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ORIGINAL ARTICLE

Comparison of diagnostic accuracy of conventional ultrasonography for characterization of axillary lymph nodes with histological findings.

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ABSTRACT… Objective: To determine the diagnostic accuracy of conventional ultrasonography for characterization of axillary lymph nodes. **Study Design:** Cross-sectional study. **Setting:** Department of Radiology, Aziz Fatima Medical and Dental Hospital, Faisalabad. **Period:** 1st of October 2022 to 31st of March 2023. **Material & Methods:** A total number of 145 female patients above the age of 18 years who reported with mastalgia and diagnosed clinically with the presence of suspicious axillary lymph nodes were included in the study. The conventional ultrasonic evaluation index was used for characterization. The ultrasonological results of characterization of axillary lymph nodes were compared with histopathological results where results of histopathology were taken as gold standard. **Results:** The Mean±SD of age in this study was 44.15±8.42 years with an age range of 29-62 years. The Mean±SD of duration of complaints was 10.17±5.60 months. USG diagnosed 89 (61.37%) patients while histopathology diagnosed 92 (63.44%) patients with metastasis of ALN. USG showed sensitivity of 86.957%, specificity 83.019%, diagnostic accuracy 86%, PPV 89.888% and NPV 78.571% in diagnosis of metastasis of axillary lymph nodes ($p < 0.000$). **Conclusion:** Conventional USG is a commonly available and affordable diagnostic tool which is useful with a good accuracy for characterization of axillary lymph nodes and detecting the metastasis.

Key words: Axillary Lymph Nodes, Characterization, Ultrasonography.

INTRODUCTION

Most common type of cancers in females is the breast cancer and the reported new cases of breast cancer in 2018 were 2.1 Million.[1] This is the leading cause of cancer related mortality in women and among cancer patients it is reported globally as 2nd leading cause of mortality with 627,000 deaths in year 2018.[2,3,4] In woman aging between 45-55 years, it is found to be a leading cause of death.[5]

Unlike developed countries where breast cancer is mostly reported after the age of 60 years, the case of developing countries is more concerning as breast cancer is reported at younger ages and at more advanced stage causing higher ratio of mortality. This is unfortunate that the cases are referred very late to the clinics having diagnostic facilities which increase the mortality rate in these women.[6] Statistics reveals that the chances of recovery and survival are increased with early diagnosis of breast cancer therefore it is considered as key to the cure.[7,8] The prognosis of the cancer greatly depend upon the stage of the disease and early diagnosis with early treatment provides better outcome and remain cost effective.[9]

For breast cancers, the investigations regarding involvement of axillary lymph nodes (ALN) is said to be important factor in the prognosis as the common pathway of metastasis of this cancer is ALN metastasis. This is because once the III–IV cancer cells capture the lymphatic vessels; they start growth and reproduction that causes obstructions in the lymphatic vessels leading to skin edema. There is also lymphatic spread as transfers of these cancer cells start to the regional lymphatic system. The status of regional LNs and specifically ALNs is decisive in deciding the stage

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of breast cancer.[10] ALN dissection is an expensive procedure and associated with some reported side effects like seroma formation, hematoma, paresthesia, lymphedema, and restricted shoulder motion. The non-invasive computer imaging techniques for characterization of ALN are important to improve the prognosis of breast cancer while avoiding the harmful surgical process of LN dissection.[11] Imaging techniques has therefore emerged over last few years for this purpose including ultrasonography (USG), CT scan, nuclear scintigraphy and MRI.[11,12]

Among USG conventional ultrasound, ultrasound elastography and virtual touch tissue imaging quantification are the techniques used for analysis of these lesions. The pathological LNs of the breast cancer are detected in USG during the examination involving ipsilateral axilla. The criteria include size, form and internal structure of the pathological LNs. With the newly introduced techniques such as spatial compounding and harmonic scanning the utilization of USG is now more extended.

However, among these, conventional ultrasound is a primary imaging technique. It is commonly available and hence a preferably used technique for the purpose of clinical evaluation of breast lesions and characterization of ALNs.[13,14] The presence of fibro adenoma along with incidental axillary lymphadenopathy must lead to differential diagnosis of malignancy of the tumor. Characterization of LNs as normal or metastatic becomes necessary and conventional USG can help to evaluate the suspicious ALNs and can save patients from undergoing sentinel node procedure. Patients will be preceded later with full ALN dissection if needed. USG is therefore an easily available and affordable imaging option which can detect the characteristic of ALN. Although the morphologic criteria like cortical thickening, compression of the hyperechoic medullary region, hilar effacement and non−hilar cortical blood flow are also important, the accuracy of USG largely rely on the size of LNs.[15] When the ALN are found to be non-palpable during a clinical examination, it must be considered for investigations. There are established criteria for differentiating the normal and malignant lesions using the gray scale USG.[16] The normal cortical thickness of LN is 1-2 millimeter and for an abnormal LN it is found to be >2.3 mm. Hence histology is indicated when changed cortical thickening is observed.[17] For defining different stages of cancer, a Tumor-Node-Metastasis system has been used by the American joint committee on cancer. This system depends on the size and extent of the primary tumor along with the involvement of regional lymph nodes for staging of cancers.[18]

