Research Article

Diagnostic Accuracy of Ultrasound in Detecting Axillary Lymph Nodes in Patients with Early Breast Cancer Taking Histopathology as a Gold Standard

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Abstract: Background: Axillary Ultrasound plays an essential role in assessment of axillary lymph nodes metastasis in early breast cancer. It is considered as important prognostic factor in the recurrence of the disease and survival of the patient.

Objective: The study was aimed to determine ultrasonography's diagnostic accuracy taking histopathology as a Gold Standard in finding axillary lymph nodes in early CA breast patients.

Materials and Methods: Study was designed as cross-sectional, conducted at Department of radiology, Liaquat National Postgraduate Medical Center, Karachi. The sample size calculated for the study was 271. Patients of age between 18-65 years were included in the study. Sensitivity, specificity, PPV, NPV and diagnostic accuracy were calculated.

Result: The mean age of the participants was 46.28 ± 9.76 years. The age range from 25 years to 78 years. The study has yield a sensitivity of 76.9% whereas specificity was reported 68.2%. The overall diagnostic accuracy of AUS was observed as 74%. A positive predictive value and negative predictive value was 88.8% and 52.7% respectively.

Conclusion: The findings of this study provides information related to the diagnostic accuracy of AUS as a detection tool for early breast cancer. The findings of this study are consistent with the existing literature showing high sensitivity and accuracy of the tool pointing out that AUS can serve as a reliable means of identification of patients who have axillary metastasis.

Keywords: Axillary ultrasound, Histopathology of breast cancer, Diagnostic tools, Axillary lymph nodes, Metastasis, Human Papilloma Virus.

INTRODUCTION

Breast cancer is utmost frequent cancer among females globally [1, 2]. Breast cancer accounts for 15% of all new diagnosed cases of cancer in the advance countries likes UK [3]. Furthermore, breast cancer is the second leading cause of death among women and the fourth leading cause of cancer death in the UK reported in years 2018, accounting for about 7% of all deaths due to cancer. In UK, approximately 98% of people, diagnosed with CA breast at the earliest stage live for at least for more five years, however the five-year survival rate reduces to round about 26% for those detected at a later stage [4]. The prognostic estimate and all in all, the survival of breast cancer patients is majorly influenced by the existence of metastases in axillary lymph node (LN) [5].

Axillary lymph node dissection (ALND) for axillary staging in CA breast was once the standard but involves a higher risk of adverse effects. Sentinel lymph node biopsy (SLNB) is now considered as the gold standard for early-staging of CA breast [6]. It is associated with a fewer adverse events after the procedure [7]. SLNB not only prevents unnecessary ALND but also supports in determining the number of lymph nodes that are involved in it. It is very crucial for selecting adjuvant therapy in CA breast. On the other hand, 1–15% of all the patients with negative SLNB even have diseased lymph nodes in the same site, mainly due to extensive metastases in nodes as the first node to drain [7].

Axillary ultrasound (AUS) is commonly used in baseline evaluations in early CA breast. It is recommended by the current guidelines. It plays an essential role in assessment of axillary lymph nodes condition [8]. It is considered as important prognostic factor in the recurrence of the disease and survival of the patient. Emerging strategies, such as targeted axillary dissection (TAD) and axillary marking, are intended to identify patients that do not require ALND requiring pre-therapeutic AUS identification and post-neoadjuvant re-evaluation [9]. The evaluation of the benefits and effectiveness of ALND is the ACOSOG Z0011 trial, done to demonstrate that ALND could be omitted in case of limited SLN metastasis without affecting the survival of women undergoing the BCS. AUS has been shown to have different sensitivities and specificities in identifying the presence of lymph node involvement [10]. For instance, Riedle *et al.* reported sensitivity 53.3% and specificity 93.7% [11]. According to the study of Reshkallah *et al.* the sensitivity, specificity and diagnostic accuracy were found to be 59.6%, 95.1% and 82.2% respectively [12].

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Although the histopathological assessment is the gold standard to establish diagnosis of lymph node involvement, however, due to the invasive nature of histopathological examination and the potential complications that may be associated with it, ultrasound has become a non-invasive and cost-effective alternative to assess lymph node involvement [13]. By matching the ultrasound findings to finding results from histopathology, the research study aimed to find the accuracy of ultrasound which can reduce the need for invasive procedures and enhance breast cancer management protocols. The study has the potential to significantly impact patient care by providing a more efficient diagnostic pathway and improving treatment planning. Therefore, the study was aimed to determine ultrasonography's diagnostic accuracy taking histopathology as a Gold Standard in finding axillary lymph nodes in early CA breast patients.

