ORIGINAL ARTICLE

Frequency of Hematological Malignancies Based on Bone-Marrow Aspiration and Trephine Biopsy in Patients Presenting to Tertiary Care Hospital

KOMAL IQBAL¹, ZARMINA HUSSAIN², SAIRA NASR MALIK³, ANSA KALSOOM RAHMAN⁴, MASHAL RIAZ⁵, HAMEEDA QURESHI⁶, MOHTASIM BILLAH⁷, ASSAD ULLAH⁸

¹Assistant professor (hematology), Bacha Khan Medical College Mardan

²Assistant Professor (hematology), Bacha Khan Medical College Mardan

³Assistant Professor (hematology), Khyber medical college/ KTH Peshawar

4Assistant Professor (Hematology), Kabir Medical College/MMC-General Hospital

⁵Lecturer hematology, Bacha Khan Medical College Mardan

⁶Associate Professor, Northwest General Hospital and Research Center, Peshawar

⁷Professor (pathology), Bacha Khan Medical College Mardan

⁸Veterinary Officer, Civil Veterinary Hospital Gumbat, kohat, KP Pakistan

Corresponding author: Zarmina Hussain, Email: zarmiina@hotmail.com

ABSTRACT

Background: Hematological disorders are found commonly in the general population existing on both ends of the spectrum with minute disorders like iron deficiency anemia to as severe as bone marrow infiltration

Objective: To assess the frequency of hematological malignancies based on bone-marrow aspiration and trephine biopsy in patients presenting to tertiary care hospital

Methodology: The current study was cross-section descriptive study carried out at the Pathology department of Bacha Khan Medical College, Mardan from April 2013 to October 2021. Bone-marrow aspiration and trephine biopsy was done for all the patients. Data regarding gender, age, clinical examination and diagnosis was recorded on a proforma designed for this research. Results were analyzed by using IBM SPSS (version 23).

Results: In our study, a total of 182 patients were included. The mean age (±SD) in the current study was 41 (12.6) years. Based on the malignant hematological disorder, acute myelogenous leukemia was diagnosed in 15 (23.08%) patients, acute lymphoblastic leukemia in (23.08%) patients, chronic myeloid leukemia in 14 (21.54%) patients, acute leukemias in 3 (4.62%) patients, Myeloproliferative neoplasms in 6 (9.23%) patients, Lymphoproliferative disease in 11 (16.92%) patients while plasma cell myeloma was diagnosed in 1 (1.54%) patients.

Conclusion: Our study concludes that acute myelogenous leukemia (AML) and acute lymphoblastic leukemia (ALL) is the most common hematological malignancies in Bacha Khan Medical College followed by chronic myeloid leukemia (CML) which is the second highest malignancies in Bacha Khan Medical College in this specific time.

Keywords: hematological malignancies, bone-marrow aspiration, trephine biopsy

INTRODUCTION

Hematological disorders are found commonly in the general population^{1, 2} existing on both ends of the spectrum with minute disorders like iron deficiency anemia to as severe as bone marrow infiltration ³⁻⁶ Although hematological disorders vary among the developed and developing countries, worldwide and predominantly in the developing countries, anemia is a common disorder⁷. In any age group hematological malignancies present primarily with anemia⁸

In most clinical setups, the most frequently met hematological disorders are Megaloblastic anemia, idiopathic thrombocytopenia purpura, aplastic anemia, and leukemias ¹. All of which can be detected through bone marrow investigation. Bone marrow investigation not only assists in the diagnosis, staging and prognosis of hematological malignancies⁹, it also reveals infections in many cases and aids in establishing the diagnosis of storage diseases¹⁰. Moreover, it confirms chromosomal abnormalities^{11, 12} and helps in diagnosing metastatic non-hematopoietic malignancies related with bone marrow¹³ Furthermore, the interpretation of cytopenias and hematopoiesis which remain unidentified can also be made through bone marrow investigation¹⁴.It also remains productive in the diagnostic assessment of Pyrexia of unknown origin (PUO)¹⁵

