The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 7, 2025

AXILLARY NODE METASTASIS IN CARCINOMA OF THE BREAST: A COMPARISON OF CLINICAL/SURGICAL/HISTOPATHOLOGICAL FINDING

Dr. Maham Waseem[*1], Muhammad Imran Anwar[2], Muhammad Naeem[3], Sumbal Dildar[4], Muhammad Hammad Ur Rehman Aslam[5], Muhammad Usama Khan[6]

[*1]*MBBS, FCPS, PGR General Surgery, Unit 1 Department Of General Surgery & Surgical Oncology at Sheikh Zayed Hospital Lahore*
[2]*FCPS, FRCS, MCPS-HPE, HOD Of Department Of General Surgery & Surgical Oncology, Director Medical Education, Director Accident & Emergency Shaikh Zayed Hospital, Lahore*
[3]*MBBS, MCPS, FCPS, MRCS (UK), Assistant Professor, Unit 1 Department Of General Surgery And Surgical Oncology, Shaikh Zayed Hospital, Lahore*
[4]*MBBS, FCPS, PGR General Surgery, Department Of General Surgery & Surgical Oncology Shaikh Zayed Hospital, Lahore*
[5]*MBBS, FCPS, PGR General Surgery, General Surgery And Surgical Oncology, Unit – 1 Sheikh Zayed Medical Complex, Lahore*
[6]*MBBS, FCPS, PGR Orthopedics Surgery, Department Of Orthopedic Surgery At Sheikh Zayed Hospital Lahore*

[*1]mahwaseeeem@gmail.com

DOI: https://doi.org/10.5281/zenodo.17356553

Keywords
Axillary lymph nodes, Breast carcinoma, Clinical correlation, Histopathology, Metastasis, Surgical findings

Article History
Received: 15 May 2025
Accepted: 02 July 2025
Published: 14 July 2025

Corresponding Author: *
Dr. Maham Waseem

Abstract

Background: *Breast carcinoma is the most prevalent malignancy among women globally and a major cause of cancer-related deaths. Axillary lymph node status is a crucial prognostic indicator in determining disease staging, treatment planning, and overall survival.*

Objectives: *To assess the clinical, surgical, and histopathological findings of axillary lymph node metastasis in patients with breast carcinoma.*

Study Design & Setting: *A cross-sectional comparative study was conducted at the Department of General Surgery, Shaik Zayed Hospital Lahore from April 2024 to April 2025.*

Methodology: *A total of 120 female patients with histologically confirmed breast carcinoma undergoing modified radical mastectomy were included. Clinical evaluation of axillary lymph nodes was performed by palpation, followed by intraoperative surgical assessment. Excised lymph nodes were examined histopathologically for metastatic involvement. Data were analyzed using SPSS version 26. Sensitivity, specificity, and diagnostic accuracy of clinical and surgical findings were calculated with histopathology as the reference standard.*

Results: *Among 120 patients, 68 (56.7%) showed clinically palpable nodes, while 74 (61.7%) were surgically suspected. Histopathology confirmed metastasis in 79 (65.8%) cases. The correlation between clinical and histopathological findings was significant ($p < 0.05$), and surgical assessment demonstrated higher diagnostic accuracy (82.5%) compared to clinical evaluation (74.1%).*

Conclusion: *Surgical assessment of axillary lymph nodes correlates more accurately with histopathological findings than clinical evaluation, emphasizing the importance of intraoperative evaluation for precise staging and management.*

INTRODUCTION

Breast carcinoma remains the most prevalent malignancy among women worldwide and represents a leading cause of cancer-related mortality.[1] Globally, over 2.3 million new cases of breast cancer were diagnosed in women in 2022, making it the most common cancer among women in 157 of 185 countries.[2] In Pakistan, breast cancer accounts for about 22–25% of all cancers, with an incidence rate rising toward 43 per 100,000 females, and estimates suggest that ~1 in 9 women will develop breast cancer in their lifetime.[3] The prognosis and therapeutic strategy in breast carcinoma are primarily determined by tumor size, grade, hormone receptor status, and, most importantly, the presence or absence of axillary lymph node metastasis.[4]