In Pakistan the situation is even more serious as the incidence is found to be the highest among Asian countries and one in every nine women is estimated to be at risk of breast cancer in their life time. As per report published in 2018, new cases of breast cancer reported in Pakistan were 34066.[7] Despite these high reported incidences, the advanced diagnostic facilities for breast cancer in Pakistan are very limited. This emphasizes the need for a study the accuracy of conventional USG in the diagnosis and staging of breast cancer. The purpose of this study was therefore was to determine the characteristics of ALNs as normal or metastatic using conventional USG.

MATERIAL & METHODS

The study was conducted at the department of Radiology, Aziz Fatima Medical and Dental Hospital, Faisalabad over a period of 6 months from 1st of October 2022 to 31st of March 2023.

The study design was cross-sectional. Sample size was calculated by using sensitivity and specificity calculator.

Sensitivity= 71.74%, Specificity= 84.62%, Accuracy=77.65%, Positive predictive value (PPV)= 84.62%, Negative predictive value (NPV)= 71.74%. The prevalence of metastatic lymph nodes =54.12% and margin of error =10%. Sample size was calculated as 145.[19]

A total number of 145 female patients above the age of 18 years who reported with mastalgia and diagnosed clinically with the presence of

suspicious ALN were included in the study.

Patients reported with malignancies except of breast, TB, lymphoma and patients on any chemotherapy or radiotherapy prior to this clinical diagnosis were excluded from the study.

The clinical diagnosis of ALN was done by use of vernier calipers by taking the 2 perpendicular diameters. The conventional ultrasonic evaluation index was used. The method marks, If ratio of the longitudinal and lateral axes of LNs ≥2 (1 point), <2 (2 points). Where the CT was <3 mm, it was given "1 point" and if the CT was ≥3 mm, it was given "2 points".[21]

All the USG was done by an experienced female sonologist.

All these biopsy specimens were then sent for histopathology. The pathologist was unaware of the USG findings.

Ethical approval was taken for conducting the study from ethical committee of the hospital.
A written consent was taken from each patient for the participation in the study (IEC/250-23).

The ultrasonological results of ALN were compared with histopathological results where results of histopathology were taken as reference. The primary outcomes were sensitivity, specificity, PPV, NPV and diagnostic accuracy. All quantitative data was expressed in Mean±SD while frequency and percentage was used to express qualitative data. Fisher's exact 2 × 2 tests were applied with 95% confidence interval while taking p-value < 0.05 as statistically significant.

RESULTS

The Mean±SD of age in this study was 44.15±8.42 years with an age range of 29 to 62 years. Details of demographic and clinical findings are given in Table-I.

USG diagnosed 89 (61.37%) patients while histopathology diagnosed 92 (63.44%) patients with metastasis of ALN as shown in Table-II.

Demographics & Clinical Finding			
1	Age (years) Mean±SD		44.15±8.42
2	Marital Status	Married n (%)	112 (77.24)
		Widow n (%)	15 (10.34)
		Divorced n (%)	11 (7.58)
		Unmarried n (%)	7 (4.82)
3	BMI	Obese n (%)	71 (48.96)
		Overweight n (%)	38 (26.20)
		Normal n (%)	22 (15.17)
		Underweight n (%)	14 (9.65)
4	Family History of Breast Cancer	Yes n (%)	34 (23.44)
		No n (%)	111 (76.55)
5	Duration of complaint (Months) Mean±SD		10.17±5.60

Table-I. Demographics and clinical findings n=145

Metastasis of ALN	USG n (%)	Histopathology n (%)
Positive	89 (61.38%)	92 (63.45%)
Negative	56 (38.62%)	53 (36.55%)
Total	145 (100%)	145 (100%)

Table-II. Overall results of USG and histopathology in diagnosis of metastasis of ALN n=145

USG showed sensitivity of 86.957%, specificity 83.019%, diagnostic accuracy by 86%, PPV 89.888% and NPV 78.571% in diagnosis of metastasis of ALN ($p < 0.000$) as shown in Table-III.

USG	Results
Sensitivity (%)	86.957
Specificity (%)	83.019
Diagnostic accuracy (%)	86%
Positive predictive Value (%)	89.888
Negative predictive Value (%)	78.571

Table-III. USG sensitivity, specificity and predictive values n=145

Comparison of USG versus histopathology for diagnosis of metastasis of ALN is given is Table-IV.