For bone marrow examination; Aspiration and trephine biopsy are the two methods that can be adopted. While Bone marrow aspiration (BMA) is a simpler, more consistent, and a fast method for evaluation of marrow that can be done from sternum with patient lying on his back, and pillow under the shoulder, ideally it is avoided due to the increased risk of damage to the vital organs associated with sternal aspirate. In children up to 2 years of age, BMA can also be done from tibia¹⁶

BMA being a safe invasive procedure, makes up for the more routinely employed modality in hospitals for the diagnosis

and management of hematological disorders ^{7, 8, 17}Bone marrow aspiration not only gives an insight about the cytological and numerical features of marrow cells that are suitable to further assessment by molecular and flow cytometric methods and cytogenetics, it is also well able to decipher any unexplained cytopenias and leukemias. With little to no risk of bleeding, it can safely be done in cases of severe thrombocytopenia⁸. However, BMA has a drawback relating to its low sensitivity in diagnosis of lymphoma and solid tumor metastasis ^{18, 19}

On the other hand, Bone marrow trephine biopsies (BMB) provide tremendous understanding of the overall bone marrow structure and spatial interactions between cells. Conditions like insufficient or an unsuccessful aspirate, evaluation of cellularity and bone marrow architecture call for a trephine biopsy, while diagnosing a suspected focal lesion and bone marrow fibrosis also depend on BMB²⁰ Besides, trephine biopsy is mandatory for the staging of lymphomas²¹

The processing of biopsy takes at least 48–72 hours and is a painful procedure. Hence, performing trephine biopsies in all patients may not be cost effective, or an efficient use of physician or laboratory staff time and efforts, and above all leads to patient discomfort²² Also the Interpretation is reliant on multiple factors including quality of tissue section and availability of additional techniques like immunohisto-chemistry, special staining and a good coordination between²⁰ hematopathologists and histopathologists.

Nowadays, for a complete study of bone marrow, obtaining aspirate and trephine biopsy specimens are considered complementary. The frequency of different hematological diseases varies from region to region. Therefore, this study was conducted with a rationale to determine the frequency of various hematological disorders through bone marrow examination in our region.

MATERIALS AND METHODS

The current study was cross-section descriptive study carried out at the Pathology department of Bacha Khan Medical College, Mardan. The duration of study was 8 years from April 2013 to October 2021. Method of sampling was through non-probability sampling technique. In the current study, totally 182 patients were included. The inclusion criteria for our study were all the patients of both gender and all ages referred from outpatients department and wards (for bone marrow aspirate and trephine biopsy) by the clinicians after taking their detail history and examination and willing to take part in our study. The exclusion criteria for our study were all the patients with benign hematological disorders and patients not willing to take part in our study. The study approval was taken from the institutional review board of the hospital. After approval informed consent was signed from the enrolled patients and study main objective was explained to all the patients. A peripheral blood sample of 2ml was taken from all the patients in EDTA tubes and sent to the laboratory for the CBC, reticulocyte and peripheral smear examination. Bone-marrow aspiration and trephine biopsy was done for all the patients. Slides were prepared from the aspirate and examined under microscope. Data regarding gender, age, clinical examination and diagnosis was recorded on a proforma designed for this research. Results were analyzed by using IBM SPSS (version 23). For variables such as gender, frequency and percentages were determined while for other variables like age, means and standard deviation were calculated.

