ORIGINAL ARTICLE

Bone Marrow Examination at Tertiary Care Center: A Four-Year Experience Highlighting Diagnostic Trends and Specimen Adequacy

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Abstract

Background: Bone marrow (BM) examination is a cornerstone in the diagnosis, staging, and monitoring of hematologic and systemic disorders. Its diagnostic yield is influenced by both procedural execution and clinical context.

Objective: To analyze the indications, diagnostic outcomes, and specimen quality of bone marrow examinations conducted over four years in the hematology department of a tertiary care hospital.

Methodology: A retrospective cross-sectional study was conducted in the Hematology Department of Liaquat National Hospital, Karachi, analyzing 1,162 BM procedures performed between January 2020 and December 2023. Data were extracted from BM reports, procedure forms, and trephine slides. Incomplete records were excluded. Descriptive analysis was conducted using IBM SPSS (version 20).

Results: Among 1,162 procedures, 728 (62.6%) were performed in males and 434 (37.3%) in females, with a mean patient age of 43.8 years ± 20.24. The majority were conducted by postgraduate trainees (year 2: 443; 38.1%, year 3: 385; 33.1%) under local anaesthesia (1,069; 92.0%). Non-staging indications accounted for 962 (82.8%) cases, with acute leukaemia being the most common. Malignancies were diagnosed in 484 (41.6%) cases, predominantly acute leukaemia. Among benign disorders (250; 21.5%), Immune thrombocytopenia was most frequent, followed by aplastic anaemia and hypoplastic marrow. Despite adequate sampling, 95 (8.2%) cases remained inconclusive. BM aspirates were particulate in 948 (81.6%) cases, while 881 (75.8%) trephine biopsies met the WHO-recommended length.

Conclusion: BM examination remains a vital diagnostic tool in a wide array of hematologic and systemic conditions. High specimen adequacy and diverse diagnostic yield underscore procedural competence and the value of training programs in tertiary care settings.

Keywords: *Bone marrow aspirate, bone marrow biopsy, bone marrow procedure, quality.*

INTRODUCTION

Bone marrow (BM) examination is a fundamental diagnostic tool in hematology, aiding in the diagnosis, staging, and monitoring of a wide range of benign and malignant conditions. It is performed for various indications, including unexplained cytopenias, hematologic malignancies, metastatic cancers, and infectious or storage disorders [1, 2]. BM procedures typically yield two complementary specimens: bone marrow aspirate (BMA) and bone marrow biopsy (BMB). The aspirate provides detailed morphological evaluation, and differential cell counts, and supports advanced studies such as flow cytometry, cytogenetics, and molecular diagnostics. In contrast, the core biopsy is essential for assessing marrow architecture, fibrosis, cellularity, and infiltration, particularly in cases where aspirates are dilute or dry taps occur [1, 3-5].

The diagnostic yield of BM biopsy depends on multiple factors, including patient-related variables, procedural techniques, and operator expertise. The World Health Organization (WHO) provides recommendations for specimen adequacy, emphasizing the importance of obtaining a core biopsy of at least 1.5–2.5 cm in length or 10 preserved intertrabecular spaces, along with a sufficiently cellular and undiluted aspirate [6, 7]. Inadequate specimens can impact diagnostic accuracy, particularly in cases of lymphomas, metastatic diseases, and myeloid malignancies [8, 9].

Bone marrow procedures are routinely performed for a wide range of hematologic, oncologic, and systemic diseases. At our institution, bone marrow biopsies are primarily carried out by hematology residents with assistance from trained staff, using a 16G lumbar puncture needle for aspiration and a disposable T-shaped trephine needle for biopsy. The posterior iliac crest is the preferred site for both aspiration and biopsy, ensuring optimal sample quality and patient comfort. The majority of these procedures are conducted under local anesthesia in a dedicated procedure room, with a small proportion performed under sedation or general anesthesia at the bedside, depending on clinical requirements.

Despite the central role of bone marrow procedures in hematology diagnostics, variations in procedural techniques, operator expertise, and adherence to quality standards can impact diagnostic accuracy [8, 10]. A systematic evaluation of biopsy indications, diagnostic trends, and specimen adequacy is essential for identifying gaps, refining practices, and enhancing

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diagnostic reliability. This study aimed to assess the clinical indications, diagnostic outcomes, and specimen quality of bone marrow examinations over four years in the hematology department of a tertiary care hospital.