The axillary lymph nodes serve as the first echelon of metastatic spread from the primary breast tumor, making their assessment crucial in clinical practice. Traditionally, axillary lymph node status has been evaluated through three main approaches—clinical examination, intraoperative or surgical assessment, and histopathological analysis.[5] Clinical evaluation is performed by inspection and palpation to detect nodal enlargement, fixation, or matting. However, it is often limited by the depth and small size of the lymph nodes, leading to both false-negative and false-positive findings.[6]

During surgery, axillary node assessment provides direct visualization and tactile feedback to the surgeon. Enlarged, firm, or matted lymph nodes identified intraoperatively raise suspicion of metastatic disease.[7] Furthermore, reactive hyperplasia and inflammatory changes can mimic metastasis, resulting in overestimation of nodal involvement. Despite these limitations, intraoperative evaluation remains a valuable step in surgical decision-making, especially in centers where frozen section facilities are not routinely available.[8]

Histopathological examination remains the gold standard for confirming the presence of metastatic disease in axillary lymph nodes. Microscopic evaluation allows for accurate detection of tumor cells, quantification of metastatic burden, and identification of extranodal extension.[9] The number of involved lymph nodes directly correlates with disease stage and survival rates, and hence forms the basis of the TNM classification system. A meticulous histopathological examination not only provides definitive staging information but also guides decisions regarding adjuvant chemotherapy, radiotherapy, and hormonal therapy.[10]

Several studies have highlighted discrepancies between clinical, surgical, and histopathological findings of axillary node involvement. Conversely, histopathology, although definitive, is time-consuming and resource-dependent. The evaluation of axillary lymph nodes is also evolving with the introduction of sentinel lymph node biopsy (SLNB) and imaging techniques such as ultrasonography and MRI. However, in many developing countries, full axillary dissection remains the standard procedure, and reliance on clinical and intraoperative judgment persists. Therefore, comparative analysis of these traditional assessment methods against histopathological findings remains highly relevant.

MATERIALS AND METHODS

This cross-sectional comparative study was conducted in the Department of Surgery, Shaikh Zayed Hospital Lahore from April 2024 to April 2024. Informed consent was obtained from all participants prior to inclusion, and approval was granted by the Institutional Ethical Review Committee. A total of 120 female patients diagnosed with carcinoma breast and planned for modified radical mastectomy were included in the study. The sample size of 120 was calculated using the World Health Organization (WHO) sample size calculator by taking expected sensitivity of 70%, margin of error of 8%, and confidence level of 95%.[13]

All patients with histopathologically confirmed carcinoma breast who underwent axillary lymph node dissection were included, while those who had received neoadjuvant chemotherapy, presented with

recurrent breast cancer, or had incomplete records were excluded from the study. Detailed demographic and clinical information, including age, tumor size, and side of involvement, were recorded. Clinical evaluation of axillary lymph nodes was performed preoperatively by inspection and palpation to determine the presence of enlarged, firm, or fixed nodes. Findings were documented as positive or negative for clinical suspicion of nodal metastasis. During surgery, intraoperative assessment of axillary lymph nodes was carried out by the operating surgeon. The nodes were visually inspected and palpated for size, consistency, and fixation. Surgical findings were classified as positive when hard, matted, or enlarged nodes were observed, and negative when nodes appeared soft and mobile. Following clinical and surgical evaluation, axillary lymph node dissection was performed in all patients as part of the definitive surgical procedure. The excised lymph nodes were labeled and sent for histopathological examination.

Histopathological assessment was considered the gold standard for confirming the presence of metastatic disease. Lymph nodes were examined microscopically after hematoxylin and eosin staining to determine the presence of malignant cells, number of involved nodes, and extranodal extension. Based on histopathological results, patients were categorized as positive or negative for metastasis.