MATERIALS AND METHODS

The study was designed as cross-sectional investigation. It was conducted after approval from Ethical Review Committee (ERC) (Ref: App#1129-2024-LNH-ERC) of the Liaquat National Hospital, Karachi. It was conducted at Department of Radiology, Liaquat National Postgraduate Medical Center, Karachi, Pakistan. The study duration was from March, 2025 to May 2025. Prevalence of lymph nodes in early breast cancer was 34.7% [11], margin of error 10% (sensitivity and specificity 59% and 88.4% respectively [14]), and confidence level 95%. The sample size calculated for the study was 269. Sampling technique used was non-probability consecutive. Patients of age between 18-65 years were included in the study. Patients those were diagnosed with early breast cancer were considered part of study. Patients excluded from the study were known metastatic disease, recurrent breast cancer and patients on chemotherapy or radiotherapy. All patient diagnosed with early breast cancer referred to radiology department for axillary ultrasound and met the inclusion criteria were enrolled. Prior to enrolment complete details of the study were explained to the patients and written informed consent was taken before using the diagnostic tools.

After taking consent baseline demographic and clinical details such as age, residence and laterality were taken. All patient with early breast cancer were undergone axillary ultrasound performed by expert sonologist, who was having more than 5 years of experience in the field of sonography, and findings regarding the lymph node were noted. A high-frequency (7–15 MHz) linear-array transducer was used to examine both breasts using ultrasound. All quadrants, the retroareolar area, and the axillary tail were methodically scanned in the radial and antiradial planes. When appropriate, color Doppler assessment was added to real-time grayscale imaging to determine lesion features and vascularity. After ultrasound all patient were undergone histopathology for confirmation of diagnosis. Later findings of ultrasound and histopathology were compared to calculate the diagnostic accuracy.

STATISTICAL ANALYSIS

Data was analyzed using SPSS version 25. Frequency and percentage were reported for qualitative variables such as laterality, stage of cancer, lymph node on ultrasound and lymph node on histopathology. While mean (SD) or median (IQR) were calculated for quantitative variables such as age on the basis of normality using Shapiro Wilk test. Sensitivity, specificity, PPV, NPV and overall diagnostic accuracy were computed with their 95% confidence interval for assessing diagnostic accuracy.

RESULT

A total of 271 patients were studied. Study finds shows the mean age of the participants was 46.28 ± 9.76 years. The age range from 25 years to 78 years. The family history of breast cancer was reported in 99 (36.5%) of the patients as shown in Table **1**.

Table 1. Characteristics of Participants and Clinical Findings.

Characteristics		**N (%)**
Age	46.06 +/- 9.08*	
Laterality	Left	131 (48.3%)
	Right	140 (51.6%)
Family History	Yes	99 (36.5%)
	No	172 (63.4%)

*Age: Mean ± SD.

Patients diagnosed with axillary U/S were 180 (66.4%), while on histopathology diagnosis of the early metastases into the axillary lymph nodes were made in 208 (76.7%) of the cases as shown in Table **2**. Fig. (**1**) displays details of histopathological findings. Fig. (**2**) depicts ultra sound findings. Fig. (**3**) shows evidence of malignancy on histopathology.

Table 2. Diagnosis of Early Breast Cancer with U/S and Histopathology.

	Findings	**Ultrasound**	**Histopathology**
Early Breast Cancer	Positive, n(%)	180 (66.4%)	208 (76.7%)
	Negative,n(%)	91 (33.5%)	63 (23.2%)

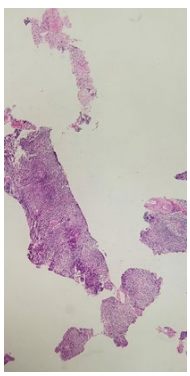

Fig. (1). This Photomicrograph Depicts Lymphoid Cells Showing a Neoplastic Lesion Arranged in Cohesive Clusters and Nests. Tumor Cells show Altered Nuclear-to-Cytoplasmic (N:C) ratio, Nucleomegaly and Hyperchromasia, Manifesting Malignant Transformation.