RESULTS

In our study, a total of 182 patients were included. The mean age (\pm SD) in the current study was 41 (12.6) years. The maximum age was 80 years while the minimum age was nine months. Based on hematological diagnosis, 65 (35.71%) patients were diagnosed as malignant while 117 (64.29%) patients were diagnosed as non-malignant. (Figure 1) Amongst the 65 malignant patients, 36 (55.38%) patients were male while 29 (44.62%) patients were female. (Figure 2) Distribution based on the malignant hematological disorder, acute myelogenous leukemia was diagnosed in 15 (23.08%) patients, acute lymphoblastic leukemia in (23.08%) patients, chronic myeloid leukemia in 14 (21.54%) patients, acute leukemias in 3 (4.62%) patients, Myeloproliferative neoplasms in 6 (9.23%) patients, Lymphoproliferative disease in 11 (16.92%) patients while plasma cell myeloma was diagnosed in 1 (1.54%) patients. (Figure 3)

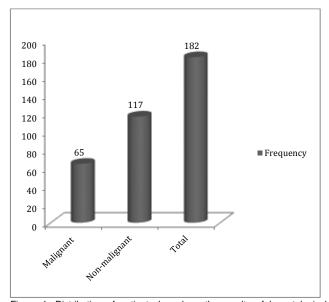


Figure 1: Distribution of patients based on the results of hematological diagnosis

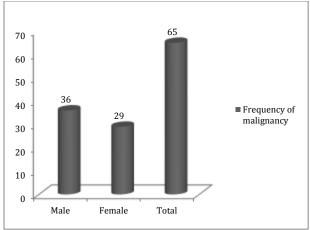


Figure 2: Gender wise distribution of malignant patients

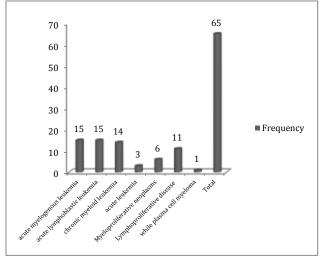


Figure 3: Distribution based on the frequency of malignant hematological disorder

DISCUSSION

Hematological diseases are prevalent among the general public ¹. In the general population, a wide variety of hematological diseases may be found ranging from mild problems such as such as iron deficiency anemia to severe condition, such as bone marrow infiltration ^{3-5, 23}. Most hematological illnesses may be definitively diagnosed with a bone marrow aspiration and biopsy, which is one of the most useful diagnostic procedures available ²⁴. It is a common invasive procedure used in hematology used routinely ²⁵. Following this treatment, reports of bleeding, infection, or any other complications are very uncommon ²⁶.

In our study, a total of 182 patients were included. The mean age (±SD) in the current study was 41 (12.6) years. The maximum age was 80 years while the minimum age was nine months. Based on hematological diagnosis, 35.71% patients were diagnosed as malignant while 64.29% patients were diagnosed as non-malignant. Amongst the 65 malignant patients, 55.38% patients were male while 44.62% patients were female. Distribution based on the malignant hematological disorder, acute myelogenous leukemia was diagnosed in 15 (23.08%) patients, acute lymphoblastic leukemia in (23.08%) patients, chronic myeloid leukemia in 14 (21.54%) patients, acute leukemias in 3 (4.62%) patients, Myeloproliferative neoplasms in 6 (9.23%) patients, Lymphoproliferative disease in 11 (16.92%) patients while plasma cell myeloma was diagnosed in 1 (1.54%) patients. A

previous study was carried out by Mehwish Sajjad et al. on 333 patients refereed to the hematology department for the bone marrow aspiration and biopsy. In their study 292 case were malignant while 41 cases were non malignant. There were more male participants as compared to female participants in their study. In their study Acute lymphocytic leukemia was diagnosed in majority of the patients (n=63) followed by Acute myeloid leukemia and Chronic myeloid leukemia. These findings are in accordance with our findings ²⁷. A comparable research published by Zeeshan et al. found that amongst 24.76% of the patients whose bone marrow was tested, acute lymphoblastic leukemia was the most prevalent hematological malignancy, which is in line with our findings 28. In line with our analysis, a previous study also found that acute leukemia was more common than chronic leukemia 29. A previous study carried out by Fazlur Rahim et al. also reported comparable reports to our findings. They reported that amongst the malignant patients diagnosed in their study, acute lymphoblastic leukemia was observed in 76 (17.92%) cases, followed by acute myeloid leukemia in 27 (6.36%) patients $^{\rm 30}$. Other studies in China and India reported lower prevalence of acute lymphoblastic leukemia as compared to our study ^{31, 32}. A previous study was carried out by Harish Chandra et al. on malignant patients. There were more male in their study than females. They reported acute lymphoblastic leukemia in only 17% of the patients while reported myeloproliferative neoplasm in majority (49%) of their patients which is not in accordance with our study 33.