METHODOLOGY

Study Design

This was a retrospective cross-sectional study. It was conducted in the Hematology Department at Liaquat National Hospital, a leading tertiary care teaching hospital in Karachi, Pakistan.

Data Collection

For this research, we analyzed 1,162 consecutive in-house BM specimens collected between January 2020 and December 2023. BMA and trephine biopsy slides, corresponding BM reports finalized by consultant hematologists, and BM procedure proformas filled at the time of sampling were retrieved for evaluation. Specimens with incomplete slides, missing reports or missing proformas were excluded from the study. The quality of bone marrow aspirates was assessed based on documentation in the finalized BM reports and correlated with BM aspirate slides where needed. Clinical indications for the procedures were obtained from the proformas filled at the time of sample collection, while the final diagnoses were recorded from the corresponding BM reports. Core biopsy specimen measurements were performed directly on glass slides using a standardized transparent ruler and recorded in centimetres (cm) to ensure consistency and accuracy.

Operational Definitions

Adequate BMA

A BMA is considered adequate if it contains well-preserved marrow particles for cytological evaluation, including differential count, and detection of abnormal cells under a microscope.

Adequate BMB

A BMB is considered adequate if it meets the WHO recommended length of at least 1.5 cm after fixation and processing [6, 7].

Statistical Analysis

Data was taken from the hematology department BM records, entered on a Microsoft Excel sheet, imported on IBM SPSS software (version 20), and then analyzed. Categorical variables, including gender, age group, residence, indications, diagnoses, and procedural details (type of sedation, procedure operator, marrow quality, and trephine biopsy length), were reported as frequencies and percentages. Pearson Chi-square (χ^2) test or Fisher's exact test was used to evaluate the relationship between categorical variables. A p-value < 0.05 was considered statistically significant.

The study was done after getting approval from the Ethical Review Committee at Liaquat National Hospital with Ref. letter No. 0914-2023-LNH-ERC. All procedures performed in studies involving human participants were following the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed written consent was taken from the patients/guardians before the performance of the procedure.

RESULTS

During the four-year study period, a total of 1162 BM procedures were performed There were (728) 62.65% males and (434) 37.34% females with a male-to-female ratio of 1.7:1. The patients' ages ranged from 1 to 93 years with a mean age of 43.8 years in which (106) 9.12% were children aged less than 14 years. The majority of the procedures were performed by year 2 and year 3 postgraduate trainees under local anesthesia.

Table 1: Patient demographics and bone marrow procedure log.

Patient and Procedural Variables	Frequency	Percentage
Sex		
Male	728	62.65
Female	434	37.34
Age group		
Children	106	9.12
Adult	1056	90.87
Residence		
Karachi	541	46.6
Hyderabad	2	0.2
Sindh (rural)	291	25.0
Punjab	16	1.4
KPK	28	2.4
Balochistan	213	18.3
Afghanistan	71	6.1
Patient's group		
Primary patient	483	41.56
Referred patient	679	58.43
Type of Sedation		
Local anesthesia	1069	91.99
General anesthesia	93	8.03
BM Procedure Operator		
R1	241	20.74
R2	443	38.12
R3	385	33.13
R4	93	8.03

R1, 1st year Postgraduate (PG) trainee; R2, 2nd year PG trainee; R3, 3rd year PG trainee; R4, 4th year PG trainee