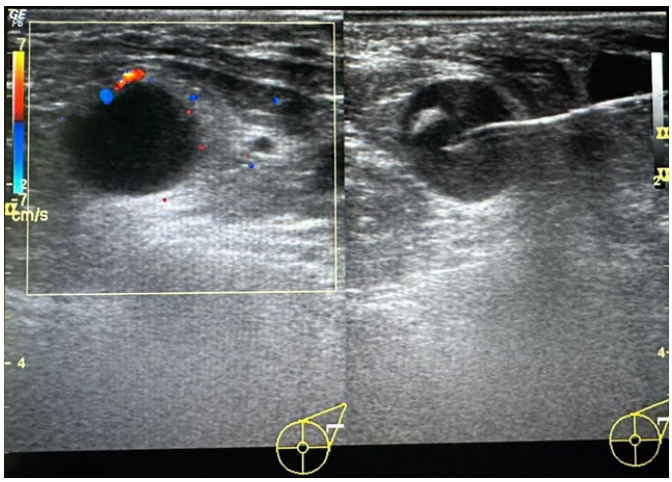

Fig. (2). This is Ultrasound Image of Left Axilla Showing a Rounded Hypoechoic Axillary Lymph Nodes with Loss of Fatty Hila. Color Doppler Imaging (CDI) Exhibits Peripheral Vascularity, Suggestive of a Metastatic Lymph Node.

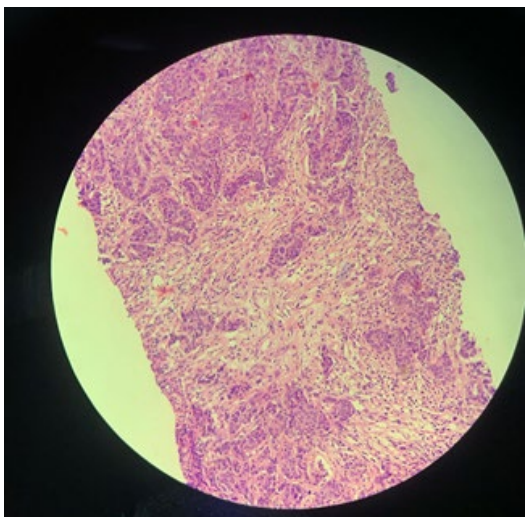

Fig. (3). Linear Fragments of Small to Medium Size Lymphocytes with no Evidence of Malignancy.

The comparison of axillary U/S and histopathology showed 160 true positive cases and false negatives were 48 as show in Table **3**. The sensitivity of the diagnostic tool was found to be 76.9% and specificity as 68.2%. Positive predictive value PPV was as 88.8% in diagnosed cases with a p-value of <0.001 as shown in Table **4**.

Table 3. Screening Results of U/S and Histopathology Test.

U/S	Histopathology		
	Positive	**Negative**	**Total**
Positive, n	TP (160)	FP (20)	180
Negative, n	FN (48)	TN (43)	91

TP: True positive, FP: False positive, FN: False negative, TN: True negative.

Table 4. Diagnostic Accuracy of U/S in Detecting Early Breast Cancer Cases.

Sensitivity (%) with 95% CI	76.9 (71-82)
Specificity (%) with 95% CI	68.2 (56-78)
Diagnostic Accuracy (%) with 95% CI	74.9 (69-80)
Positive Predictive Value (%) with 95% CI	88.8 (83-89)
Negative Predictive Value (%) with 95% CI	52.7 (37-59)

DISCUSSION

The Axillary Ultrasound (AUS) is considered as an affordable diagnostic tool in low resource settings [15]. It is frequently available and can be used in diagnosing breast cancer at early stage. The evaluation of breast cancer stage can be predicted on the basis of Lymph Node (LN) status. The variations in morphology of cortex in LN provides information about the metastasis [16]. Several studies conduct have discussed the suspected breast lesions and the presence of cancer by using the ultrasound. It especially supports in the diagnosis of metastasis in Axillary Lymph Node (ALN) [17-19]. The study has assessed the diagnostic performance of AUS in detecting axillary lymph node metastasis in breast cancer patients. The study has yield a sensitivity of 76.9% whereas specificity was reported 68.2%. The overall diagnostic accuracy of AUS was observed as 74% and a positive predictive value (PPV) of 88.8% and a negative predictive value (NPV) of 52.7%.

