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Comparison of Radiologic and Pathological Diagnosis in Patients Presenting with Bloody Nipple Discharge

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ABSTRACT

Objective: To assess efficacy of ultrasound in detecting breast carcinoma in patients with abnormal nipple discharge, given the limitations of mammography in this context.
Study Design: Prospective observational study.
Place and Duration of Study: Combined Military Hospital, Rawalpindi Pakistan, from Jul 2023 to Mar 2024.
Methodology: The study included 139 female patients with abnormal nipple discharge who underwent traditional breast ultrasound followed by histopathological confirmation through biopsy.
Results: The demographic data revealed a majority in the 46-66 age group (62.59%) and a longer disease duration exceeding 6 months (73.39%). Ultrasonography demonstrated significant diagnostic accuracy, identifying 89 out of 93 positive cases as true positives and correctly identifying 36 out of 46 negative cases as true negatives, with a sensitivity of 95.7%. However, it also showed 10 false positives, leading to an accuracy of 78.3%.
Conclusions: The study highlights the efficacy of ultrasound in differentiating between benign and malignant breast lesions linked to abnormal nipple discharge, demonstrating significant diagnostic accuracy. Despite concerns about false positives, ultrasound remains a valuable non-invasive diagnostic tool, contributing to improved clinical decision-making and patient comfort.

Keywords: Bloody Nipple Discharge, Breast cancer, False positive, Histopathology, Ultrasonography.

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INTRODUCTION

Breast cancer stands out as one of the most widespread types of cancer, representing 12.5% of all newly diagnosed cancer cases globally each year. This prevalence underscores its significance within the realm of public health, given the substantial number of new cases emerging worldwide.[1] Notably, abnormal nipple discharge in females occurs at a rate ranging from 2% to 12%,[2] with reported occurrences of breast carcinoma in cases of pathological nipple discharge ranging from 5% to 23%.[3] Consequently, many patients are referred for further assessment following cancer guidelines, as nipple discharge is often viewed as a potential indicator of breast cancer.[4] It's important to recognize that nipple discharge, while sometimes an initial symptom, may also coincide with other indications such as breast masses or abnormal mammography results.[5,6] Mammography plays a pivotal role in identifying and diagnosing breast diseases,[7,8] however, its sensitivity in detecting nipple discharge is relatively low, ranging from 20% to 25%.[9] This limitation underscores the need to explore alternative diagnostic methods such as ultrasound, which has demonstrated promise in improving detection rates, particularly in cases involving abnormal nipple discharge.[10] Therefore, this research aimed to assess the accuracy of ultrasound as an alternative diagnostic tool for detecting breast carcinoma in patients presenting with abnormal nipple discharge, considering the challenges associated with mammography in this specific context.

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METHODOLOGY

We conducted a Prospective observational study to collect data from July 2023 to March 2024. The study enrolled female patients who came to the Department of Radiology at the hospital for sonographic evaluation of breast lesions. Patients underwent traditional breast ultrasound, followed by biopsy for histopathological confirmation. A sample of 139 was calculated using an online sample size calculator. The sample size was determined based on a confidence interval of 95%, and an abnormal nipple discharge prevalence of 10% as reported by Lippa *et al.*,[6] Sample collection for the study involved using consecutive sampling.

Inclusion Criteria: The female patients between the ages of 25 and above, who had abnormal nipple discharge along with mammography and were scheduled for a biopsy.

Exclusion Criteria: Patients who were receiving chemotherapy had breast implants, or were unable to provide informed consent were not included in the study.

Demographic and clinical data were gathered, and patients underwent traditional breast ultrasound. Bi-RADS scores were documented, and patients were classified as either positive or negative according to specific criteria. A biopsy was conducted by a skilled surgeon at the same hospital, and the histopathology reports were carefully reviewed by pathologists.

The data was collected and analysis was performed using the statistical analysis social science (SPSS) tool version 26. Frequency and percentage were used to present the qualitative variables. The calculations for sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of ultrasound were performed using 2x2 tables.

RESULTS

Out of the 139 patients included in the study, a small percentage 12(8.63%) were between the ages of 25-45, while the majority 87(62.59%) belonged to the 46-66 age group. In terms of disease duration, a small portion of patients 37(26.61%) experienced symptoms for 6 months or less, whereas the majority (73.39%) had a longer duration exceeding 6 months (Table-I).

