Original Article

Spectrum of Hematological and Non-Hematological Diseases on Bone Marrow Examination-A Study on 220 Cases at a Tertiary Care Centre

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Author's Contribution

[1] Conception of study
[2] Experimentation/Study conduction
[2] Analysis/Interpretation/Discussion
[1] Manuscript Writing
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Abstract

Background: Bone marrow examination is an invaluable tool in the diagnosis of hematological and non-hematological diseases. Referral is made based on the clinical evaluation followed by after analysis of CBC and peripheral film.

Objective: This study aims at evaluating the spectrum of diseases diagnosed on bone marrow biopsy at a tertiary care hospital of Rawalpindi, Pakistan.

Materials and Methods: This descriptive, cross-sectional study was carried out at the pathology department of Holy family hospital for a duration of 1 year after ethical approval from IRF. All 220 cases requiring bone marrow examination were included in the study by consecutive sampling technique. Variables such as age, gender, presenting complaints, examination findings, CBC, peripheral blood film, indications and diagnosis of bone marrow examination were noted. Data were analyzed using SPSS v22.

Results: Mean age was 29.15±20.9 years. 117(53.2%) specimens were of males and 103(46.8%) were of females. Spectrum of hematological and non-hematological diseases found on bone marrow examination ranged from acute leukemia in 37(16.8%) to megaloblastic anemia in 29(13.1%).The relationship between indications of referral and diagnosis of bone marrow examination was found to be statistically significant showing that suspected diagnosis made by the clinician was same as the final diagnosis in many cases. Pancytopenia was found as the major indication in most diseases (32.7%).

Conclusion: Bone marrow examination is a useful tool in ascertaining diagnosis of various hematological. Pancytopenia was found to be major indication whereas, acute leukemia and megaloblastic anemia were most common malignant and benign hematological disorders on bone marrow examination, respectively.

Keywords: Bone marrow, Hematological disorders, Acute leukemia, Megaloblastic anemia, Pancytopenia.

Introduction

Bone marrow examination is a detailed procedure for analyzing the pathologies of bone marrow samples obtained through bone marrow aspiration and biopsy (often termed as trephine biopsy). Bone marrow aspiration is utilized for obtaining specimens for cytological evaluation, with analysis being directed toward the assessment of morphology and for obtaining a differential cell count. It further allows the samples to be directed towards other specialized tests, such as cytogenetics, molecular studies, microbiologic cultures, immunohistochemistry, and flow cytometry.[1,2] Bone marrow aspiration and biopsy is the most frequent and safe invasive procedure carried out in hospitals for the diagnosis of hematological and non- hematological diseases.[3,4] The hematological diseases include acute leukemia, myeloproliferative disease (MPD), lymphoid neoplasm and various nutritional deficiency diseases whereas non-hematological diseases include infectious diseases infiltrating the bone marrow such as tuberculosis, parasitic infections, metastatic deposits and metabolic storage diseases.[5] Although a peripheral blood smear is carried out in patients with suspicion of hematological diseases, it alone does not reflect on the nature of disease process. Thus, a bone marrow biopsy is indicated based on the suspicion from clinical picture and peripheral blood smear.[6] This study aims at evaluation the spectrum of diseases diagnosed on bone marrow biopsy at a tertiary care hospital of Rawalpindi, Pakistan.

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.[7] Rationale of the study is to 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

A descriptive cross-sectional study was conducted at the pathology department of Holy Family Hospital. All 220 cases requiring bone marrow examination for various hematological disorders were included in the study, from March 2016 to March 2017. Patients having contraindications for bone marrow aspirations such as skin infection at site of sample, osteomyelitis, active bleeding were excluded from study. Ethical approval was taken from the ethical review board before proceeding with data collection. The bone marrow examination was carried out in the group of patients who were referred to the pathology department because of unexplained anemia, pancytopenia, hematological malignancies, leukemia or thrombocytopenia. A detailed history, examination and all the relevant investigations were done. Peripheral blood smears, complete blood count and hematological parameters were performed prior to bone marrow aspiration. A written consent was taken from the patients by the concerned department. Bone marrow was collected by bone marrow aspiration needle under aseptic conditions after giving local anesthesia. An aspirate smear was prepared and stained. The slide was observed under the microscope and the findings were noted.

Data were entered and analyzed using SPSS v22. Mean and standard deviation were calculated for quantitative variables. Frequencies and percentages were calculated for qualitative variables, such as for diagnosis and gender. A chi-square test of independence was applied to find out the association between indications of referral and diagnosis of bone marrow examination. The p-value to be considered statistically significant for the test was set at ≤ 0.05. A post-hoc comparison was further carried out between indications and hematological diseases with p-value being $\leq .0004$ by Bonferroni correction.

