Original Article

DOI: 10.7860/JCDR/2023/64980.18352

Pathology Section

An Audit of the Length of Bone Marrow Trephine Biopsy in Adult Patients: A Cross-sectional Study

VANDANA BHATTI[1], ASHIMA[2], GAGANDEEP DEVAL[3], ROMA ISAACS[4]

BY-NC-ND

ABSTRACT

Introduction: A bone marrow trephine biopsy is a minor surgical procedure used to diagnose various haematological and non haematological diseases, such as leukaemia, multiple myeloma, and parasitic disorders like histoplasmosis and leishmaniasis. It is often performed alongside bone marrow aspiration to gather additional information about cellularity, the arrangement of marrow components, and the presence of focal diseases. According to the World Health Organisation (WHO), the recommended minimum adequate length for a trephine biopsy is ≥1.5 cm (before processing).

Aim: To conduct an audit of trephine biopsy lengths and assess their diagnostic utility among adult patients.

Materials and Methods: This cross-sectional study analysed all bone marrow biopsies from adult patients received at the Department of Pathology, Christian Medical College and Hospital in Ludhiana, Punjab, India, over a three-year period (January 2019 to December 2021). The biopsies were categorised into three groups based on their length at the time of grossing: Group A (≥1.5 cm), Group B (1-1.4 cm), and Group C (0.5-0.9 cm). The length of each trephine biopsy was recorded and its diagnostic usefulness was evaluated.

Results: The study included 1,155 trephine biopsies performed over the three-year period. Out of these, 1042, 97, and 16 biopsies were allocated to Groups A, B, and C, respectively. Biopsies meeting the recommended length (>1.5 cm) accounted for 90.2% of the cases. Longer biopsies were associated with a higher rate of conclusive diagnosis compared to shorter biopsies (p-value=0.02). However, when comparing Groups A and B individually, no significant difference was observed in terms of the conclusive diagnosis (p-value=0.9).

Conclusion: Trephine biopsy is a vital tool for diagnosing haematological disorders, particularly focal lesions. Obtaining longer trephine biopsies should be emphasised, as they contribute to a more definitive diagnosis.

Keywords: Biopsy length, Diagnostic concordance, Haematological disorders

INTRODUCTION

Bone marrow examination is an important investigation in any haematological diagnosis. It plays a crucial role in diagnosing conditions such as leukaemia, lymphoma, multiple myeloma, unexplained anaemia, and myelodysplastic syndrome [1-4]. It also aids in the diagnosis of fungal and parasitic disorders like histoplasmosis, leishmaniasis, and cryptococcosis [5-7]. In some cases, the aspiration technique may fail to yield sufficient marrow particles, even when performed by experts. This can result in dry taps or the inability to make a diagnosis based on the aspirate alone [8].

To address the issue of "dry tap," where inadequate or no material is obtained during the aspiration procedure, McFarland W and Dameshek W introduced a method of obtaining bone marrow core biopsies in the late 1950s [9]. Additionally, histological examination of the trephine biopsy can provide valuable information about various types of focal bone marrow diseases, including lymphomas, metastases, granulomas, and myelomas [2,10-12]. In conditions like myelodysplasia, the trephine biopsy offers additional information about cellularity, the arrangement of marrow elements, and focal disease [13]. Trephine biopsies can also be used for performing immunohistochemistry, which is beneficial in the diagnostic evaluation of haematological disorders involving the bone marrow [14]. Due to these advantages, bone marrow trephine biopsy is a commonly performed procedure. The posterior iliac crest is the preferred anatomical site for bone marrow aspiration and trephine biopsy [15]. Other sites that may be used include the anterior iliac crest, sternum, or medial surface of the tibia in infants [1,16]. The bone marrow trephine biopsy can be performed before or after the aspirate [1]. The recommended length of the core trephine biopsy from an adult is ≥1.5 cm, as recommended by the WHO [17]. The biopsy specimen shrinks by approximately 20% after processing. This study presents an audit of trephine biopsy length and diagnostic concordance among different biopsy lengths.