USG	Histopathology		Total
	Positive	Negative	
Positive	80 (TP)	9 (FP)	89
Negative	12 (FN)	44 (TN)	56
Total	92	53	145

Table-IV: Comparison of USG versus Histopathology for diagnosis of metastasis of ALN n=145

TP=True positive, **FP**=False positive
FN=False negative, **TN**=True negative

DISCUSSION

USG is now a day among the most frequently available and affordable mean of diagnosing breast cancer. The status of LN is an important predictor for evaluating the stage of breast cancer as focal cortical variations in morphology provide good details. Several studies have therefore discussed the role of USG in assessing the presence of malignancy in suspected lesions and especially the metastasis of ALN.

Park YM conducted a study to determine the diagnostic usefulness of strain elastography in differentiating benign Vs metastatic ALN in patients suspected of breast cancer. The patients who were suspected for metastatic ALN on the basis of conventional USG were then examined using strain elastography. The results were then compared with biopsy results which showed that conventional USG was more useful than strain elastography alone ($p < 0.001$) in determining abnormal ALNs.[20]

Singh R studied the usefulness of USG for assessment of size of ALN in breast cancer patients keeping histopathology as gold standard. The largest dimension of ALN was taken for clinical, sonological and pathological assessment. The results showed a strong correlation between sonological and pathological ALN assessment ($p=<0.001$). The researcher therefore concluded that both clinical and ultrasonological assessment of ALN were as good as pathological assessment in diagnosing breast cancer.[21]

Berg WA after mentioning the fact that mammography is not widely available and USG is in larger use compared the results obtained by USG with the results revealed by mammography. A total of 2662 woman completed the study. The women were studied for detection of breast cancer, recall and PPV was determined. On the basis of the results, the researchers concluded that although the false positives were more common with USG, detection of blood cancer with USG was comparable with that of mammography.[22]

Wang J studied the usefulness of different USG techniques to identify the ALN metastasis keeping pathological findings as gold standard. The results showed a sensitivity of 71.74%, specificity of 84.62% and accuracy of 77.65%. The PPV was reported to be 84.62% while NPV was 71.74%.[19]

In a recent study published in December 2022, spectral Doppler USG was assessed for its diagnostic accuracy in prediction of malignancy in shape of evaluating the solid breast lesions while keeping histopathology as gold standard. The age range in this study was 18-60 years and Mean±SD of age was 42.965±7.66 years. The results show the sensitivity of 84.8% and specificity of 95% with diagnostic accuracy as 92%. The results also shared a PPV of 88.6% and NPV of 93%. Study concluded that spectral Doppler USG has significant role in diagnosis of metastasis and help in distinguishing benign tumors lesions and malignant tumors.[23]

The study conducted by Coronado-Gutiérrez D was aimed to noninvasively determine the potential of ultrasound techniques in finding the involvement of ALN in breast cancer. The results were compared with biopsy findings and reported an accuracy of the method as high as 86.4% while the sensitivity and specificity were reported as 84.9% and 87.7% respectively. The study therefore demonstrated the potential of USG in detection of the compositional and microstructural changes in ALN due to metastasis.[24]

The Mean±SD of age in our study was 44.15±8.42 years with an age range of 29-62 years while the Mean±SD of duration of complaints was 10.17±5.60 months. Majority of patients were married (77.24%) and 48.96% of them were obese (as assesses by their Body mass Index). Only 34 (23.44%) women had a family history of breast cancer. USG diagnosed 89 (61.37%) patients with metastasis of ALN while histopathology reported 92 (63.44%) patients. USG showed sensitivity of 86.957%, specificity of 83.019% and diagnostic accuracy by 86%. The PPV for USG was 89.888% while NPV was 78.571% in diagnosis of metastasis of ALN ($p < 0.000$). Out of 89 cases diagnosed with USG 80 were true positive (TP) while 9 were false positive (FP) while out of 56 patients diagnosed negative with USG 44 were true

negative (TN) and 12 were false negative (FN). The results of our study are in line with the results of studies discussed above which mentions USG as a reliable tool to diagnose the metastasis of ALN.[20,21,22] Similarly the sensitivity, specificity, accuracy, PPV and NPV found in our study are also similar to results reported previously in studies conducted over the topic.[19,23,24] These results show that conventional USG provides a good diagnostic tool for diagnosis in females reported with the suspect of breast cancer.

The limitations of our study include the small sample size. Studies with larger number of patients will be helpful in future to determine the usefulness of USG in characterizing ALN and diagnosing the stage of breast cancer.

CONCLUSION

Early diagnosis of breast cancer provides better outcome and is vital to the cure. Conventional USG is commonly available and affordable diagnostic tool which is useful with a good accuracy for characterization of ALN and detecting the metastasis thereby offering a non-invasive method without procedural complications.

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