Results

A total of 220 patients, aged between 1 to 90 years, underwent bone marrow biopsy examination during the study period of 1 year,. Mean age was 29.15±20.9 years. 117(53.2%) were male and 103(46.8%) were females with male to female ratio of 1.13:1. Major presenting complaints were fever in 159(72.3%), generalized weakness in 75(34.1%), dyspnea in 46(20.9%), bleeding in 72(32.7%), and weight loss in 27((12.3%) cases. Other minor presenting complaints included abdominal pain, vomiting, loose motion and body aches. On systemic examination, pallor was found in 168(76.3%), jaundice in 21(9.5%), lymphadenopathy in 41(18.6%), hepatomegaly in 73(33.2%), splenomegaly in 95(43.2%), and bruises in 34(15.5%).

The blood cell counts were highly variable (Table-I). On peripheral blood film examination, 24 had a normocytic normochromic picture, 38 had a microcytic hypochromic picture, 18 were macrocytic, and 140 had a dimorphic picture. The most frequent indications for which the patients were referred for bone marrow examination were pancytopenia in 113(51.3%), hematological malignancy in 53(24%) and anemia in 32(14.5%) cases (see Figure-1). 86% of the specimens showed hypercellularity of bone marrow. The spectrum of hematological and non-hematological diseases as found on bone marrow examination ranged from acute leukemia in 37(16.8%), megaloblastic anemia in 29(13.1%) to some very rare diseases as Diamond Blackfan syndrome and Bernard-Soulier syndrome in 1 specimen each (see Table-II). Among the 10 cases of patients suffering from anemia of chronic disease, 4 (40%) had a past history of tuberculosis. When examining the association between indications for which referral was made and definitive diagnosis on bone marrow examination, a chi-square test of independence revealed that the relationship between these variables was statistically significant $\chi 2(112, N=220) = 264.9$, p-value < .001. A post-hoc comparison was further carried out with p-value set as ≤ .0004 by bonferroni correction. The results are shown in Table-III and Table-IV. The results show that the referral indication by the clinician based on complete blood count and peripheral blood film, was same as the final diagnosis of bone marrow examination in 29.5% cases. Moreover, pancytopenia was found to be the major indication in most diseases (32.7%), commonest being in megaloblastic anemia, followed by aplastic anemia.

Table-I Blood cell counts

Blood Cell Indices (Normal Values)	**Minimum Value**	**Maximum Value**	**Mean**
TLC (4-11 x $10^3/\mu L$)	0.40	328.7	25.9
Hemoglobin (12-17 g/dL)	2.1	19.5	7.97
Hematocrit (37.5-51%)	2.8	63.8	24.99
Platelets (150-450 x $10^3/\mu L$)	2.0	1899.0	130.2

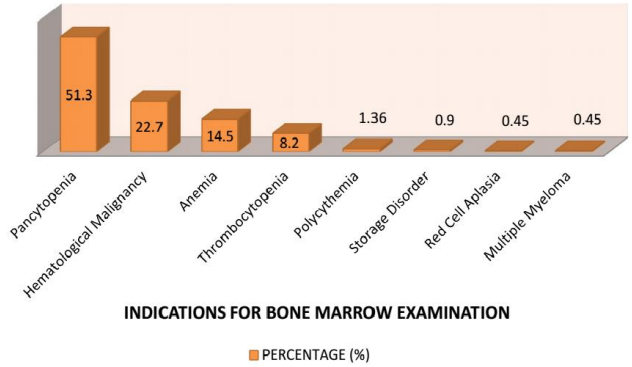

Figure-1 Spectrum of diseases with indication for bone marrow examination-indications

Table-II Hematological and non-hematological diseases on bone marrow examination

A. Malignant hematological diseases (N=72/220)	
Acute myeloid leukemia (AML)	34 (15.45%)
Acute lymphocytic leukemia (ALL)	3 (1.36%)
Chronic myeloid leukemia (CML)	21 (9.54%)
Chronic lymphoid leukemia (CLL)	8 (3.63%)
Myelodysplastic syndrome (MDS)	5 (2.27%)
Multiple myeloma	1 (0.45%)
B. Benign hematological diseases (N=138/220)	
Megaloblastic anemia	29 (13.1%)
Iron deficiency anemia	5 (2.27%)
Anemia of chronic disease	10 (4.5%)
Hemolytic anemia	15 (6.8%)
Aplastic anemia	20 (9.09%)
Peripheral destruction of platelets (itp)	22 (10%)
Hypersplenism	12 (5.45%)
Reactive changes	16 (7.2%)
Polycythemia	3 (1.36%)
Hemophagocytic syndrome	2 (0.9%)
Fanconi anemia	2 (0.9%)
Diamod Blackfan syndrome	1 (0.45%)
Bernard Soulier syndrome	1 (0.45%)
C. Non- hematological diseases (N=10/220)	
Storage disorder	4 (1.81%)
Visceral leishmaniases	6 (2.72%)