Limitation of the study: As the current research was only done at a single institution, it may not have accurately represented the total number of cases of hematological malignancies in the country.

CONCLUSION

Our study concludes that acute myelogenous leukemia (AML) and acute lymphoblastic leukemia (ALL) is the most common hematological malignancies in Bacha Khan Medical College followed by chronic myeloid leukemia (CML) which is the second highest malignancies in Bacha Khan Medical College in this specific time. Hematological disorders may be effectively diagnosed by using bone marrow aspiration and trephine biopsy. As a result, it plays a crucial diagnostic role in the hematological workup.

REFERENCES

- Khan MI, Ahmad N, Fatima SH. HAEMATOLOGICAL DISORDERS: ANALYSIS OF HEMATOLOGICAL DISORDERS THROUGH BONE MARROW BIOPSY EXAMINATION. The Professional Medical Journal. 2018;25(06):Medical and Dental College-Islamabad.
- Bedu-Addo G, Amoako YA, Bates I. The Role od Bone Marrow Aspirate and Trephine Samples in Haematological Diagnoses in Patients Referred to a Teaching Hospital in Ghana. Ghana Med J. 2013:47(2):74-8.
- 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.
- Syed NN, Moiz B, Adil S, Khurshid M. Diagnostic importance of bone marrow examination in non-hematological disorders. Journal of Pakistan Medical Association. 2007;57(3):123.
- 5. Štifter S, Babarović E, Valković T, Seili-Bekafigo I, Štemberger C, Načinović A, et al. Combined evaluation of bone marrow aspirate and biopsy is superior in the prognosis of multiple myeloma. Diagn Pathol.
- Khan A, Aqeel M, Khan TA, Munir A. Pattern of hematological diseases in hospitalized paeditric patients based on bone marrow examination. Journal of Postgraduate Medical Institute. 2008;22(3).
- Egesie O, Joseph D, Egesie U, Ewuga O. Epidemiology of anaemia necesitating bone marrow aspiration cytology in Jos. Nigerian Medical Journal. 2009;50(3):61.
- Kibria S, Islam M, Chowdhury A, Ali M, Haque M, Mustanzid S, et al. Prevalence of hematological disorder: a bone marrow study of 177 cases in a private hospital at Faridpur. Faridpur Medical College Journal. 2010;5(1):11-3.
- Phillips L, Opie J. The utility of bone marrow sampling in the diagnosis and staging of lymphoma in South Africa. International 9. Journal of Laboratory Hematology. 2018;40(3):276-83.

