Original articles

The role of bone marrow biopsy and patterns of bone marrow involvement in patients with lymphoma at Da Nang Hospital

Truong The Diem Trinh[1], Cao My Duyen[1], Hoang Thi Anh Thu[2], Le Phan Minh Triet[2*]

[1]Department of Hematology, Da Nang Hospital

[2]Department of Hematology, University of Medicine and Pharmacy, Hue University

***Corresponding author:** Le Phan Minh Triet. Email: lpmtriet@huemed-univ.edu.vn

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Abstract

Background: Bone marrow biopsy (BMB) is essential for diagnosis and monitoring of hematologic disorders, particularly hematologic malignancies and solid tumors with bone marrow involvement. Since January 2024, the Department of Hematology at Da Nang Hospital has implemented BMB combined with immunohistochemistry, improving diagnostic accuracy.

Objectives: To evaluate the diagnostic role of BMB, with emphasis on dry tap aspiration and patterns of bone marrow involvement (BMI) in lymphoma.

Methods: A cross-sectional descriptive study was conducted on 214 patients undergoing BMB at Da Nang Hospital from January to December 2025.

Results: Among 214 patients who underwent both bone marrow aspiration (BMA) and BMB, the mean age was 65.0 ± 14.4 years, most were older than 40 years, and BMB demonstrated a significantly higher diagnostic yield than BMA. Dry tap aspiration occurred in 19.6% of cases, the majority of which were subsequently diagnosed as malignant by biopsy. In patients with lymphoma, BMB identified BMI in 33 cases, including 9 cases with negative BMA due to marrow fibrosis or focal infiltration. Diffuse and mixed patterns of marrow involvement were the most common forms of BMI and may reflect advanced disease.

Conclusion: BMB provides superior diagnostic and prognostic value, particularly in infiltrative hematologic neoplasms. In lymphoma, BMB is indispensable for accurate detection and characterization of BMI and forms the basis for immunophenotypic classification and treatment strategies.

Keywords: *bone marrow biopsy; lymphoma; bone marrow involvement patterns.*

1. BACKGROUND

Bone marrow examination, including aspiration (BMA) and biopsy (BMB), is a fundamental diagnostic tool in both hematologic and non-hematologic disorders. BMA provides cytomorphologic evaluation and is widely used for rapid assessment; however, it has inherent limitations in cases of marrow fibrosis, focal infiltration, hypocellularity, or "dry tap." BMB, by contrast, enables assessment of marrow architecture, cellularity, stromal alterations, and patterns of infiltration, and permits immunohistochemical (IHC) studies essential for disease classification according to the WHO 2022 criteria [1, 2]. In the context of lymphoma, in addition to detecting and characterizing bone marrow involvement (BMI), BMB is essential for disease staging, prognostication, and treatment planning [3]. Large histopathologic studies have shown that BMB not only contributes to definitive lymphoma diagnosis but also provides independent prognostic value beyond clinical stage [4]. In Viet Nam, due to technical and expertise requirements, BMB has been primarily established at major tertiary centers such as National Institute of Hematology and Blood Transfusion, Blood Transfusion and Hematology Hospital Ho Chi Minh City, and Hue Central Hospital. At Da Nang Hospital, a regional general hospital in central Da Nang, BMB with IHC has been implemented since January 2024. Accordingly, this study aimed to evaluate the role of BMB in the diagnosis of hematologic disorders and to characterize the patterns of BMI in patients with lymphoma.

2. MATERIALS AND METHODS

2.1. Materials: Patients who were clinically indicated for BMB at the Department of Hematology, Da Nang Hospital (DNH) in 2025. Patients agreed to participate in the study. BMB was performed under strict aseptic conditions by board-certified hematopathologists with specialized training. Each biopsy specimen met the minimum adequacy criterion of a core length ≥ 1 cm.

2.2. Methods

Study design: A cross-sectional study. Sample size and collecting samples methods: Using convenience

sampling from January to December 2025, we identified 214 patients who met the inclusion criteria.