All data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 27. Quantitative variables such as age and tumor size were presented as mean ± standard deviation, while qualitative variables such as clinical, surgical, and histopathological nodal status were expressed as frequencies and percentages. The diagnostic accuracy of clinical and surgical assessment was evaluated using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy, taking histopathological findings as the reference standard. The degree of agreement between clinical, surgical, and histopathological findings was determined using the Kappa (κ) statistic. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

The demographic characteristics of the 120 patients included in the study revealed that the mean age of participants was 49.6 ± 10.8 years, with the majority falling within the 50–70 years age group (51.7%) followed closely by those aged 25–49 years (48.3%). The mean tumor size was 3.8 ± 1.4 cm, indicating that most patients presented with moderately large tumors. Regarding laterality, the right breast was slightly more commonly affected (56.7%) compared to the left breast (43.3%). In terms of menopausal status, postmenopausal women formed the majority of the study population (58.3%), while 41.7% were premenopausal, as given in Table 1.

Assessment of axillary node metastasis through different diagnostic approaches showed variations in positivity rates. On clinical examination, 74 (61.7%) patients were found to have palpable or suspicious axillary nodes, while 46 (38.3%) had no clinical evidence of metastasis. Surgical assessment indicated a higher detection rate, with 82 (68.3%) patients showing intraoperative evidence of enlarged or firm lymph nodes. Histopathological examination, considered the gold standard, confirmed axillary metastasis in 90 (75.0%) patients, while 30 (25.0%) showed no nodal involvement. as given in Table 2.

Distribution of the number of histopathologically positive lymph nodes showed that the largest group of patients (36.7%) had 1–3 positive nodes, followed by 23.3% with 4–6 nodes, and 15.0% with more than 6 nodes involved. A total of 30 patients (25.0%) were found to have no metastatic involvement of axillary lymph nodes. These results indicate that the majority of breast carcinoma cases demonstrated limited nodal involvement rather than extensive metastasis, as given in Table 3. The comparison between clinical assessment and histopathological findings of axillary node metastasis revealed that among 74 (61.7%) patients clinically diagnosed as positive, 68 (56.7%) were confirmed to have metastasis on histopathology, while 6 (5.0%) were false positives. Conversely, of the 46 (38.3%) patients clinically assessed as negative, 22 (18.3%) were later found positive and 24 (20.0%) true negatives on histopathological examination, as given in Table 4.

Intraoperative or surgical assessment demonstrated better agreement with histopathological findings compared to clinical evaluation. Out of 82 (68.3%) patients suspected intraoperatively to have nodal metastasis, 76 (63.3%) were confirmed positive, while 6 (5.0%) were false positives. Among the 38 (31.7%) patients judged negative during surgery, 14 (11.7%) turned out positive and 24 (20.0%) were true negatives on histopathology, as given in Table 5.

The diagnostic accuracy analysis, taking histopathology as the gold standard, showed that clinical assessment had a sensitivity of 75.6%, specificity of 80.0%, and an overall accuracy of 76.7%. In comparison, surgical assessment yielded higher diagnostic performance with a sensitivity of 84.4%, specificity of 80.0%, and overall accuracy of 83.3%. The positive predictive value was 91.9% for clinical and 92.7% for surgical evaluation, while the negative predictive values were 52.2% and 63.1%, respectively. The Kappa (κ) coefficient demonstrated moderate agreement for clinical assessment (0.52) and substantial agreement for surgical assessment (0.63) with histopathological results, indicating better reliability of intraoperative findings in detecting nodal metastasis, as given in Table 6.

Table 1: Demographic Characteristics of the Study Population (n = 120)

Variable	Mean ± SD / n (%)
Age (years)	
Mean±SD	49.6 ± 10.8
25–49 years	58 (48.3%)
50–70 years	62 (51.7%)
Tumor Size (cm)	3.8 ± 1.4
Side of Involvement	
Right Breast	68 (56.7%)
Left Breast	52 (43.3%)
Menopausal Status	
Premenopausal	50 (41.7%)
Postmenopausal	70 (58.3%)

Table 2: Frequency of Axillary Node Metastasis Based on Clinical, Surgical, and Histopathological Assessment (n = 120)

Assessment Method	Positive for Metastasis	Negative for Metastasis
Clinical Assessment	74 (61.7%)	46 (38.3%)
Surgical Assessment	82 (68.3%)	38 (31.7%)
Histopathological Assessment	90 (75.0%)	30 (25.0%)

Table 3: Distribution of Number of Histopathologically Positive Lymph Nodes

Number of Positive Nodes	Frequency (n)	Percentage (%)
1–3 Nodes	44	36.7
4–6 Nodes	28	23.3
>6 Nodes	18	15.0
No Metastasis	30	25.0
Total	120	100