MATERIALS AND METHODS

This retrospective cross-sectional study was conducted in the Department of Pathology at a tertiary care centre in North India over a three-year period (January 2019 to December 2021). The study received approval from the Institutional Research and Ethics Committee (ref CMC/4693).

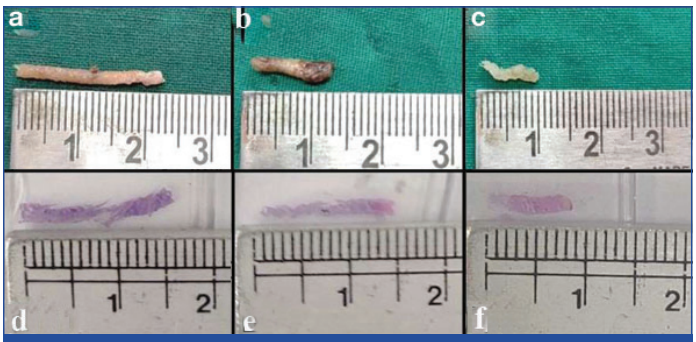
Inclusion criteria: All bone marrow trephine biopsies performed on adult patients (>18 years of age) were included in the study.

Exclusion criteria: Biopsies from children (<18 years of age) were excluded from the study.

Procedure details: After obtaining consent from the patient, trained physicians/physician assistants performed the trephine biopsies using a trephine biopsy needle (Jamshidi needle of gauge 11G/13G) from the posterior superior iliac spine. The biopsies were then placed in 10% formalin for fixation and sent to the histopathology department. The length of the biopsies was measured, and they were subsequently decalcified in 10% formic acid for 24 hours. After decalcification, the biopsies were processed in a Leica automatic tissue processor following standard protocols, and then embedded in paraffin wax. Thin sections measuring 3-4 µm were cut, and slides were prepared. The slides were stained with Haematoxylin and Eosin (H&E) as per routine procedure.

These H&E slides were retrieved from the records and studied. Relevant information was obtained from bone marrow requisition

forms and bone marrow reports in the departmental records. The biopsies were divided into three groups based on their measured length at the time of grossing: Group A (≥1.5 cm), Group B (1-1.4 cm), and Group C (0.5-0.9 cm) [Table/Fig-1]. The conclusive diagnosis of the trephine biopsy was noted and compared among the three groups. A conclusive diagnosis was defined as one in which the pathologist was able to provide an opinion based on the trephine biopsy that contained sufficient bone marrow tissue for evaluation.



[Table/Fig-1]: (a-c) Gross images of bone marrow trephine biopsies of different lengths in groups A, B, and C, respectively; (d-f): Haematoxylin and Eosin (H&E) stained slide of bone marrow trephine biopsies of different lengths in groups a, b, and c, respectively.

STATISTICAL ANALYSIS

The data were analysed using GraphPad InStat Version 3.06 statistical software. Percentages and proportions were calculated, and descriptive analysis was performed with measures of variance including mean, median, and standard deviation for continuous variables. Nominal variables were expressed as percentages. The Chi-square test was used to calculate the p-value.

RESULTS

A total of 1155 biopsies were included in the study, comprising 685 males (59.3%) and 470 females (40.7%) with a male-to-female ratio of 1.4:1. The age of the patients ranged from 18 to 94 years, with a mean age of 51.7±16.6 years. The indications for bone marrow examination are presented in [Table/Fig-2]. Among the biopsies, 659 were malignant and 496 were non malignant. The most common indication for malignant biopsies was leukaemia, while for non malignant biopsies, it was cytopenia under evaluation.