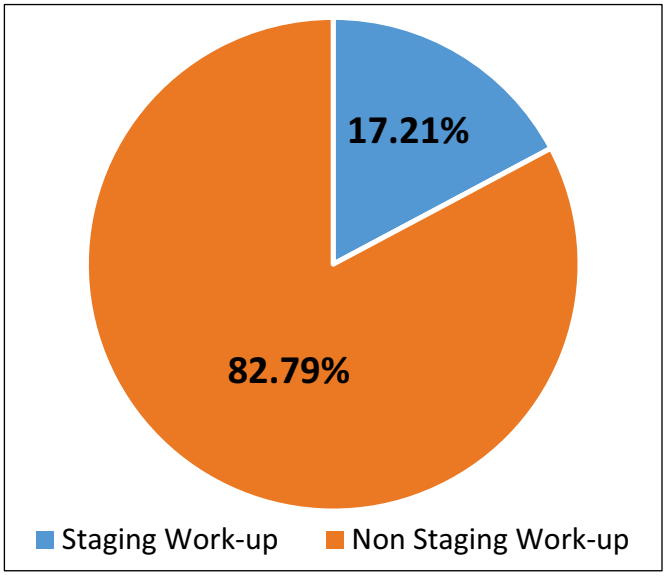

Fig. (1A): Distribution of clinical indications for bone marrow examinations. Staging work-up refers to the evaluation of known malignancies (*e.g.*, lymphoma), while non-staging includes the initial work-up of unexplained cytopenias, suspected leukemia, or systemic illnesses *etc.*

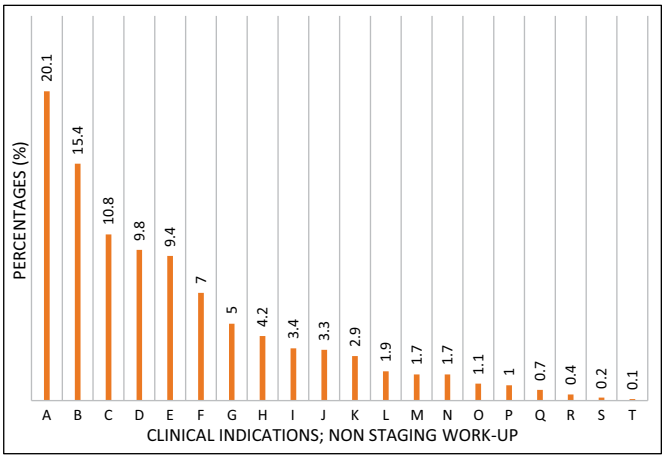

Fig. (1B): Distribution of clinical indications for bone marrow examination; non-staging work-up. A – Acute Leukemia, B – Pancytopenia, C – Metastatic Disease, D – Multiple Myeloma, E – Aplastic Anemia, F – Thrombocytopenia, G – Lymphoproliferative Disorder, H – Clinical Indication Not Provided, I – Anemia, J – Immune Thrombocytopenic Purpura, K – Chronic Myeloid Leukemia, L – Myelodysplastic Neoplasm, M – Bicytopenia, N – Polycythemia Vera, O – Myeloproliferative Neoplasm, P – Essential Thrombocythemia, Q – Tuberculosis, R – Neutropenia, S – Chronic Myelomonocytic Leukemia, T – Juvenile Myelomonocytic Leukemia.

Table **1** summarizes patients' demographics and BM procedure logs.

Clinical indications for BM examination were categorized into staging workups and non-staging workups. Staging workups, performed to assess bone marrow involvement in known cases of malignancies such as lymphoma or solid tumours, accounted for (200)17.21% of all samples. The remaining (962)

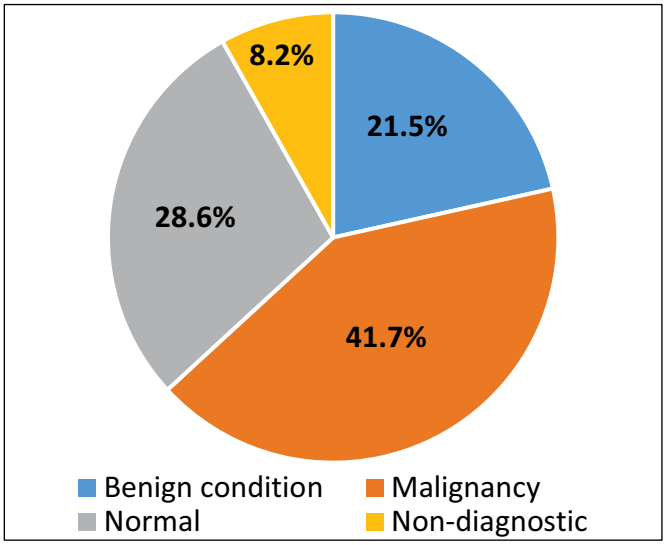

Fig. (2A): Diagnostic outcomes of bone marrow examinations. Diagnoses are categorized into malignancies, benign hematological conditions, normal findings, and non-diagnostic samples. The chart shows that malignancy was the most frequent diagnostic outcome, followed by normal marrow findings, benign conditions, and a small proportion of non-diagnostic cases.