Table 4: Cross-tabulation Between Clinical and Histopathological Findings of Axillary Node Metastasis (n = 120)

Clinical Findings	Histopathology Positive	Histopathology Negative	Total
Positive	68 (56.7%)	6 (5.0%)	74 (61.7%)
Negative	22 (18.3%)	24 (20.0%)	46 (38.3%)
Total	90 (75.0%)	30 (25.0%)	120 (100%)

Table 5: Cross-tabulation Between Surgical and Histopathological Findings of Axillary Node Metastasis (n = 120)

Surgical Findings	Histopathology Positive	Histopathology Negative	Total
Positive	76 (63.3%)	6 (5.0%)	82 (68.3%)
Negative	14 (11.7%)	24 (20.0%)	38 (31.7%)
Total	90 (75.0%)	30 (25.0%)	120 (100%)

Table 6: Diagnostic Accuracy of Clinical and Surgical Assessment Taking Histopathology as Gold Standard

Parameter	Clinical Assessment	Surgical Assessment
Sensitivity	75.6%	84.4%
Specificity	80.0%	80.0%
Positive Predictive Value	91.9%	92.7%
Negative Predictive Value (NPV)	52.2%	63.1%
Overall Accuracy	76.7%	83.3%
Kappa (κ) Value	0.52	0.63

DISCUSSION

Breast carcinoma is the most common malignancy among women worldwide and a major cause of cancer-related mortality. The presence or absence of axillary lymph node metastasis remains the most significant prognostic factor influencing staging, treatment, and survival. Clinical, surgical, and histopathological assessments are routinely used to evaluate nodal status. While clinical and intraoperative evaluations provide rapid guidance, histopathology serves as the gold standard for confirmation. However, variations among these methods can affect management decisions and treatment outcomes. Correlating these assessments helps improve diagnostic accuracy and optimize patient care.

Our findings are in agreement with those of Laiq et al. (2025), who reported that axillary ultrasonography (US) demonstrated 84.2% sensitivity, 48.1% specificity, and 67.6% overall accuracy in detecting nodal metastasis, where cortical thickness >3 mm and absence of fatty hilum were strong predictors ($p < 0.05$). These findings support our observation that although clinical and imaging assessments are valuable screening tools, histopathology remains the diagnostic gold standard for confirming ALN metastasis.[12] In a study by Naz et al. (2024), 60% of patients presented with

macrometastases and 45% with extracapsular extension, while micrometastases were noted in 30% of cases. Their findings showed lymph node involvement as a key prognostic factor (hazard ratio = 2.5), with 5-year survival rates of 60% in metastasis-positive patients versus 85% in those without nodal spread. The 75% positivity in our histopathological findings closely aligns with their data, emphasizing that lymph node metastasis strongly influences survival outcomes in breast cancer.[13]

Baran et al. (2020) evaluated 305 breast cancer patients and reported that mean tumor diameter (Dmax = 3.4 ± 1.8 cm) and tumor volume (vTm = 17.9 ± 35.9 cm^3) significantly predicted nodal metastasis, with AUC values ranging from 0.709 to 0.748.[14] Similarly, our study found that larger tumor size correlated with increased lymph node positivity, reinforcing tumor dimension as an important predictive parameter. Fayyaz et al. (2019) observed that US-guided FNAC achieved a sensitivity of 77.2%, specificity of 92.6%, and diagnostic accuracy of 85.0% for detecting metastatic nodes.[15] These values are comparable to our surgical accuracy (83.3%), suggesting that both intraoperative assessment and image-guided cytology provide dependable diagnostic information for axillary staging.

Our demographic findings also coincide with Soomro et al. (2021), who studied 55 patients with carcinoma breast and reported 87% clinically palpable axillary lymph nodes, with 42.8% histopathological positivity among clinically negative cases. Their results highlight the limitations of clinical evaluation alone, consistent with our finding that 18.3% of clinically negative patients were histologically positive.[16] The role of tumor biology in nodal metastasis was also emphasized by Üreyen et al. (2018), who found a significantly higher frequency of lymphovascular invasion in node-positive patients (57%) than in node-negative ones (13%) ($p = 0.003$).[17] Our results similarly revealed that histopathologically confirmed lymphovascular invasion was strongly associated with axillary metastasis, confirming the prognostic relevance of tumor micro-invasion features.