Table-III Diseases with indication of referral and definitive diagnosis on bone marrow examination

Bone marrow diagnosis	Indications for referral (p-value ≤ .0004)		
Hematological malignancies (AML, ALL, CML, CLL, MDS)	Hematological Malignancy 42 (59.2 %)	Pancytopenia 24 (33.8 %)	Others 5 (7%)
Peripheral destruction of platelets	Thrombocytopenia 16 (72.7 %)		Others 6 (27.3 %)
Storage disorder	Storage disorder 2 (50 %)	Pancytopenia 2 (50%)	
Polycythemia	Polycythemia 3 (100 %)		
Multiple myeloma	Multiple myeloma 1 (100 %)		
Diamond black fan syndrome	Red cell aplasia 1 (100 %)		

Table-IV Diseases with pancytopenia as the major indication of referral

Hematological and non-hematological diseases	Pancytopenia as the major indication for referral
Megaloblastic anemia	23 (79.3 %)
Hypersplenism	12 (100 %)
Visceral leishmaniases	4 (66.7 %)
Fanconi's anemia	2 (100 %)
Aplastic anemia	16 (80 %)
Reactive changes	10 (62.5 %)
Iron deficiency anemia	3 (60 %)
Hemophagocytic syndrome	2 (100 %)

Discussion

Bone marrow examination is an important tool in diagnosis of various hematological and non-hematological diseases.[8,9] This study basically aimed at determining spectrum of diseases diagnosed on bone marrow examination and finding the most common indication of referral in our setup. A total of 220 patients were included in our study with a male to female ratio of 1.13:1. Mean age was 29.15±20.9 years, compared to mean age of 38±2.33 years in another study.[10]

Common clinical presentations were fever, generalized weakness, dyspnea, weight loss and bleeding manifestations. These were similar to the findings of the studies done by Prajapati et al and Belai et al.[11,12] Pancytopenia has been one of the biggest diagnostic dilemmas for clinicians and presents as the most frequent indication (51.3%) for bone marrow examination in our study. Similar to this, pancytopenia was the major indication of referral in a study done by Pudasaini et al and Ghartimagar.[3,13] However, it was in contrast to the study from Saudi Arabia[10], in which acute leukemia was the most common indication. Bone marrow was found to be hypercellular in most cases (86%), followed by hypocellular (12%) and normocellular (2%). This was similar to the study conducted by Pudaisani et al.[3]

On bone marrow examination, benign hematological diseases (62.7%) comprised of most cases, followed by malignant hematological diseases (32.7%) and non-hematological diseases (4.5%). This was similar to a study conducted by Gandapur et almand Meena, in which benign hematological diseases contributed to 73.2% of all diagnoses.[14,15] However, it was contrary to studies conducted in Saudi Arabia and India where malignant hematological diseases were the most common diagnosis (82.5%).[10,16] Among the benign hematological diseases, megaloblastic anemia was the most frequent diagnosis observed, seen in 29 cases. Similarly, megaloblastic anemia was also the commonest condition (found in 37 cases) in a study conducted in Peshawar.[17] In a study conducted in Khyber Pakhtunkhwa, hemolytic anemias were the commonest condition.[18] In another study, megaloblastic anemia was the second most common diagnosis comprising of 16.6% of the cases.[19] Among the malignant hematological diseases, the highest numbers of cases (34) were those of acute myeloid leukemia, followed by chronic myeloid leukemia. In another study, similar results were found, acute leukemia being the most prevalent hematological malignancy (34.6%) followed by chronic myeloid leukemia (28.8%).[12]

Our study showed that referral indication by the clinician based on complete blood count and peripheral blood film, was same as the final diagnosis of bone marrow examination in 29.5% of the cases. This shows that these investigations alone can lead to diagnosis in many cases. However, bone marrow examination is still necessary for the confirmation of final diagnosis. Moreover, it was found out that pancytopenia was the major indication in most diseases (32.7%), commonest being in megaloblastic anemia, followed by aplastic anemia, as shown in Table-IV. Likewise, the commonest cause for pancytopenia was megaloblastic anemia (79%) followed by aplastic anemia (18%) in a study conducted by Gayathri et al.[20]

Conclusion

Herein, indications of bone marrow examination were pancytopenia, followed by hematological malignancies. Spectrum of diagnosis at bone marrow examination ranged from malignant hematological diseases, benign hematological diseases to non-hematological diseases like storage disorders and visceral leishmaniasis. Thus, our study concludes that bone marrow examination is an important diagnostic tool for various diseases.