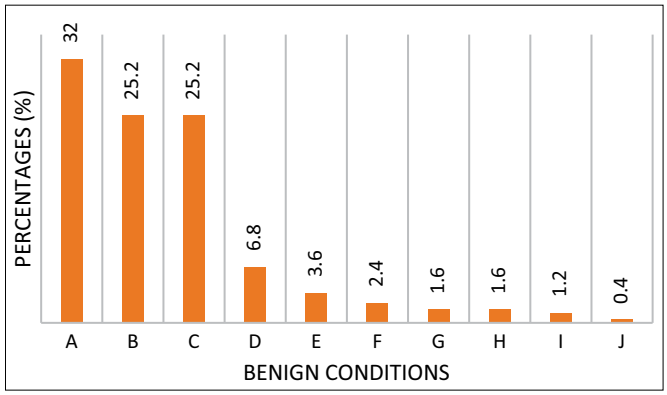

Fig. (2B): Distribution of benign hematological conditions diagnosed on bone marrow examination. A – Immune Thrombocytopenic Purpura, B – Aplastic Anemia, C – Hypoplastic Marrow, D – Megaloblastic Anemia, E – Hemolytic Anemia, F – Pure Red Cell Aplasia, G – Tuberculosis, H – Hemophagocytic Lymphohistiocytosis, I – Chronic Granulomatous Inflammation, J – Leishmaniasis.

82.79% of samples were performed for non-staging clinical indications (**Fig. 1A**). The distribution of non-staging indications is shown in **Fig. (1B)**, with the most common being Acute Leukemia, followed by Pancytopenia, Metastatic disease and Multiple Myeloma.

The distribution of the diagnoses made based on the bone marrow examination is shown in **Fig. (2A)**. Out of 1162 BM specimens, (250) 21.5% of biopsies were found to have benign conditions while (484) 41.6% had malignancy. Immune Thrombocytopenia (ITP) was found to be the most common benign condition followed by Aplastic Anemia and hypoplastic marrow whereas Acute Leukemia was found to be the most common

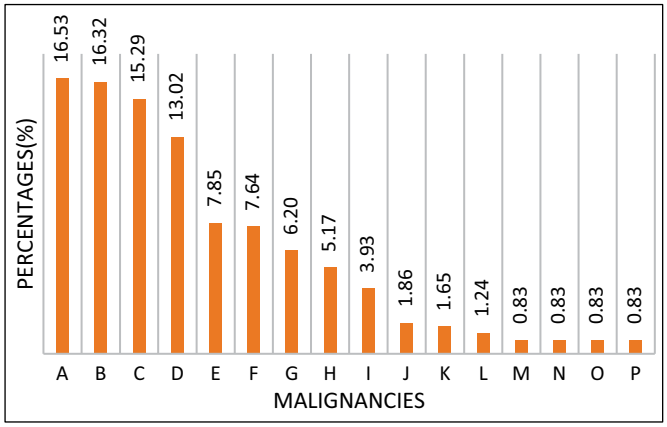

Fig. (2C): Distribution of malignant hematological conditions diagnosed on bone marrow examination. A – Acute Leukemia, B – Metastatic Disease, C – Lymphoproliferative Disorder, D – Multiple Myeloma, E – Acute Myeloid Leukemia, F – Chronic Myeloid Leukemia, G – Acute Lymphoblastic Leukemia, H – Myelodysplastic Neoplasm, I – Primary Myelofibrosis, J – Burkitt's Lymphoma, K – Myeloproliferative Neoplasm, L – Hodgkin's Lymphoma, M – Polycythemia Vera, N – Essential Thrombocythemia, O – Non-Hodgkin Lymphoma – Diffuse Large B-cell Lymphoma, P – Acute Promyelocytic Leukemia.

