 (9)
No viceromegly with enlarged inguinal lymph nodes	58 (39)

Table-3: Different haematological parameters of participants.

Haematological Parameter		Non-suspicious	Suspicious
Platelets Count	Thrombocytopenia	79	20
	Normal PLT count	6	26
	Thrombocytosis	3	16
Haemoglobin level	Anaemia	76	52
	Normal Hb level	12	10
Total Leukocyte Count	Leukopenia	46	6
	Normal TLC	37	23
	Leucocytosis	5	33

Table-4: Correlation amongst abnormal lab parameters, GPE with bone marrow aspirate findings.

Abnormal Haematological Parameter	General Physical Examination Findings	Findings on Peripheral Blood Film	Finding on Bone Marrow Aspirate	Frequency (n) %
Anaemia Thrombocytopenia Leucocytosis	Hepatosplenomegaly Cervical Lymphadenopathy	Blasts +++ TLC will be upto 200 x 10^9ltr Erythrocytes; normocytic normochromic Platelets; markedly decreased	Acute leukaemia	17 (11%)
	Splenomegaly & lymphadenopathy	Erythrocytes: normocytic normochromic Leucocytes: neutrophilic leucocytosis Platelets: decreased or normal	Hodgkin's and Non-Hodgkin lymphoma	6 (4%)
	Myeloproliferative neoplasm MPN (U)	Erythrocytes: TRBC increased Leucocytes: increased Platelets: increased		1 (0.7)%
Pancytopenia	No viceromegaly	Erythrocytes: Decreased Leucocytes: decreased Platelets: decreased	Hypo cellular Marrow (aplastic anaemia)	8 (5%)
		Erythrocytes: RBC Fragmentation, Microspherocytes, dimorphia Leucocytes: decreased Platelets: decreased	Autoimmune haemolyticanaemia	2 (1.3%)
		Erythrocytes: Ovalocytes, Dimophia: Leucocytes: hypersegmented neutrophils Platelets: decreased	Megaloblastic anaemia	3 (2%)
	Massive splenomegaly	Erythrocytes: Decreased Leucocytes: normal/decreased Platelets: decreased	Hypersplenism	16 (10.6%)
Anaemia with thrombocytosis	Cervical lymphadenopathy Splenomegaly	Erythrocytes: normocytic normochromic Leucocytes: complete spectrum of granulocytic precursors (blasts, mylocytes, promylocytes), increased basophils Platelets: markedly increased	CML	20 (13%)
Anemia	No viceromegaly	Erythrocytes: Macrocytic hypochromic, blasts + Leucocytes: neutrophils show psedopelgar Platelets: large / small decreased	MDS	15 (10%)
		Erythrocytes: normocytic normochromic, rouleaux formation ++ Leucocytes: decreased Platelets: decreased	Multiple myeloma	17 (11%)
		Erythrocytes: Anisocytosis ++, pokiliocytosis ++, target cells ++, pencil cells ++, dimorphia + Leucocytes: Normal Platelets: Normal	Mixed deficiency anaemia	1(0.7)
Bicytopenia (anaemia with thrombopenia)	Mild splenomegaly	Erythrocytes: dimorphia ++, target cells +, tear drop + Leucocytes: normal Platelets: normal	CKD	4 (2.7%)
	Fever & hepatosplenomegaly	Erythrocytes: leucoerythroblastic blood picture Leucocytes: neutrophilic leucocytosis Platelets: increased	Marrow showing reactive changes	18 (12%)

DISCUSSION

A variety of malignant and non-malignant disorders that directly or indirectly affect the bone marrow are manifested commonly as abnormal lab parameters as well as clinical signs and symptoms which necessitate bone marrow intervention to make a definite diagnosis (Bharuthram N, *et al*).[2019] In our study, there were abnormal lab parameters which finally led to bone marrow aspiration and biopsy simultaneously. The results correspond to the study conducted at Dessie Town North East Ethiopia by (Hussen Ebrahim, *et al*.)[2022] where the results of abnormal parameters finally ended up in bone marrow examination and it was later ruled out that patients did have either malignant or non-malignant haematological disorders. Furthermore, our results are completely in agreement with the study conducted in Turkey by (Dogan A, *et al*).[2022] Our findings are also consistent with the study conducted by (Bharuthram N, *et al*)[2019] at Uludag University, Department of Haematology where abnormal haematological parameters (MAHA, Thrombocytopenia and unexplained cytopenias) lead to bone marrow examination and final results were in accordance to our findings. Where non-haematological malignant disorders were finally diagnosed by performing bone marrow aspirate and biopsy simultaneously. Consequently, our findings are inconsistent with the findings of (Sami A *et al*).[2021] Where bone marrow aspirate showed a relatively decreased sensitivity to NHL and non-hemopoietic metastasis. The results obtained in our study showed a correlation between abnormal lab parameters as well as bone marrowaspirate results which were nearly similar e.g. in acute leukaemia there will be spillage of blasts in the peripheral blood which will be presented amongst lab parameters as increased TLC with anaemia and thrombocytopenia respectively, which requires bone marrow intervention to make a definitive diagnosis.

CONCLUSION

This study revealed that initial abnormal lab findings and clinical presentation of a patient lead to bone marrow examination to make a definite diagnosis in certain malignant as well as non-malignant haematological disorders.

AUTHOR'S CONTRIBUTION

SB & FA: Data acquisition, data analysis, data interpretation, critical review, and approval of the final version. MS & MA: Conception, Study design, drafting the manuscript, approval of the final version.ZT & FA: Drafting, data interpretation, critical review, and approval of the final version.

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