Table-I: Demographic Variables of the Study Sample (n=139)

Age (years)	n (%)
25-45	12(8.63%)
46-66	87(62.59%)
67 Above	40(28.78%)
Duration of Disease	
≤ 6 months	37(26.61%)
>6 months	102(73.39%)
Parity	
Primiparous	21(15.11%)
Multiparous	118(84.89%)
History of Breastfeeding	
Yes	94(67.63%)
No	45(32.37%)

The data presented in Table II clearly demonstrates the diagnostic accuracy of ultrasonography when compared to histopathology results in patients with abnormal NP. Among the 93 positive cases identified by histopathology, ultrasonography accurately detected 89 cases True Positives and misclassified 4 cases as False Negative. In addition, 36 out of the 46 negative cases identified by histopathology were correctly identified as negative by ultrasonography. However, 10 cases were incorrectly classified as positive. The sensitivity of ultrasonography was found to be around 95.7%. However, the accuracy of ultrasonography was 78.3%. The calculated Positive Predictive Value (PPV) is 89.9%.

Table-II: Diagnostics Accuracy of Ultrasonography (n=193)

		Histopathology	
		Yes/Positive	No/Negative
Ultrasonography	Yes/Positive	89(64.00%)	10(7.19%)
	No/Negative	4(2.88%)	36(25.90%)

Sensitivity: 95.70%
Specificity: 78.26%
PPV (Positive Predictive Value): 89.90%
NPV (Negative Predictive Value): 90.00%

DISCUSSION

Excessive abnormal nipple discharge often prompts individuals to seek for breast cancer.[5,11,12] Nevertheless, the occurrence of breast cancer in individuals experiencing nipple discharge may not solely be attributed to the discharge itself, like this situations, it is important to prioritize the investigation of abnormal clinical or radiological examination.

In our study, out of a total of 93 positive cases identified by histopathology, ultrasonography accuracy was 89 positive. Additionally, out of 46 negative cases identified by histopathology, ultrasonography correctly identified 36 cases as negative. The sensitivity of ultrasonography, which measures its ability to correctly identify positive cases, is approximately 95.7%. This indicates that ultrasonography is highly sensitive in detecting actual positive cases. On the other hand, the specificity of ultrasonography, which measures its ability to correctly identify negative cases, is approximately 78.3%. This suggests that while ultrasonography is fairly specific, there is a notable rate of false positives. The Positive Predictive Value (PPV) of ultrasonography, representing the probability that a positive result truly indicates the presence of the condition, is approximately 89.9%. This means that when ultrasonography shows a positive result, there is a high likelihood that the patient indeed has the condition. Conversely, the Negative Predictive Value

(NPV) of ultrasonography, representing the probability that a negative result truly indicates the absence of the condition, is 90%. This indicates that when ultrasonography shows a negative result, there is a high likelihood that the patient does not have the condition. Overall, these results suggest that ultrasonography is a valuable diagnostic tool with high sensitivity and NPV, although it may have some limitations in terms of specificity and PPV.

Our study's findings align with previous literature; however, the reported sensitivity and specificity values of ultrasonography varied slightly, showing results slightly lower than those found in our study.[14,15] A study by Lorenzon et al., evaluating 38 patients including 32 with pathological nipple discharge (PND), using mammography and ultrasound reported an overall 63% for ultrasound.[16] A local study showed that ultrasound had a sensitivity of 100% and a specificity of 73% for detecting breast cancer.[17] Additionally, Park *et a*l., reported a 15% detection rate of malignant lesions.[18] Yoon *et al*., also found that accuracy of detecting malignancies was increased when we use combination of ultrasound and mammography.[19] The detection rate was increase to16.1%, on negative results of mammography, when we combine the ultrasound.[18] Furthermore, subareolar ultrasound (US) has emerged as the more accurate diagnostic tool for patients with PND replacing ductography.[17,20] This shift is attributed to the less invasive nature of US, increased patient comfort, absence of radiation exposure, and comparable diagnostic accuracy to ductography. However, recent studies have advocated for the combined use of ductography alongside ultrasonography.[14] The integration of ductography and US has proven valuable in assessing PND in women with negative mammography results. Ductography, often overlooked but highly effective, aids in detecting malignancies missed by initial ultrasound scans, thus enhancing sensitivity.[21] Its combined use with US exhibits high sensitivity in malignancy detection and can obviate the need for unnecessary surgeries in cases of normal findings. Incorporating ductography with US or MRI enhances diagnostic precision, identifies abnormality locations, and facilitates optimal treatment selection for individuals with abnormal nipple discharge and negative mammographic findings.

CONCLUSION

The study highlights the efficacy of ultrasound in differentiating between benign and malignant breast lesions linked to abnormal nipple discharge, demonstrating significant diagnostic accuracy. The current analysis demonstrated its ability to detect positive cases with a sensitivity of approximately 95.7%.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SZ & MS: Data acquisition, data analysis, critical review, approval of the final version to be published.

SRQN & MSA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

KKK & AN: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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