Ultrasound is a radiation-free and non-invasive imaging technique that can be utilized for breast cancer detection [20]. Some previously conducted studies showed similar results which are consistent with the results of our study. A study conducted in Aga Khan University Hospital reported accuracy of AUS as 75%. The sensitivity reported was 61% and specificity of 84.4% [21]. Diagnostic accuracy reported is similar to the reported accuracy of current study. A Study conducted in China, a population based study that involved around 1049 breast cancer cases found that AUS showed sensitivity of 69.9%, while specificity of 81.8%. The overall diagnostic accuracy reported was 77% [22] which was comparable with the results of this study. Another study conducted on UK breast cancer cases showed the diagnostic accuracy of AUS was found to be 71% which is near to the finding of our study. But the reported sensitivity of 54% was found to be lower than the results of our study [23]. In a study conducted on Iranian women showed the diagnostic accuracy of AUS was 76% [24] which is very similar to the results of our study, suggesting consistency in diagnostic accuracy across different healthcare settings.

In resource limited settings, one recent meta-analysis on 76,958 patients revealed that overall pooled sensitivity and specificity was 80.1% and 88.4% respectively, which demonstrates that AUS could be a best primary diagnostic tool for early breast cancer detection [25]. In a breast cancer trails being conducted in over six different settings including China, Nigeria, Argentina and Malaysia showed AUS sensitivity of 89.25 and specificity of 99.1% which is here yield that the findings of our study [26].

The results may vary because in these settings the patients are younger in age and the disease is diagnosed at more advance stage. In a study conducted on patients with Human Papilloma Virus (HPV) metastases of ALN showed Diagnostic sensitivity of 71.7%, specificity of 84.6%, and diagnostic accuracy of 77.6% [27] keeping pathological findings as the Gold standard for diagnosing the ALN metastases.

There is a variability in the existing literature and the finding of the current study. Authors in the literature suggest these variation in the diagnostic accuracy depends on the level of experience of individual examiner performing the procedure. The results are also influenced by the evaluation criteria used during the examination. Studies supported that high sensitivities reported were consistent with the low specificities within the studies and the results were vice versa. The overall global performance of AUS in diagnosing the ALN metastases was not considerably improved.

LIMITATIONS

The study has few limitations that includes progression of the disease cannot be evaluated based on the study design as the current study is a cross-sectional in nature. Another limitation of this study is utilization of AUS in the up-follow of disease progression, which can be eliminated in future researches by using the prospective or follow-up study designs. Further added to the limitation, the study is not generalizable as it was a single center study which hinders the external validation of the data on entire targeted population.

CONCLUSION

The findings of this study provides information related to the diagnostic accuracy of AUS as a detection tool for early breast cancer. The findings of this study are consistent with the existing literature showing high sensitivity and accuracy of the tool pointing out that AUS can serve as a reliable means of identification of patients who have axillary metastasis. Future researches would need to address standardizing AUS protocols, educating monographers to increase diagnostic accuracy and studying adjunctive imaging modalities to enhance axillary lymph node metastasis detection in patients with breast cancer

ABBREVIATIONS

ALND: Axillary lymph node dissection.

AUS: Axillary Ultrasound.

CA: Cancer.

HPV: Human Papilloma Virus.

IQR: Inter-quartile Range.

NPV: Negative Predictive Value.

PPV: Positive Predictive Value.

SLNB: Sentinel Lymph Node Biopsy.

SD: Standard Deviation.

TAD: Targeted Axillary Dissection.

AUTHORS' CONTRIBUTION

Ambreen Shaikh: Conceptualization, Study design, Writing draft, Final approval, final proof to be published.

Saleha Anwar: Study design, Critical review and revision the manuscript, Final approval, final proof to be published.

Hasnain Ali and **Raisa Altaf Malik**: Writing draft, Final approval, final proof to be published.

Humaira Erum and **Bisma Rizwan**: Methodology, Data analysis and interpretation, Final approval, final proof to be published.

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Declared none.

ETHICAL DECLARATIONS

Data Availability Statement

Data will be available from the corresponding author upon a reasonable request.

Ethical Approval

ERC approvals were taken before the start of this study (Ref: App#1129-2024-LNH-ERC).

Consent to Participate

All the study participants were enlisted with their written informed consent.

Consent for Publication

All authors give consent for the publication of this work.

Conflict of Interest

None

Competing Interest/Funding

None

Use of AI-Assisted Technologies

The authors declare that no generative artificial intelligence (AI) or AI-assisted technologies were utilized in the writing of this manuscript, in the creation of images/graphics/tables/captions, or in any other aspect of its preparation.

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