

## ORIGINAL ARTICLE

**EVALUATION OF BONE MARROW ASPIRATE, TREPHINE BIOPSY AND IMMUNOHISTOCHEMISTRY IN NON- HAEMOPOIETIC MALIGNANCIES****Aiza Saadia, Maham Arshad, Sunila Tashfeen, Sidra Naveed , Warda Furqan, Fahad Ahmed**

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**Background:** Bone marrow involvement in non-haematopoietic malignancies is rare but clinically significant. Accurate diagnosis is crucial for assessing disease progression and prognosis. This study evaluates the diagnostic effectiveness of bone marrow aspiration and trephine biopsy in detecting non-haematopoietic malignancies. Objective of this study was to assess bone marrow aspiration and trephine biopsy findings in metastatic solid tumours and confirm diagnoses using immunohistochemistry. **Methods:** This cross-sectional study was conducted at Pathology (Haematology) Department, Pak Emirates Military Hospital, Rawalpindi, from Apr 2021 to Jun 2023. Data were collected from patients undergoing bone marrow biopsy who were provisionally diagnosed with metastatic solid tumours. Statistical analysis was performed using SPSS-22, with quantitative data expressed as Mean±SD and qualitative data as frequencies and percentages. Chi-square test was applied and  $p \leq 0.05$  was considered statistically significant. **Results:** There were 21 patients in the study, 18 (85.7%) male and 3 (14.3%) female. The mean age was 63.81±11.82 years (range: 40–86). Common symptoms included pallor (52.4%), weight loss (28.6%), and fever (19.0%). Bone marrow trephine biopsy revealed metastatic tumours in 8 patients (38.1%), anaemia of chronic disease in 3 (14.3%), peripheral platelet destruction in 1 (4.8%), and reactive changes in 6 (28.26%). **Conclusion:** Metastatic solid tumours were found in 38.1% of cases, highlighting the importance of bone marrow evaluation in disease monitoring and prognosis. Understanding marrow metastasis patterns supports research and targeted therapies.

**Keywords:** Bone Marrow, Immunohistochemistry, Trephine BiopsyPak J Physiol 2025;21(1):56–9, DOI: <https://doi.org/10.69656/pjp.v21i1.1771>**INTRODUCTION**

Bone marrow examination is a convenient and beneficial analytical technique in Pathology practice for the diagnosis of both haematological disorders as well as non-haematological solid malignancies. The bone marrow examination helps in either confirmation of the already formed diagnosis or may provide the earlier unanticipated diagnosis.<sup>1</sup>

Bone marrow metastatic malignancies are usually all non-haematological solid tumours that originate in other parts of the body and metastasize to the bone marrow through blood or lymphatic circulation.<sup>2</sup>

Many frequently arising solid tumour reveals great incidence of bone marrow involvement in their later stages.<sup>3</sup> In adults, the most common metastatic solid tumours seen in bone marrow are from breast, prostate, lung and gastrointestinal tract and in children from neuroblastoma. Diagnosis of metastatic solid tumours in bone marrow can be challenging, as in certain cases they may not always produce visible symptoms and may not show up on imaging studies.<sup>4</sup> In some cases of advanced disease, bone marrow metastasis is diagnosed before the primary tumour site due to cytopenias.<sup>5</sup>

Bone marrow aspiration is adequate for diagnosing megaloblastic anaemia and the majority of haematological malignancies. On the other hand, bone marrow trephine biopsy is better suited for identifying conditions involving focal marrow abnormalities, such as lymphoproliferative disorders, lymphoma staging, metastatic tumours, granulomatous diseases, and hypoplastic marrow. To ensure the highest level of diagnostic precision, performing both procedures together is strongly advised.<sup>6</sup> Bone marrow trephine biopsy provides a way to directly visualize and analyse the bone marrow tissue for the presence of cancer cells. The biopsy allows for the discovery of small deposits of tumour cells that may not be detectable by other diagnostic methods. The biopsy can help determine the extent of tumour involvement in the bone marrow, which is important for determining the stage of the cancer and planning appropriate treatment. Bone marrow involvement in solid tumours is a poor prognostic factor and can influence treatment decisions. Majority of cancer deaths occur as a result of expansion of irredeemable metastasis.<sup>7</sup>

In this article, we will discuss role of bone marrow trephine biopsy in diagnosing metastatic solid tumours in bone marrow and reliability of bone marrow trephine biopsy in diagnosis of metastatic solid tumours.

## METHODOLOGY

It was a cross-sectional study, carried out at the Department of Pathology (Haematology), Pak Emirates Military Hospital, Rawalpindi for a duration of 2 years, from Apr 2021 to Jun 2023, after taking approval from the Ethical Review Committee (ERC/ID/265). A total of 745 bone marrow biopsies performed during the study period were analysed. A total of 21 cases of suspected metastatic bone marrow infiltration were retrieved. Non probability consecutive sampling technique was used.