Indication	N (%)
Malignant	
Leukaemia	301 (26.1)
Plasma cell dyscrasia	158 (13.7)
Lymphoma	84 (7.3)
Myeloproliferative disorder	78 (6.8)
Myelodysplastic syndrome	38 (3.3)
Non malignant	
Cytopenia under evaluation	279 (24.2)
Anaemia under evaluation	75 (6.5)
Immune thrombocytopenic purpura	73 (6.3)
Pyrexia of unknown origin	24 (2.0)
Tuberculosis	19 (1.6)
Metastasis	6 (0.5)
Aplastic anaemia	5 (0.4)
Organomegaly	3 (0.3)
Others*	12 (1.0)

[Table/Fig-2]: The indications of bone marrow examination.
*Others include Pure red cell dysplasia-2, Eosinophilia under evaluation-2, Haemophagocytic lymphohistiocytosis-3, Leucocytosis under evaluation-5

The number of biopsies in Groups A, B, and C were 1042 (90.2%), 97 (8.4%), and 16 (1.4%), respectively. When comparing these three groups, a significant p-value of 0.02 was obtained, suggesting an association between the length of the trephine biopsy and a conclusive diagnosis [Table/Fig-3].

Group (cm)	No. of biopsies in each group (N=1155) (%)	Biopsies optimal for conclusive diagnosis (%)	p-value
A (>1.5)	1042 (90.2)	1019/1042 (97.8)	p-value=0.02 (Significant)
B (1-1.4)	97 (8.4)	95/97 (97.9)	
C (0.5-0.9)	16 (1.4)	14/16 (87.5)	
		1128/1155	

[Table/Fig-3]: Association of trephine biopsy length with a conclusive diagnosis.

In Group A, a conclusive diagnosis was given in 97.8% of cases, in Group B, it was 97.9% of cases, while in Group C, a conclusive diagnosis was given in 87.5% of cases. However, when Groups A and B were compared, no difference was observed in terms of trephine biopsy length and a conclusive diagnosis, as the p-value was not significant (p-value=0.9) between these two groups. This suggests that even a trephine biopsy length of 1 to 1.4 cm, with adequate tissue for examination, yielded comparable results to that of a trephine biopsy length >1.5 cm.

It was observed that 27 out of 1155 (2.33%) trephine biopsies were suboptimal and did not yield a conclusive diagnoses. These included 2.21% (23/1042), 2.06% (2/97), and 12.50% (2/16) biopsies in Groups A, B, and C, respectively. No diagnosis could be given for these biopsies, and they were reported as suboptimal for comments.

DISCUSSION

Bone marrow examination is a commonly performed procedure for diagnosing various haematological and non haematological disorders. It helps in obtaining specimens to assess bone marrow morphology and cellularity, as well as for special tests such as cytogenetic studies, molecular studies, and flow cytometric immunophenotyping [11]. Bone marrow trephine biopsy, when performed in conjunction with bone marrow aspiration, provides better information on cellularity and is better at detecting focal lesions [1,18].

The length of the trephine biopsy is one factor that can affect its diagnostic yield. Firstly, a longer biopsy provides a larger amount of tissue for evaluation. Secondly, it may contain more representative tissue, leading to a more accurate evaluation. A study by Ur Rehman S et al., on 393 trephine biopsies showed that the rate of diagnostic positivity on trephine biopsies is directly proportional to the length of the biopsy [19]. A larger size of trephine biopsy also allows for a more comprehensive evaluation of the architecture of the bone marrow, its cellular composition, and the identification of focal lesions involving the marrow. In a study by Campbell JK et al., they found that the rate of conclusive diagnosis of lymphoma (which can have focal involvement of the marrow) increased with the increasing length of the biopsy. They noticed that 20% of biopsies <2 cm in length yielded a positive diagnosis of lymphoma, while the percentage increased to 35% in biopsies ≥2 cm (p-value=0.023) [20].

Present study analysed 1155 trephine biopsies performed on patients with an average age of 51.7±16.6 years. The most common indication for bone marrow examination was leukaemia, while other indications are listed in [Table/Fig-1].