References

1. Malempati S, Joshi S, Lai S, Braner DA, Tegtmeyer K. Bone marrow aspiration and biopsy. N Engl J Med. 2009;361(15):28.
2. Gupta AK, Gupta S, Gupta R, Kumar V. Diagnosis of Non-Neoplastic Haematological Disorders using Bone Marrow Aspiration and Trephine Biopsy.
3. Pudasaini S, Prasad K, Rauniyar S, Shrestha R, Gautam K, Pathak R, et al. Interpretation of bone marrow aspiration in hematological disorder. Journal of Pathology of Nepal. 2012;2(4):309-12.
4. Riley RS, Hogan TF, Pavot DR, Forysthe R, Massey D, Smith E, et al. A pathologist's perspective on bone marrow aspiration and biopsy: I. Performing a bone marrow examination. Journal of clinical laboratory analysis. 2004;18(2):70-90.
5. Shah NV, Goswami F, Rathod P, Nasit J, Singh M, Gidwani R. Diagnostic spectrum of Bone Marrow Aspiration in Evaluation of Haematological and Non-hematological disorders.
6. Raina JS, Kundal R, Puri P, Puri A, Kumar K, Attri HK. Correlation between Different Blood Investigations-Peripheral Blood Film and Bone Marrow Findings in Cases of Pancytopenia.
7. Agrawal S, Bhandari R, Gowda VN, Gupta A, Singh N, Chowdhury N, et al. Hematological and biochemical predictors of bone marrow metastases in non-hematological malignancies: a clinico-pathological analysis. medRxiv. 2020.
8. Syed NN, Moiz B, Adil SN, Khurshid M. Diagnostic importance of bone marrow examination in non-hematological disorders. JPMA The Journal of the Pakistan Medical Association. 2007;57(3):123-5. PubMed PMID: 17432015.
9. Khan SP, Sajjad G, Shareefa A. Bone marrow aspiration in haematological disorders: study at a tertiary care centre. Int J Res Med Sci. 2018;6:2363.
10. Qahtani FA, Syed NN. An audit- indications and diagnosis of bone marrow biopsies at a tertiary care hospital in Saudi Arabia. Hematology & Transfusion International Journal. 2018;6.
11. Prajapati Z, Kokani MJ, Gonsai R. Clinicoepidemiological profile of hematological malignancies in pediatric age group in Ahmedabad. Asian Journal of Oncology. 2017;3(01):054-8.
12. Belai N, Ghebrenegus AS, Alamin AA, Alamin AA, Embaye G, Andegiorgish AK. Patterns of bone marrow aspiration confirmed hematological malignancies in Eritrean National Health Laboratory. BMC hematology. 2019;19:8. doi: 10.1186/s12878-019-0138-3. PubMed PMID: 31073409; PubMed Central PMCID: PMCPmc6498504.
13. Ghartimagar D, Ghosh A, Thapa S, Sapkota D, Jhunjhunwala AK, Narasimhan R, et al. Clinicohematological Study of Pancytopenia in a Tertiary Care Hospital of Western Region of Nepal. Journal of the Nepal Medical Association. 2017;56(207).
14. Gandapur AS, Nadeem S, Riaz M, Modood-ul-Mannan. Diagnostic importance of bone marrow examination in haematological malignant and non-malignant disorders. J Ayub Med Coll Abbottabad. 2015;27(3):692-694.
15. Meena S, . S, Bhati S, Patni A. Diagnostic importance of bone marrow aspiration in haematological disorders - tertiary care centre based study. IJMBS. 2019;3(6):204-7.
16. Donald S, Kakkar N. Dry tap on bone marrow aspiration: a red flag. J. Hematop. 2021;14(2):125-30.
17. Khan MI, Ahmad N, Fatima SH. Haematological disorders; analysis of hematological disorders through bone marrow biopsy examination. Professional Medical Journal. 2018;25(6).
18. Ghori MR, Khan H, Marwat M. Distribution of non-malignant hematological disorders by sex, age groups and type of disease based on bone marrow aspiration in population of Khyber Pakhtunkhwa, Pakistan. Gomal Journal of Medical Sciences. 2019;17(2):29-36.
19. Munir AH, Qayyum S, Gul A, Ashraf Z. Bone marrow aspiration findings in a tertiary care hospital of peshawar. Journal of Postgraduate Medical Institute (Peshawar-Pakistan). 2015;29(4).
20. Gayathri BN, Rao KS. Pancytopenia: a clinico hematological study. Journal of laboratory physicians. 2011;3(1):15-20. doi: 10.4103/0974-2727.78555. PubMed PMID: 21701657; PubMed Central PMCID: PMCPmc3118050.