2.3. Collecting data

Following enrollment, all participants underwent both BMA and BMB. All procedures were performed under sterile conditions by experienced hematologist–pathologists. BMA and BMB were obtained from the posterior superior iliac spine following standard protocols. Aspirate smears were stained with Giemsa for cytomorphologic evaluation. Biopsy specimens were formalin–fixed, decalcified, paraffin–embedded, and stained with hematoxylin–eosin. Reticulin staining was performed when myelofibrosis was suspected. IHC was conducted using an automated platform when indicated, with antibody panels selected according to the suspected disease entity. All staining procedures followed manufacturer instructions with appropriate quality controls.

Study variables: Collected variables included demographic characteristics (age, sex), disease status (newly diagnosed, remission, persistent disease, relapse), final WHO 2022–based diagnosis, and BMA and BMB findings. In lymphomas, the morphology and histological pattern of infiltration was categorized as diffuse, nodular, interstitial, paratrabecular, sinusoidal, and mixed patterns.

2.4. Data analysis: The data were entered in Microsoft Excel 365 and analyzed using SPSS version 27.0, with descriptive statistics including frequencies, percentages, means, and standard deviations.

2.5. Ethical considerations: This study was conducted in accordance with the ethical principles of the Ministry of Health and was approved by the Scientific Committee and the Institutional Review Board of DNH (H2025/312).

3. RESULTS

3.1. Characteristics of patients undergoing bone marrow biopsy

In our study, a total of 214 patients were subjected to both bone marrow aspiration and biopsy. The mean age was 65.0 ± 14.4 years (range 17–96 years), with patients aged ≥ 65 years comprising the majority (51.4%). The male-to-female ratio was 1:1.18. (Figure 1)

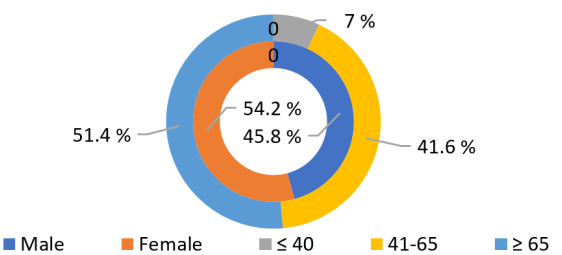

Figure 1. Age and sex distribution (N=214)

BMB demonstrated a significantly higher detection rate of malignant and infiltrative marrow disorders compared with BMA, particularly in multiple myeloma, lymphoma, and myeloproliferative neoplasms (15.4% vs. 5.6%, 15.4% vs. 11.2%, and 13.1% vs. 10.3%, respectively). Aplastic anemia was identified exclusively by biopsy, whereas aspiration more frequently yielded hypocellular and normal marrow results. (Figure 2)

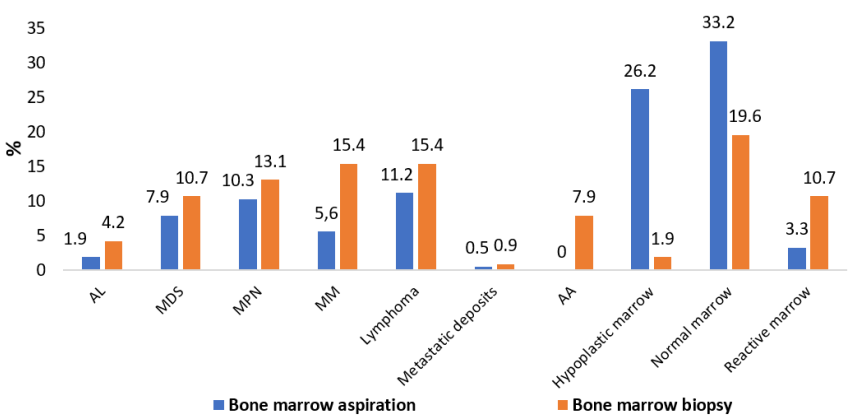

Figure 2. Diagnostic results of bone marrow aspiration and biopsy (N = 214)
(AL Acute leukemia, MDS Myelodysplastic syndrome, MPN Myeloproliferative neoplasm, MM Multiple myeloma, AA aplastic anemia)