According to WHO guidelines, the recommended length for a trephine biopsy is >1.5 cm [17]. In present study, 90.2% of the trephine biopsies were of the recommended length. In contrast, Ur Rehman S et al., found that only 22.3% of biopsies were of the recommended length in their study [19]. Authors observed that out

of the 90.2% of biopsies that were of the recommended length, 97.8% were optimal for a conclusive diagnosis, while the rest were mixed with fibro-collagenous tissue and skeletal muscle fibres and showed crush artifacts, hence they were considered suboptimal.

It was noted that out of the 8.4% of biopsies in the range of 1-1.4 cm (Group B), 97.9% were optimal for a conclusive diagnosis. When comparing Group A and Group B, the p-value was not significant, suggesting that there was not much difference in the rate of conclusive diagnosis between the two groups. Similar findings were observed by Ur Rehman S et al., [19]. Thus, even biopsies in the length range of 1-1.4 cm can provide a conclusive diagnosis if there are adequate inter-trabecular spaces for evaluation.

When all three groups were compared for the rate of conclusive diagnosis, a significant p-value was obtained. This suggests that as the length of the biopsy increases, the rate of obtaining a conclusive diagnosis also increases. Longer biopsies provide more material for evaluation, resulting in a higher rate of conclusive diagnosis compared to smaller biopsies. Similar findings were observed by Campbell JK et al., and Ur Rehman S et al., [19,20].

In present study, 27 out of 1155 (2.33%) trephine biopsies were suboptimal and yielded an inconclusive diagnosis. These included 2.21% (23/1042), 2.06% (2/97), and 12.50% (2/16) biopsies in groups A, B, and C, respectively. Most of these suboptimal biopsies were from Group C, which had a length of less than 0.5 cm (12.5%). Ur Rehman S et al., observed that 6.5% of biopsies were suboptimal, with the majority (50%) being 0.5 cm in length, which was similar to present study findings [19].

Limitation(s)

This study included biopsies from adult patients only, and biopsies from children (under 18 years of age) were not included. Another limitation was that the representation of cases in Group B and C was lower compared to Group A.

CONCLUSION(S)

Trephine biopsy plays a vital role in diagnosing haematological disorders, especially focal lesions. Longer trephine biopsies are beneficial in reaching a conclusive diagnosis, so physicians should prioritise obtaining longer trephine biopsies. While WHO recommends a trephine biopsy length of more than 1.5 cm, it is worth noting that a trephine biopsy length of 1-1.4 cm, with sufficient tissue for evaluation, can also provide a conclusive diagnosis.