Inclusion criteria was patients of age 45 to 75 years, of both genders, with suspicion of metastatic solid tumour in bone marrow trephine which was later confirmed by immunohistochemistry. Exclusion criteria was no confirmed evidence of solid metastatic bone marrow tumour on aspiration.

The patients' history, physical findings, haematological and bone marrow trephine findings were reviewed retrospectively and were noted down on proforma. Clinical profile included information about patients' age, gender, physical findings and provisional diagnosis on aspiration. Peripheral blood counts and blood films were reviewed. Bone marrow aspirations and subsequent trephine biopsies were performed in all the patients. The bone marrow aspiration findings were correlated with trephine biopsy results. Results were later confirmed by applying relevant immunohisto-chemistry markers.

Data was analysed on SPSS-22. Quantitative data was represented using Mean±SD and qualitative data was represented by using percentage and frequency. Chi-square test (for comparison of qualitative variables) was applied and  $p \leq 0.05$  was taken as statistically significant.

## RESULTS

A total of 21 patients were included in the study, 18 (85.7%) patients were male and 3 (14.3%) were female. The mean age of the patients was  $63.81 \pm 11.82$  years ranging from 40 to 86 years. Majority of the patients had pallor history 11 (52.4%) followed by weight loss 6 (28.6%) and fever 4 (19.0%). Of the total lymph nodes biopsy was done in 8 (38.1%) patients and not done in 13 (61.9%) patients. The detail of patients' history and lymph nodes biopsy shown in Table-1. However, out of 21 patients, CRP raised in 11 patients (52.4%), Serum Alk Phosphatase in 7 patients (33.3%), and LHD raised in 13 patients (61.9%).

The CK7 marker was positive in 10 patients (47.6%) followed by Pan Ck (n=9; 42.9%), PAS (n=8; 38.1%), CK20 (n=8; 38.1%) and can 5.2 (n=3; 14.3%). The following table shows Immunohistochemistry markers applied (Table-2).

Eight (38.1%) patients had metastatic tumour, 3 (14.3%) had anaemia of chronic disorder, 1 (4.8%) had peripheral destruction of platelets, 1 (4.8%) had iron deficiency anaemia, 1 (4.8%) had mixed deficiency anaemia, and 1 patient (4.8%) had few clumps of atypical non-haemopoetic cells seen. The details of aspiration results are shown in Table-3.

Out of 21 Patients, 8 (38.09%) patients had metastatic tumour/metastatic carcinoma, 3 (14.3%) patients had adenocarcinoma prostate infiltrating bone marrow, 1 (4.8%) patient had peripheral destruction of platelets, and 3 (14.3%) patients had anaemia of chronic disorder. The details of trephine reports/results are shown in Table-4.

Out of the total, 6 (28.57%) patients showed metastatic tumour/metastatic carcinoma in both aspirate and trephine, followed by anaemia of chronic disorder (2, 9.6%), and reactive change (4, 19.0%). There were statistical significant differences between aspirate and trephine reports of the patients ( $p=0.003$ ) as shown in Table-5.

**Table-1: The detail of patient's history and lymph nodes biopsy (n=21)**

Variables	Frequency	Percentage
<b>Patient's history</b>		
Pallor	11	52.4
Weight loss	6	28.6
Fever	4	19.0
<b>Lymph nodes biopsy</b>		
Yes	8	38.1
No	13	61.9

**Table-2: Immunohistochemistry markers in patients (n=21) [n (%)]**

Markers	Positive	Negative	Inconclusive
Pan Ck	9 (42.9)	7 (33.3)	5 (23.8)
PAS	8 (38.1)	4 (19.0)	9 (42.9)
Can 5.2	3 (14.3)	9 (42.9)	9 (42.9)
CK 7	10 (47.6)	3 (14.3)	8 (38.1)
CK 20	8 (38.1)	4 (19.0)	9 (42.9)

**Table-3: Diagnosis on bone marrow aspiration (n=21)**

Entities	Frequency	Percentage
Diluted Marrow	2	9.5
Metastatic tumour	8	38.1
Anaemia of chronic disorder	3	14.3
Peripheral destruction of platelets	1	4.8
Reactive changes	4	19.0
Iron deficiency anaemia	1	4.8
Mixed deficiency anaemia	1	4.8
Few clumps of atypical non-hemopoetic cells seen	1	4.8

**Table-4: Diagnosis on bone marrow trephine biopsy (n=21)**

Entities	Frequency (%)
Adenocarcinoma prostate infiltrating marrow	3 (14.3)
Metastatic tumour/metastatic carcinoma	8 (38.09)
Reactive change	6 (28.6)
Peripheral destruction of platelets	1 (4.8)
Anaemia of chronic disorder	3 (14.3)