Among 48 cases with dry tap on BMA, BMB established a definitive diagnosis in the majority, with malignant hematologic disorders predominating; multiple myeloma was the most frequent diagnosis (22.9%), followed by myelodysplastic syndromes and myeloproliferative neoplasms (each 16.7%), and lymphoma (14.6%). (Figure 3)

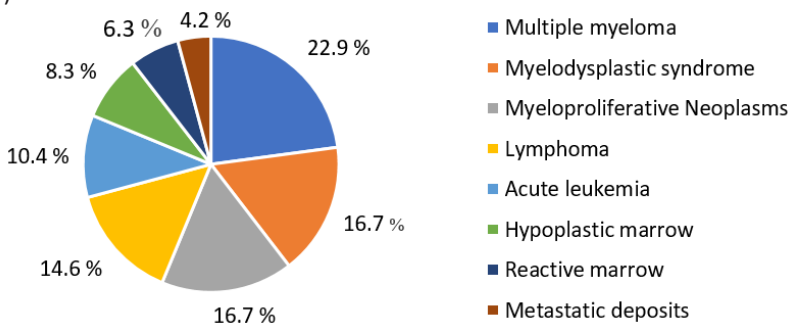

Figure 3. Diagnostic findings of bone marrow biopsy in cases of dry tap aspiration (n = 48)

In our study, analysis of the distribution of benign, malignant, and equivocal findings on BMA and BMB revealed that out of 78 benign cases on BMA, 25 were reclassified as malignant, and 53 were benign on BMB. In 56 equivocal cases on BMA, 29 were confirmed as benign and 23 were malignant on biopsy, and 80 cases were diagnosed as malignant on both. (Table 1)

Table 1. Distribution of benign, malignant, and equivocal findings on bone marrow aspiration and bone marrow biopsy (N = 214)

Bone marrow aspiration	Bone marrow biopsy
78 benign	53 benign, 25 malignant
80 malignant	80 malignant
56 equivocal	29 benign, 23 malignant, 4 equivocal

3.2. Bone marrow involvement in patients with lymphoma

Bone marrow biopsy identified marrow involvement in all 33 patients with lymphoma, whereas bone marrow aspiration detected involvement in only 24 cases (72.7%), with 9 cases (27.3%) reported as normal on bone marrow aspiration. (Figure 4)

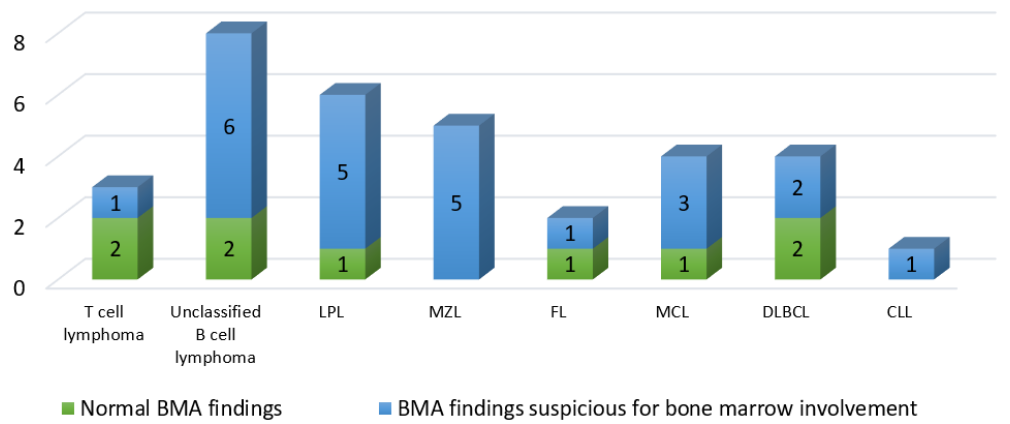

Figure 4. Diagnostic results of bone marrow aspiration and biopsy in the assessment of marrow involvement in patients with lymphoma (n=33)
(LPL Lymphoplasmacytic lymphoma, MZL Marginal zone lymphoma, FL Follicular Lymphoma, MCL Mantle cell lymphoma, DLBCL Diffuse large B-cell lymphoma, CLL chronic lymphocytic leukemia)