- Ruchlemer R, Mittelman M, Zimran A. Gaucher disease, myelodysplastic syndrome and ICUS. Blood Cells, Molecules, and Diseases. 2020;80:102373.
- Nishijima A, Noguchi Y, Narukawa K, Takano H, Oshikawa G. Aggressive B-cell lymphoma with IGH/MYC, IGH/BCL2, and IGH/CCND1 translocations. [Rinsho Ketsueki] The Japanese Journal of Clinical Hematology. 2019;60(10):1425-30.
- Shao X, Chen D, Xu P, Peng M, Guan C, Xie P, et al. Primary Philadelphia chromosome positive acute myeloid leukemia: A case report. Medicine. 2018;97(44).
- Elnahass Y. Youssif L. Cytogenetic features in primary myelodysplastic syndrome Egyptian patients. Journal of Advanced Research, 2018:10:77-83.
- Le Clef Q, Menter T, Tzankov A. Our approach to bone marrow biopsies in cytopenia. Pathology-Research and Practice. 2019;215(7):152447
- Kumar V, Bhatia A, Madaan GB, Marwah S, Nigam A. Role of bone marrow examination in the evaluation of infections: Clinicohematological analysis in a tertiary care centre. Turk patoloji dergisi. 2020;36(1):17-22.
- Fend F, Kremer M. Diagnosis and classification of malignant lymphoma and related entities in the bone marrow trephine biopsy. Pathobiology. 2007;74(2):133-43.
- Laishram S, Shimray R, Sharma A, Pukhrambam G, Singh A, Sharma L. Neoplastic lesions in the bone marrow: a 10 year study in a teaching hospital. JIACM. 2008;9(3):175-8.
- 18. Bain BJ, Bates I, Laffan MA. Dacie and lewis practical haematology e-book: Elsevier Health Sciences; 2016.
- 19. Atla BL, Anem V, Dasari A. Prospective study of bone marrow in haematological disorders. 2015.
- 20. Bain B. Bone marrow trephine biopsy. Journal of clinical pathology. 2001:54(10):737-42.
- F F. Diagnosis and classification of malignant lymphoma and related 21 entities in the bone marrow trephine biopsy. Pathobiology. 2007:74(2):133-43.
- Goyal S, Singh UR, Rusia U. Comparative evaluation of bone marrow aspirate with trephine biopsy in hematological disorders and determination of optimum trephine length in lymphoma infiltration. Mediterranean journal of hematology and infectious diseases. 2014;6(1).
- 23. Afzal K, Muhammad A, Taj Ali K, Arshia M. Pattern of hematological diseases in Hospitalized pediatric patients based on bone marrow examination. 2008.
- Tschautscher MA, Jevremovic D, Buadi FK, Lacy MQ, Gertz MA, Dispenzieri A, et al. Utility of repeating bone marrow biopsy for confirmation of complete response in multiple myeloma. Nature Publishing Group; 2020. p. 1-3.
- Bienzle D. Bone Marrow Examination: Why, How, and What to Expect from the Pathologist. Veterinary Clinics: Equine Practice. 2020:36(1):35-52
- Stensby J, Long J, Hillen T, Jennings J. Safety of bone marrow 26. aspiration and biopsy in severely thrombocytopenic patients. Skeletal Radiol. 2021;50(5):915-20.
- Sajjad M, Kouser S, Khan T, Al Abideen Z, Qadir H, Mehmood M. Pattern of malignant hematological disorders using bone marrow aspirate and biopsy at tertiary care hospital, Karachi. Journal of Muhammad Medical College. 2022;12(2):145-8.
- Zeeshan R, Irshad B, Aslam MA, Khan MT, Bhatti HW, Chaudhary NA. A spectrum of hematological disorders in children with pancytopenia based on bone marrow examination in a tertiary care hospital. Cureus. 2019;11(7).
- Mattsson M, Sandin F, Kimby E, Höglund M, Glimelius I. Increasing prevalence of chronic lymphocytic leukemia with an estimated future rise: A nationwide population-based study. Am J Hematol. 2020;95(2):E36-E8.
- Fazlur R, Irshad A, Saiful I, Muhammad H, Taj Ali Khan K, Qudsia B. Spectrum of hematological disorders in children observed in 424 consecutive bone marrow aspirations/biopsies. 2005.
- Gaynon PS, Bostrom BC, Hutchinson RJ, Lange BJ, Nachman JB, 31. Steinherz PG, et al. Duration of hospitalization as a measure of cost on Children's Cancer Group acute lymphoblastic leukemia studies. J Clin Oncol. 2001;19(7):1916-25.
- Rajajee S, Desikulu M, Pushpa V. Brief report. Survival of childhood acute lymphoblastic leukemia: experience in Chennai. J Trop Pediatr. 1999:45(6):367-70.
- Chandra H, Kunnumbrath A, Bharati V, Singh N, Nath UK, Gupta AK. Patterns of haematological malignancies on bone examination: A 3-year institutional experience. Journal of Medical Evidence. 2022;3(2):141.