Table 2: Quality of Bone marrow aspirate and core biopsy.

Variables	Total	Percentage
Quality of Aspirate		
Particulate	948	81.58
Aparticulate	20	1.72
Hemodiluted with marrow particles	194	16.69
Trephine biopsy Length		
Short length (<1.5cm)	281	24.18
Adequate length (>1.5cm)	881	75.81

malignant condition followed by Metastatic disease and Lymphoproliferative condition (**Figs. 2B&C**). A conclusive diagnosis could not be reached in (95) 8% of cases, despite an adequately performed bone marrow examination.

The quality of bone marrow aspirates and the length of core biopsies are summarized in Table **2**. A total of (948) 81.58% of aspirate samples were deemed adequate, showing particulate material. Likewise, (881) 75.81% of trephine biopsies had an adequate post-processing length of ≥ 1.5 cm.

DISCUSSION

Our institution is a tertiary care hospital offering over 35 specialized services under one roof. The Hematology Department routinely conducts bone marrow examinations for a wide range of hematological and non-hematological conditions, serving both pediatric and adult populations. Due to the high volume of procedures performed, it is crucial to uphold rigorous quality standards in specimen collection, processing, and reporting to ensure diagnostic accuracy and optimal patient outcomes. In alignment with the study's objective to systematically assess the indications, diagnostic trends, and specimen quality of bone marrow examinations, we conducted a comprehensive analysis of 1,162 cases in a training-focused environment. This represents one of the largest datasets from the region and provides valuable insights into current clinical practices while identifying key areas for improvement.

Regarding the clinical indications, non-staging workups accounted for the majority (82.78%) of procedures, with Acute Leukemia, Pancytopenia, and Metastatic disease being the most common reasons for bone marrow (BM) examination. This trend is consistent with the high burden of hematological malignancies and marrow involvement in systemic diseases [11]. However, the findings are unexpectedly high in contrast with local studies, which identified anemia as the most common indication [2, 12]. On the other hand, these findings align with various international studies conducted both in neighbouring countries like Iran [13] and India [14] and other Asian countries such as Saudia Arabia [15] and Nepal [16]. Similar trends have also been observed in studies from Africa [17] United States and Canada [18]. The discrepancy may be attributed to the improved approach to diagnosis, which is now following international standards. Clinicians are increasingly using non-invasive tests for anemia before proceeding to bone marrow examination. The relatively lower proportion of staging workups (17.21%) aligns with the decreasing reliance on bone marrow examination for staging purposes, as advanced imaging modalities such as CT scans, PET/CT scans, and MRI have become the preferred tools for staging solid tumours and lymphomas due to their higher sensitivity and non-invasive nature [19].

The distribution of bone marrow diagnoses highlights the diagnostic significance of this procedure, with 41.6% of specimens confirming malignancies and 21.5% indicating benign conditions. These findings are consistent with a local study by Omer *et al.* which also reported a higher prevalence of malignant conditions compared to benign ones. However, in our study, Acute Leukemia emerged as the most frequently diagnosed malignancy, followed by Metastatic disease and Lymphoproliferative disorders. This contrasts with the findings of Omer *et al.* where Chronic Myeloid Leukemia (CML) was the most common malignancy, followed by Multiple Myeloma [10].

Among benign cases, Immune thrombocytopenic purpura (ITP) was the most frequently observed condition, followed by Aplastic Anemia and Hypoplastic marrow. These findings are almost comparable to local and international studies [10, 15, 20]. Likely due to the common diagnostic approach and clinical indications for bone marrow examination in patients presenting with unexplained cytopenias. The similarity in diagnostic distribution may also reflect standardized referral patterns and uniform criteria for bone marrow evaluation across different healthcare settings.

The diagnostic yield of BM is 92% which is comparable to a local study [10] and notably higher than an international study [21]. This difference may be attributed to variations in patient selection, as our study was conducted in a dedicated hematology unit, where bone marrow procedures are primarily performed for well-defined indications. Additionally, the availability of ancillary diagnostic tools (*e.g.*, flow cytometry, cytogenetics, and molecular studies) may have further contributed to the higher diagnostic accuracy observed in our setting. However, 8% of cases remained inconclusive despite adequate sample collection, emphasizing the limitations of BM examination alone in certain clinical scenarios. In such cases, supplementary investigations including immunohistochemistry, next-generation sequencing (NGS), fluorescence *in situ* hybridization (FISH), and targeted gene panels may be used for definitive diagnosis and disease characterization.