The most frequent bone marrow infiltration patterns in patients with lymphoma were diffuse (45.5%) and mixed (39.4%). Within the mixed category, nodular–interstitial infiltration was the most prevalent (30.3%), followed by combined nodular–interstitial–sinusoidal patterns (9.1%). (Figure 5)

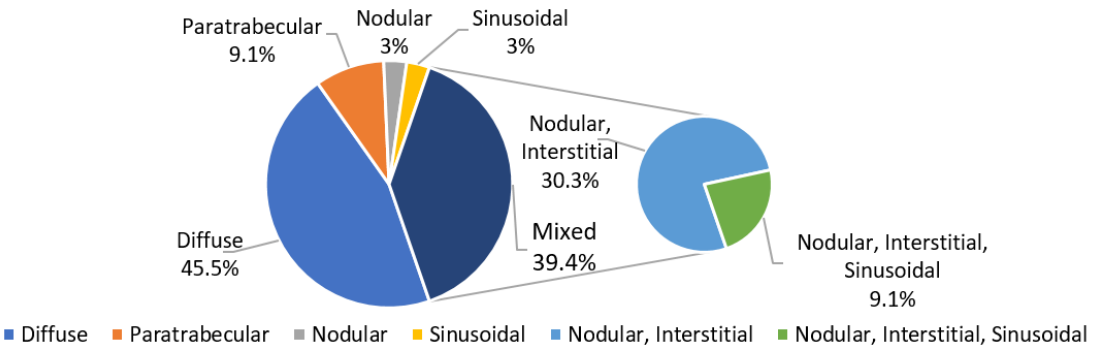

Figure 5. Distribution of bone marrow infiltration patterns in patients with lymphoma (n = 33)

Bone marrow infiltration patterns varied across lymphoma subtypes. Aggressive lymphomas, including DLBCL, MCL, and T-cell lymphoma, predominantly demonstrated diffuse and mixed infiltration patterns, reflecting extensive marrow involvement. In contrast, indolent lymphomas showed more heterogeneous patterns - FL and LPL frequently exhibited paratrabecular or diffuse infiltration, while MZL was mainly associated with diffuse and mixed patterns. (Table 2)

Table 2. Bone marrow infiltration patterns by lymphoma subtype (n = 33)

Subtype	Bone marrow infiltration patterns
T-cell lymphoma	3 mixed
Unclassified B-cell lymphoma	1 nodular, 1 paratrabecular, 2 diffuse, 4 mixed
LPL	1 paratrabecular, 3 diffuse, 1 mixed, 1 sinusoidal
MZL	4 diffuse, 1 mixed
FL	1 paratrabecular, 1 diffuse
MCL	3 diffuse, 1 mixed
DLBCL	2 diffuse, 2 mixed
CLL	1 mixed

Representative cases from our cohort are illustrated in Figures 6 and 7, including a case of dry tap associated with marrow fibrosis (Figure 6) and a BMA-negative/BMB-positive case demonstrating paratrabecular lymphoma infiltration on biopsy (Figure 7).