Comparatively, Bashir et al. (2024) assessed 133 patients and reported that the false-negative rates for detecting any nodal metastasis were 30.1% for US, 38.4% for CT, 61.2% for MRI, and 32.3% for PET-CT. The corresponding sensitivities for N2 nodal staging were 36.4%, 48.7%, 17.6%, and 53.3%, respectively. Although imaging modalities showed wide variability, the specificity for US (88.2%) and MRI (93.3%) was relatively high, comparable to our surgical specificity (80.0%), reinforcing that histopathology remains superior for diagnostic confirmation.[18] Bansal et al. (2019)[19] also demonstrated that USG-guided FNAC, due to its moderate sensitivity and high specificity and positive predictive value, can effectively diagnose axillary lymph node metastasis in clinically non- palpable cases, further supporting our findings that clinical palpation alone may miss a subset of metastatic nodes. Finally, Venkatesh et al. (2021) studied 100 breast cancer cases and reported that increased tumor size, higher T-stage, and higher histological grade were significantly associated with axillary

lymph node metastasis ($p < 0.05$).[20] These observations parallel our results, where patients with larger tumor size and advanced histopathological grade exhibited greater nodal positivity.

Overall, our study confirms that while clinical and imaging methods provide preliminary insights, surgical and histopathological assessments remain the most definitive diagnostic tools for axillary staging. The present study included a well-defined cohort of 120 patients with histopathologically confirmed breast carcinoma, allowing reliable comparison between clinical, surgical, and histopathological assessments. All patients underwent uniform surgical procedures, ensuring methodological consistency. The use of histopathology as a reference standard strengthened diagnostic validity. However, the study was limited by its single-center design and moderate sample size. In addition, inter-observer variability during clinical and intraoperative assessments could not be entirely excluded. Lack of long-term follow-up data also restricted prognostic evaluation.

CONCLUSION

Surgical assessment showed higher diagnostic accuracy than clinical examination when compared with histopathological findings. Correlation among all three methods highlights the importance of combining clinical judgment with histopathological confirmation for optimal management. Routine histopathological evaluation remains essential for accurate staging and treatment planning in carcinoma breast.

REFERENCES

Luo C, Li N, Lu B, Cai J, Lu M, Zhang Y, Chen H, Dai M. Global and regional trends in incidence and mortality of female breast cancer and associated factors at national level in 2000 to 2019. Chinese medical journal. 2022 Jan 5;135(01):42-51.

Arnold M, Morgan E, Rumgay H, Mafra A, Singh D, Laversanne M, Vignat J, Gralow JR, Cardoso F, Siesling S, Soerjomataram I. Current and future burden of breast cancer: Global statistics for 2020 and 2040. The Breast. 2022 Dec 1;66:15-23.

Arif T, Anwar N. Promoter Hypermethylation and Expression Changes of BRCA1 Gene in a Cohort of Sporadic Breast Cancer Cases among Pakistani Population. Asian Pacific Journal of Cancer Prevention: APJCP. 2020 Aug;21(8):2395.

Łukasiewicz S, Czeczelewski M, Forma A, Baj J, Sitarz R, Stanisławek A. Breast cancer—epidemiology, risk factors, classification, prognostic markers, and current treatment strategies—an updated review. Cancers. 2021 Aug 25;13(17):4287.

Dhamija E, Mohan SL, Pandey D. Approach to Imaging of Axilla in Breast Cancer. InImaging in Management of Breast Diseases: Volume 1, Overview of Modalities 2025 Apr 18 (pp. 247-268). Singapore: Springer Nature Singapore.

Stanford EF, Levine HM, Cabana MD, Anosike BI. Lymphadenopathy: Differential Diagnosis and Indications for Evaluation. Pediatrics in Review. 2024 Aug 1;45(8):429-39.