REFERENCES

[1] Lee SH, Erber WN, Porwit A, Tomonaga M, Peterson LC; International Council for Standardization InHematology. ICSH Guidelines for the standardization of bone marrow specimens and reports. Int J Lab Hematol. 2008;30:349-64.
[2] Charles KS, Winfield DA, Angel C, Goepel J. Audit of bone marrow aspirates and trephine biopsies in multiple myeloma--A single center study. Clin Lab Haematol. 2004;26:403-06.
[3] Kumar S, Rau AR, Naik R, Kini H, Mathai AM, Pai MR, et al. Bone marrow biopsy in non-Hodgkin lymphoma: A morphological study. Indian J Pathol Microbiol. 2009;52:332-38.
[4] Subramanian R, Basu D, Badhe B, Dutta TK. Role of bone marrow trephine biopsy in the diagnosis of marrow involvement in Hodgkin's disease. Indian J Pathol Microbiol. 2007;50:640-43.
[5] Apriany N, Sukorini U, Ratnaningsih T, Asdie RH, Subronto YW, Hutajulu SH, et al. Two cases of hemophagocytic lymphohistiocytosis associated with disseminated histoplasmosis presented with transient pancytopenia. Case Rep Med. 2022:28;9521128. Doi: 10.1155/2022/9521128.
[6] Zhang X, Liu Y, Zhang M, Wang Z, Feng X, Yang L, et al. Case report: Diagnosis of visceral leishmaniasis using metagenomic next-generation sequencing and bone marrow smear. Front Cell Infect Microbiol. 2022;12:1095072. Doi: 10.3389/fcimb.2022.1095072.
[7] Dharwadkar A, Vimal S, Buch AC, Panicker NK. HIV infection presenting as bone marrow cryptococcosis. Adv Biomed Res. 2014;3:144.
[8] Bain BJ. Bone marrow trephine biopsy. J Clin Pathol. 2001;54:737-42.
[9] McFarland W, Dameshek W. Biopsy of bone marrow with the Vim-Silverman needle. J Am Med Assoc. 1958;166:1464-66.
[10] Bharuthram N, Feldman C. The diagnostic utility of bone marrow examination in an infectious disease ward. South Afr J HIV Med. 2019;20:974.
[11] Malempati S, Joshi S, Lai S, Braner DA, Tegtmeyer K. Bone marrow aspiration and biopsy. N Eng J Med. 2009;361:28.
[12] Hamid GA, Hanbala N. Comparison of bone marrow aspiration and bone marrow biopsy in neoplastic diseases. Gulf J Oncolog. 2009;6:41-44.
[13] Orazi A. Histopathology in the diagnosis and classification of acute myeloid leukaemia, myelodysplastic syndromes, and myelodysplastic/myeloproliferative diseases. Pathobiology. 2007;74:97-114.
[14] Subash Chandra bose P, RamiahMadanagopaal L, Subba Rao TM. Diagnosis and classification of acute leukaemia in bone marrow trephine biopsies, utility of a selected panel of minimal immunohistochemical markers. Int J Hematol Oncol Stem Cell Res. 2016;10:138-46.
[15] The normal bone marrow. In: Bain BJ, Clark DM, Wilkins BS, editors. Bone marrow pathology. 5th ed. Hoboken, NJ: Wiley-Blackwell; 2019. Pp. 1-60.
[16] Bhaskar N. Bone marrow aspiration and biopsy in critical pediatric patients: A pathologist's perspective. Cureus. 2021;13:e17423.
[17] Arber DA, Orazi A, Hasserjian RP, Brunning RD, Le Beau MM, Porwit A, et al. Introduction and overview of the classification of myeloid neoplasms. In: Swedlow SH, Campo E, Harris NC, Jaffe ES, Pileri SA, Stein H, et al, editors. WHO Classification of tumours of haematopoietic and lymphoid tissue. 4th ed. Lyon: International Agency for Research on Cancer; 2017. Pp.16-27.
[18] Patel S, Nathani P, Nathani S, Shah CK. Diagnostic role of bone marrow aspiration and trephine biopsy in haematological practice. Guj Med J. 2015;70:37-41.
[19] Ur Rehman S, Zafar L, Kazi F, Ur Rehman Z, Luqman M. An audit of length of bone marrow trephine biopsies at a tertiary care hospital. J Ayub Med Coll Abbottabad. 2010;22:81-83.
[20] Campbell JK, Mathews JP, Seymour JF, Wolf MM, Juneia SK. Optimum trephine length in assessment of bone marrow involvement in patients with diffuse large cell lymphoma. Ann Oncol. 2003;14:273-76.

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Pathology, Christian Medical College and Hospital, Ludhiana, Punjab, India.
2. Associate Professor, Department of Pathology, Christian Medical College and Hospital, Ludhiana, Punjab, India.
3. Resident, Department of Pathology, Christian Medical College and Hospital, Ludhiana, Punjab, India.
4. Professor, Department of Pathology, Christian Medical College and Hospital, Ludhiana, Punjab, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Vandana Bhatti,
Associate Professor, Department of Pathology, Christian Medical College and Hospital, Ludhiana-141008, Punjab, India.
E-mail: vandanarajeshwar@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Apr 28, 2023
- Manual Googling: Jun 14, 2023
- iThenticate Software: Jul 18, 2023 (12%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Apr 25, 2023**
Date of Peer Review: **Jun 15, 2023**
Date of Acceptance: **Jul 20, 2023**
Date of Publishing: **Aug 01, 2023**