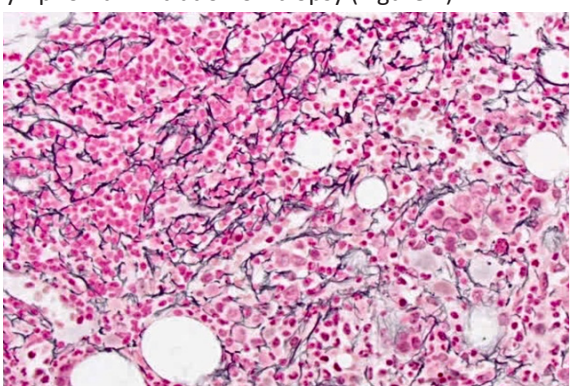

Figure 6. Reticulin stain (x40) showing grade 1 positivity in myelofibrosis

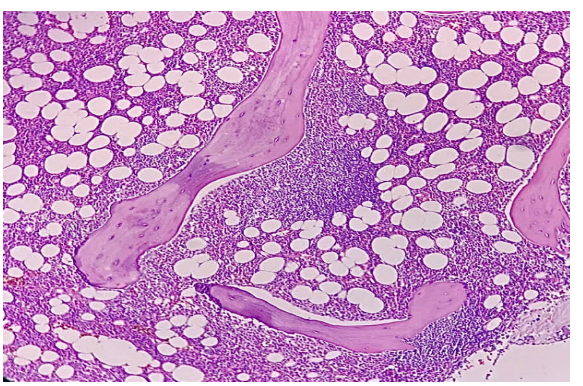

Figure 7. H&E (x40) showing paratrabecular pattern in Non-Hodgkin lymphoma

4. DISCUSSION

As shown in Figure 1, this study cohort was predominantly composed of older adults, which reflects the typical age distribution of patients undergoing BMB. This finding is consistent with those reported by Aydoğmuş, who observed a mean age of 60.3 ± 15.5 years with a range of 18 to 87 years [5], and by Prajapati, who noted that among

106 patients undergoing BMB, the most frequent age group was 50 - 59 years, followed by 60 - 69 years [6]. Similarly, Martellosio reported a mean age of 64 ± 15 years [7]. In our study, the proportion of female patients slightly exceeded that of males, with a male-to-female ratio of 1:1.18, in contrast to some reports in which males predominated. Sex distribution appears to vary according to geographic region and the specific study population.

In Figure 2, comparison of diagnostic outcomes between BMA and BMB demonstrates the superior diagnostic value of BMB across a wide range of hematologic disorders. BMB identified 17 cases of AA (8.1%) that were not detected by BMA. Notably, BMB was significantly more effective in detecting malignant and infiltrative marrow disorders, including MM, lymphoma, and MPN, thereby reducing false-negative interpretations of normal or hypocellular marrow based on BMA alone. These findings highlight the comprehensive histopathologic assessment provided by BMB, including evaluation of cellularity, trabecular architecture, degree of fibrosis, and patterns of malignant cell infiltration, whereas BMA tends to underestimate marrow pathology, particularly in disorders characterized by patchy, focal, or uneven involvement or those associated with marrow fibrosis. Multiple studies have affirmed the critical role of BMB in the diagnosis of hematologic diseases. Gilotra et al. in a comparative study of BMA and BMB in 130 patients reported that the combined use of both modalities significantly improved diagnostic accuracy, with BMB contributing to definitive diagnosis in up to 87% of cases [8]. Vijayamohanan et al. similarly demonstrated that in 21% of cases with normal BMA findings, BMB revealed significant pathology [9].

In cases with dry tap on aspiration in Figure 3, BMB provided definitive diagnoses in a substantial proportion of patients, most commonly hematologic malignancies, particularly MM, followed by MDS, MPN (Figure 6), and lymphoma. This finding underscores the superior capability of BMB in detecting marrow pathology that is difficult to assess on aspiration specimens due to malignant cell infiltration or marrow fibrosis, a condition in which normal marrow elements are replaced by fibrous tissue [10]. Singh et al. reported a lower rate of dry tap (11.8%), among which 84% were diagnosed with hematologic disorders by BMB, most commonly AL (32.8%) [11]. The higher dry tap rate observed in our study may reflect a greater prevalence of hematologic malignancies, such as lymphoma and advanced leukemia, in our patient population. In addition, marrow fibrosis or marked hypercellularity may further contribute to this finding. In such cases, BMB remains the most critical diagnostic modality, as it provides comprehensive assessment of fibrosis, and patterns of malignant infiltration.