Muthuswamy K, Fisher R, Mavroveli S, Petrou F, Khawar S, Amlani A, Hanna GB, Hadjiminas DJ, Thiruchelvam PT, Leff DR. Assessment of technical skills in axillary lymph node dissection. Annals of Surgery. 2022 Mar 1;275(3):e568-74.

Pateras IS, Igea A, Nikas IP, Leventakou D, Koufopoulos NI, Ieronimaki AI, et al. Diagnostic challenges during inflammation and cancer: current biomarkers and future perspectives in navigating through the minefield of reactive versus dysplastic and cancerous lesions in the digestive system. International Journal of Molecular Sciences. 2024 Jan 19;25(2):1251.

Safari D, Razi S, Rezaei N. Intraoperative detection of axillary metastasis of breast cancer using nucleic acid amplification methods: review of advantages and limitations. Expert Review of Molecular Diagnostics. 2025 Jul 3(just-accepted).

Kuncman W, Orzechowska M, Kuncman Ł, Kordek R, Taran K. Intertumoral heterogeneity of primary breast tumors and synchronous Axillary Lymph Node Metastases reflected in IHC- Assessed expression of routine and nonstandard biomarkers. Frontiers in Oncology. 2021 Nov 3;11:660318.

Houghton SC, Hankinson SE. Cancer progress and priorities: breast cancer. Cancer epidemiology, biomarkers & prevention. 2021 May 1;30(5):822-44.

Laiq T, Masood Z, Siddiqui H, Javed M, Mallick MJ. Prediction of axillary lymph node metastasis in breast cancer patients based on ultrasonograhic-clinicopathologic features. Pakistan Journal of Medical Sciences. 2025 Jan;41(1):96. https://doi.org/10.12669/pjms.41.1.10384

Naz S, Ahmad M, Muhammad A, Khan P, Iqbal S, Abbas F. Correlation of Histopathological Characteristics of Nodal Metastasis with Clinicopathologica Features and Survival in Breast Cancer Patients. Journal of Saidu

Üreyen O, Çavdar DK, Adıbelli ZH, İlhan E. Axillary metastasis in clinically node-negative breast cancer. Journal of the Egyptian National Cancer Institute. 2018 Dec 1;30(4):159-63. https://doi.org/10.1016/j.jnci.2018.09.001

Bashir N, Fraser D, Rezai F, Navas S, Rao A. A Retrospective Cohort Study Assessing Ability of Radiological Investigations to Predict Axillary Nodal Status in Breast Cancer. National Radiol J Pak. 2024 Oct 17;13:9-8. https://doi.org/10.37184/nrjp.3007-5181.1.7

Bansal S, Singh R, Gupta AK. Evaluation of non-palpable axillary lymph nodes metastasis with ultrasonography guided fine needle aspiration cytology in carcinoma breast and comparing with histopathological report. Int Surg J. 2021;8:2392-8. https://dx.doi.org/10.18203/2349-2902.isj20213135

Medical College Swat. 2024 Nov 11;14(4):335-40. https://doi.org/10.52206/jsmc.2024.14.4.914

Baran MT, Gündoğdu H, Demiral G, Kupik O, Arpa M, Pergel A. PET-CT and MR imaging in the management of axillary nodes in early stage breast cancer. Journal of the College of Physicians and Surgeons Pakistan. 2020;30(06):595-600. https://doi.org/10.29271/jcpsp.2020.06.595

Fayyaz MB, Niazi IK. Diagnostic accuracy of us-fnac of axillary lymph nodes in patients with primary breast cancer using sentinel lymph node biopsy as standard reference. Journal of Ayub Medical College Abbottabad. 2019 Mar 28;31(2):242-7. PMID: 31094125

Soomro SH, Abro AS, Shah Vaqar-e-Sahar, Shaikh SA, Shaikh SN, Malik E. Axillary lymph nodes and breast cancer metastasis. Professional Med J 2021; 28(7):978-982. https://doi.org/10.29309/TPMJ/2021.28.07.5919

Venkatesh PM. Association of Histopathological Parameters and Axillary Lymphnode Metastasis in Primary Breast Carcinoma. Asian Pacific Journal of Cancer Care. 2021 Oct 27;6(4):379-82. DOI:10.31557/APJCC.2021.6.4.379