**Table-5: Comparison of diagnosis on bone marrow aspiration and trephine (n=21) [n (%)]**

Aspiration	Trephine						p
	Adenocarcinoma prostate infiltrating marrow	Metastatic tumour/metastatic carcinoma	Reactive change	Peripheral destruction of platelets	Anaemia of chronic disorder	Total	
Diluted Marrow	1 (4.8)	1 (4.8)	0 (0)	0 (0)	0 (0)	2 (9.6)	0.003
Metastatic Tumour	2 (9.5)	6 (28.57)	0 (0)	0 (0)	0 (0)	8 (38.2)	
Anaemia of chronic disorder	0 (0)	0 (0)	1 (4.8)	0 (0)	2 (9.6)	3 (14.3)	
Peripheral destruction of platelets	0 (0)	0 (0)	0 (0)	1 (4.8)	0 (0)	1 (4.8)	
Reactive changes	0 (0)	0 (0)	4 (19.0)	0 (0)	0 (0)	4 (19.0)	
Iron deficiency anaemia	0 (0)	0 (0)	0 (0)	0 (0)	1 (4.8)	1 (4.8)	
Mixed deficiency anaemia	0 (0)	0 (0)	1 (4.8)	0 (0)	0 (0)	1 (4.8)	
Few clumps of Atypical non-hemopoetic cells seen	0 (0)	1 (4.8)	0 (0)	0 (0)	0 (0)	1 (4.8)	
Total	3 (14.3)	8 (38.09)	6 (28.6)	1 (4.8)	3 (4.3)	21 (100)	

## DISCUSSION

Bone marrow is a rare yet important site for metastasis of non-haematopoietic solid tumours, affecting less than 10% of patients with metastatic disease and being associated with a poor prognosis.<sup>8</sup> Bone marrow assessment for metastasis detection is conducted in two scenarios: as part of the staging process in patients identified with non-haematological malignancies or to endorse metastases in suspected cases, indicated by abnormal peripheral blood results or radiologically suspected cases of bone marrow involvement.<sup>1</sup> Most common reported non-haematological malignancies which results in bone marrow metastasis include those arising in the prostate, breast, lung and neuroblastoma.<sup>9</sup>

Present study focused on the clinical features of the patients with solid cancers and bone marrow metastasis detected on bone marrow trephine biopsy. The mean age of the patients was 63.81±11.82 years and ranged from 40 to 86 years. Khan *et al*<sup>10</sup> showed mean age of their subjects as 40±11.5 years. Patients in our study were of the same median age as was detected in a similar study conducted in Taiwan<sup>11</sup>.

In our study, prostatic adenocarcinoma (14.3%) was the most common solid cancer with bone marrow metastasis, whereas in a similar study by Hung YS *et al*<sup>11</sup> the most common primary tumour location was found to be stomach (39%) followed by prostate (19%) and lung (15%). In Kucukzeybek BB *et al*<sup>12</sup> study most cases were from primary breast carcinoma. The smaller percentage of cases of primary tumour in our study is related to the invasive nature of the procedure due to which mostly terminally ill patients and their physicians find this procedure of little to no help in treatment of the patient.

Clinically, in present study the most common symptoms experienced by the patient was body aches and bone pain (42%), followed by fever (28%) and weight loss (23%). The results in this study were in coherence with the results of parallel studies conducted by Yu-Shin Hung *et al*<sup>11</sup> and Chauhan K *et al*.<sup>13</sup>

The single biochemical marker raised in majority of the cases in present study was LDH whereas

in a study conducted by Arya L *et al*<sup>14</sup> ALP was found to be elevated in almost all cases of patients of bone marrow metastasis of solid tumours. In contrast, serum LDH was raised as established by few case reports and case series in the background of BM involvement by a solid organ cancer.<sup>15-17</sup>

It is always endorsed to execute both aspiration and biopsy and these are considered harmonizing to each other.<sup>18</sup> In the present study, out of total, 6 (28.6%) patients showed metastatic tumour both in aspirate and trephine biopsy. In the study by Rani HS *et al*<sup>1</sup> one case of metastatic malignancy was missed on trephine biopsy but detected on bone marrow aspiration owing to sparse spreading of the tumour. In the present study, primary origin of all diagnosed metastatic tumours was confirmed by immunohistochemistry.

## CONCLUSION

Trephine biopsy has higher sensitivity than bone marrow aspirates in diagnosis of marrow metastasis and should be performed in all cases for detection of bone marrow metastasis along with augmentation by relevant immunohistochemistry markers.

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### Contribution of Authors:

**AS:** Concept and drafting of work  
**ST:** Final approval of manuscript  
**WF:** Interpretation of data

**MA:** Concept and design of work  
**SN:** Reviewing the data  
**FA:** Acquisition of data

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