In Table 1, BMB showed superior diagnostic yield over BMA, particularly in resolving equivocal cases and detecting malignancy, with 25 benign and 23 equivocal BMA cases reclassified as malignant. This pattern is consistent with Gilotra et al., who reported that among 100 cases, BMB reclassified 8% of BMA diagnoses, with 7 cases initially reported as benign and 1 equivocal case subsequently confirmed as malignant [8]. Although concordance for malignant diagnoses between BMA and BMB was high, BMB demonstrated superior sensitivity for detecting marrow infiltration, particularly in focal, interstitial, or fibrotic involvement. This discrepancy reflects methodological differences, as BMA assesses cytomorphology without architectural context and is limited in dry tap, fibrosis, or patchy disease, whereas BMB preserves tissue architecture, enabling evaluation of cellularity, fibrosis, and infiltration patterns. The diagnostic revisions observed on BMB confirm its role as the gold standard and support the routine combined use of BMA and BMB in hematologic malignancies [6].

The diagnostic comparison between BMA and BMB shown in Figure 4 identified 33 cases of lymphoma with BMI detected by BMB, of which 9 had normal BMA findings, demonstrating the clear limitations of BMA in assessing marrow infiltration in lymphoma patients. Specifically, in T-cell lymphoma, unclassified B-cell lymphoma, LPL, and FL, all five cases with normal BMA results were attributable to marrow fibrosis, and in one case, neoplastic cells exhibited a paratrabecular distribution on BMB (Figure 7). In MCL and DLBCL, three cases showed no abnormalities on BMA due to focal marrow involvement and nodular-interstitial patterns of tumor cell distribution, requiring BMB combined with immunohistochemistry for definitive diagnosis. Vijayamohanan et al. reported that only 3 of 9 (33.3%) lymphoma cases were detected by BMA, whereas BMB demonstrated marrow involvement in all 9 cases [9]. Similarly, Khan et al. found that all lymphoma cases were diagnosed by BMB, but lymphoma cells were observed in only 4 of 18 (22.2%) cases on BMA [12]. In our study, the detection rate of marrow infiltration by BMA was 24 of 33 cases (72.7%), which is higher than

that reported in comparable studies. This may be related to the characteristics of our patients at a general hospital, where most lymphoma patients are referred at advanced stages and present later in the disease course.

Figure 5 demonstrates that the patterns of BMI observed in our study are consistent with the histopathological models described in lymphoma. Diffuse and mixed patterns predominated, reflecting extensive or heterogeneous marrow infiltration by neoplastic cells, which is commonly observed in advanced-stage lymphoma. Gültekin et al., in a study of 102 lymphoma cases with BMI, reported that the mixed pattern, comprising nodular and interstitial components, was the most frequent (29.1%), while the diffuse pattern was the most common isolated infiltration pattern [13], indicating a similar diversity of infiltration patterns to that observed in our study.

Table 2 shows that different patterns of BMI are associated with specific lymphoma subtypes. Aggressive lymphomas, such as T-cell lymphoma, DLBCL, and MCL, predominantly exhibited diffuse or mixed infiltration patterns. In contrast, some indolent lymphomas, such as FL and LPL, demonstrated more heterogeneous patterns, including paratrabecular, nodular, and sinusoidal involvement. Similarly, KILINÇ et al. reported that in DLBCL, infiltration patterns were predominantly diffuse (34.7%), followed by nodular (26%) and mixed (17.4%); in MCL, mixed (47.8%) and diffuse (21.7%) patterns were most common, while paratrabecular involvement was prominent in FL [13]. Notably, in our study, MZL, an indolent subtype, predominantly exhibited diffuse and mixed infiltration patterns. A study of 120 MZL patients demonstrated that there is no fixed pattern of marrow involvement in MZL, as patterns may vary according to disease stage and extent of infiltration [14]. KILINÇ et al. also observed that mixed and diffuse patterns were common across multiple lymphoma subtypes, including indolent forms when marrow involvement was extensive [13]. These findings suggest that the diffuse or mixed marrow infiltration patterns observed in MZL in our study may reflect advanced disease stage, extensive marrow involvement, or dynamic changes in infiltration patterns over the disease course, underscoring the critical role of BMB in the evaluation of marrow involvement. Although each lymphoma subtype tends to exhibit characteristic patterns of marrow involvement, these patterns alone are insufficient for definitive subtype classification; therefore, ancillary studies are required to accurately determine the lymphoma subtype.