Specimen adequacy is a critical determinant of diagnostic accuracy. In this study, 75.81% of trephine biopsies had a post-processing length of ≥1.5 cm, correlating with higher diagnostic accuracy for malignant disorders. The World Health Organization (WHO) recommends a minimum core length of 1.5 cm, a standard further supported by the International Council for Standardization in Haematology (ICSH), which advises a pre-processing core length of at least 2 cm in adults. However, a shorter core (*e.g.*, 1 cm) may sometimes provide sufficient diagnostic information [3]. Bishop *et al.* emphasized that trephine cores of at least 1.6 cm are essential for reliably detecting malignant tumours [22]. Similarly, Goyal *et al.* reported that trephine biopsies with a pre-processing length of ≥1.7 cm had a significantly higher lymphoma detection rate compared to those measuring ≤1.6 cm, highlighting the importance of technical precision in the procedure [23]. Similarly, the presence of particulate BM aspirate material directly impacts the diagnostic utility of the specimen. In our study, 81.58% of BM aspirate specimens were particulate which is comparable to another study reported by Odejide *et al.* Although the particulate specimen yield in our study was relatively high, the absence of marrow particles in a subset of cases underscores the inherent limitations of BM aspiration alone. In such instances, reliance on trephine biopsy findings becomes essential for comprehensive diagnostic evaluation.

Beyond patient-related or disease-specific variables, operator technique also plays a crucial role in specimen adequacy. Unfortunately, due to the retrospective nature of our study and the lack of intra-procedural quality checks, we were unable to objectively assess whether inadequate aspiration was due to operator-related factors. Additionally, we were unable to measure the pre-processing length of trephine cores to determine whether suboptimal post-processing lengths resulted from procedural technique or tissue loss during processing. While ancillary diagnostic tools such as flow cytometry, cytogenetics, and molecular studies are integral to comprehensive hematologic diagnosis, they were often performed later in the disease workup and not consistently recorded in the initial bone marrow reports, restricting their inclusion in our analysis. These limitations underscore the need for real-time specimen adequacy checks, proper documentation of biopsy parameters, and the establishment of standardized protocols for evaluating operator performance. We recommend the implementation of prospective quality assurance protocols and enhanced training in aspiration and biopsy techniques to improve procedural outcomes and ensure consistent diagnostic quality.

CONCLUSION

This study underscores the indispensable role of bone marrow examination in the diagnostic work-up of hematologic and systemic disorders. The high rate of specimen adequacy and broad diagnostic spectrum reflect procedural proficiency, adherence to quality control measures, and diagnostic acumen within a training-focused tertiary care setting. The active involvement of skilled specialists and structured supervision of trainees contribute significantly to diagnostic accuracy. Furthermore, the integration of ancillary techniques such as flow cytometry, cytogenetics, and immunohistochemistry enhances the interpretive value of bone marrow evaluations. Strengthening diagnostic services, reinforcing quality assurance protocols, and fostering excellence in training will further advance the accuracy and impact of hematologic diagnostics.

ETHICAL APPROVAL

Ethical approval was obtained from the Ethical Review Committee, Liaquat National Hospital and Medical College, Karachi (REF letter No. 0914-2023-LNH-ERC). All procedures performed in studies involving human participants followed the ethical standards of the institutional and/ or national research committee and the Helsinki Declaration.

CONSENT FOR PUBLICATION

Written informed consent was taken from the participants.

AVAILABILITY OF DATA

The datasets generated or analyzed during the current study are not publicly available due to institutional data protection policies.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

AUTHORS' CONTRIBUTION

SMA and NR conceived the study concept and designed the research methodology. SMA, ASK, AAM, FM, NA, ATS, MAM contributed to data collection, statistical analysis, and result interpretation. SMA, ASK, AAM, FM, NA, ATS, MAM was involved in manuscript drafting, while SMA, NR critically reviewed and revised the initial draft.

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