Study limitations: This study was conducted at a single regional hospital in Central Vietnam, which may limit the generalizability of the findings. In addition, the study did not include survival analysis or molecular correlation.

5. CONCLUSION

Bone marrow biopsy demonstrated superior diagnostic value in the evaluation of hematologic disorders, particularly malignant diseases, marrow infiltrative processes, and cases of dry tap. In lymphoma, BMB improved detection of marrow involvement and enabled characterization of infiltration patterns relevant to staging and treatment planning. These findings support the routine integration of BMB with immunohistochemistry in standard diagnostic workflows at general hospitals in Viet Nam, where access to specialized hematopathology is expanding, as exemplified by recent implementation at Da Nang Hospital.

Disclosure: The authors report no conflicts of interest in this work.

REFERENCES

1. Isher SK, Singh S, Isher IS, Kale AS. A diagnostic utility of simultaneous bone marrow aspiration and bone marrow biopsy: a retrospective study. Int J Acad Med Pharm. 2023;5(4):1606-1612.

2. Tomasian A, Jennings JW. Bone marrow aspiration and biopsy: techniques and practice implications. Skeletal Radiol. 2022;51(1):81-88.

3. Zahur U, Zafar L, Khaliq S, Rehan M, Khalid A. Frequency and pattern of bone marrow involvement among patients with non-Hodgkin lymphoma. J Ayub Med Coll Abbottabad. 2016;28(3):497-500.

4. Sovani V, Harvey C. Bone marrow trephine biopsy involvement by lymphoma: review of histopathological features in 511 specimens and correlation with diagnostic biopsy, aspirate and peripheral blood findings. J Clin Pathol. 2014;67(5):389-95.

5. Aydoğmuş BB, Özdemir Ç. Clinicopathological Correlations in Adult Bone Marrow Biopsies: Indications, Preliminary Diagnoses, and Histopathological Outcomes in 698 Cases. Preprints: Preprints; 2025. DOI: 10.20944/preprints202511.2193.v1.

6. Prajapati A, Patel N. Utility of Bone Marrow Examination in Hematological Disorders: Bone Marrow Examination in Hematological Disorders. GAIMS J. Med. Sci. 2024;4(2):35-41.

7. Martellosio J, Puyade M. Bone marrow biopsy diagnostic yield in internal medicine. Postgrad Med. 2021;133(1):89-95.

8. Gilotra M, Gupta M. Comparison of bone marrow aspiration cytology with bone marrow trephine biopsy histopathology: An observational study. J Lab Physicians. 2017;9(3):182-189.

9. Vijayamohanan L, Asotra S. Comparative utility of bone marrow aspiration and trephine biopsy in evaluation of hematological disorders. Arch Med Health Sci. 2020;8(1):15-19.

10. Islam A. Diagnostic value of preparing bone marrow smears from the small amount of material left within the aspiration needle following a dry tap. Clin Case Rep. 2018;6(12):2427-2430.

11. Singh S, Ahsan E. Demystifying the evaluation of a “dry tap”. J Hematop. 2025;18(1):17.

12. Khan TA, Khan IA. Diagnostic role of bone marrow aspiration and trephine biopsy in haematological practice. J Postgrad Med Inst. 2014;28(2):217-21.

13. Gültekin A. Lenfomalarda Kemik İliği Tutulum Paterni. Mev Med Sci. 2022;2(1):22-26.

14. Boveri E, Arcaini L. Bone marrow histology in marginal zone B-cell lymphomas: correlation with clinical parameters and flow cytometry in 120 patients. Ann Oncol. 2009;20(1):129-136.