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Original Research

Breast Carcinoma among Patients Undergoing Breast Diagnostic Ultrasonography in a Tertiary Care Hospital in Nepal

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ABSTRACT

Background Ultrasonography (US) is an important modality for investigating breast lesions, as it lacks radiation exposure, differentiates between solid tumor and fluid-filled cysts, and is particularly-useful for young females with dense breast tissue. This study aimed to determine test characteristics (sensitivity, specificity, positive and negative predictive values, and accuracy), and the prevalence of breast cancer, among patients undergoing diagnostic breast US for clinically-detected abnormalities in a tertiary care cancer hospital in Nepal, comparing US findings with histopathology and cytopathology.

Data and Methods A cross-sectional study was conducted among a convenience sample of 418 female patients who underwent diagnostic breast US between April 15 and September 10, 2022. Data were entered and analyzed on SPSS 25.0. Prevalence of cancer was determined among US patients who were referred for tissue diagnosis on the basis of clinical or US findings. Sensitivity, specificity, positive and negative predictive values, and accuracy of US in detecting breast lesions in comparison to histopathology and cytopathology findings were calculated.

Results The study respondents' age ranged from 13 to 75 (±11.8) years. Among 97 patients who underwent fine needle aspiration or biopsy based on US findings, 52 (12.4% of total) were diagnosed with breast carcinoma. The sensitivity, specificity, negative predictive value, positive predictive value, and accuracy of US to detect breast cancer were 94%, 100%, 93.7%, 100%, and 96.9%, respectively.

Conclusion Among women with breast complaints or physical examination findings, diagnostic US revealed a high prevalence in the population investigated and demonstrated very good sensitivity, specificity, and accuracy to detect breast cancer. This study confirms the important role of ultrasound in the evaluation of breast lesions, particularly in underdeveloped countries.

Keywords breast carcinoma, breast cancer, fibroadenoma, ultrasonography, US, prevalence

INTRODUCTION

Breast cancer is the most-common cancer in women (accounting for more than 1 in 10 new cancer diagnoses each year)[1,2,3] and the most-common cause of cancer death among women[4] and an emerging public health problem in developing countries. It is the second most-common cause of death among women, after heart disease.[5] Youlden et al. found breast cancer was the most-prevalent cancer among women in Asia, including Nepal.[2] Comparing developed vs. developing countries, breast cancer mortality per 100,000 was 71.7 and 29.3 respectively, and corresponding mortality rates were 17.1 and 11.8. Amongst all cancers, breast cancer is one of the leading causes of death in post-menopausal women, accounting for 23% of all cancer deaths.[6]

Long-term mortality rates from breast cancer are lowered by early identification of cancer. Five-year survival rates for breast cancer stages 0 and I are excellent (100%); for stages II and III are 93% and 72%, respectively; and for stage IV is only 22%.[1] The development of efficient techniques for screening (no symptoms or physical examination finding) and diagnostic evaluation (of patients with symptoms or physical examination findings) has made it feasible to identify breast cancer early.[7] The main approaches regarding early diagnosis include mammography, ultrasonography (US), and fine needle aspiration (FNA).[8]

Ultrasound, a non-radiating, non-invasive, cheap, and essentially-painless diagnostic tool, is particularly-useful in cases of dense breast parenchyma (common among young women)[9] or when radiation should be avoided (e.g., pregnancy). US has good sensitivity and specificity for detecting breast lesions, including those with high-likelihood of being cancer, such as enlarged axillary lymph nodes.[10] A study conducted by Gonzaga MA found the sensitivity for detecting breast lumps to be 92.5%. Additionally, the sensitivity and specificity to detect the breast cancer was 57.1% and 62.8% respectively (positive and negative predictive value was found out to be 68.1% and 99.5%).[11] Due to technological advancements, US sensitivity in detecting benign and malignant breast lesions is improving.[12] As Nepal is a low- to medium- income country, US is a feasible tool for evaluating symptomatic or palpable breast lesions,[13] owing to reasonable cost and portability to remote areas.

Our present study evaluated the prevalence of breast cancer among patients undergoing ultrasonography in a major public hospital in Nepal. We also evaluated the sensitivity, specificity, positive and negative predictive values, and accuracy of US with respect to histopathology (gold standard) to detect malignant breast masses.

DATA AND METHODS

A cross-sectional study was conducted at B.P. Koirala Memorial Cancer Hospital (BPKMCH), a tertiary-level public cancer hospital in the Chitwan district of Nepal. Established in 1992, the hospital has 500 inpatient beds, 9 surgical oncology departments, adult and pediatric medical

oncology, 8 modular operating rooms, 4 radiotherapy bunkers, radiology facilities, a pathology lab, and other auxiliary services. In 2021, approximately 13,700 outpatients attended the hospital per month.[14]

Four hundred eighteen female patients who came between April 15 to September 10, 2022 for a first-time ultrasound evaluation for breast lesions were included in this study. US was performed using the Philips Affiniti 70 device. Patients who came for follow-up ultrasound were excluded. According to a study Bujang and Adnan regarding minimum sample size for sensitivity and specificity analysis,[15] assuming histology-confirmed breast cancer prevalence of 10%, US sensitivity (from previous studies) of 60%, and histology (gold standard) sensitivity of 90% for breast cancer, then, to detect a 30% difference (e.g., US has 60% sensitivity) with power = ~90% and alpha (statistical significance) <0.05, the estimated sample size of patients to evaluate with ultrasound for breast cancer is 190, with expected findings of 19 patients (10%) with breast cancer. Clinical details related to patients were collected with an informed consent form.

Patients who underwent US and were found to have normal findings were not referred for FNA or biopsy. All patients whose US-identified lesion was deemed by the interpreting radiologist as being high-likelihood of cancer were referred for FNA or biopsy. Patients with the following characteristics proceeded to surgical excision followed by chemotherapy and radiotherapy, depending on tissue analysis: Age >35 years, immobile or poorly circumscribed mass, mass >2.5 cm, biopsy not definitive for fibroadenoma, Fibroadenoma >3cm. For fibroadenomas <2 cm, treatment with Vitamin E and follow-up was advised.

For definitional purposes: (i) True positive (TP) = patient with both US highly-suspicious for breast cancer and histopathology positive for breast cancer, (ii) False positive (FP) = patient with US highly-suspicious for breast cancer but histopathology negative for breast cancer, (iii) True negative (TN) = patient with both US not suspicious for breast cancer and histopathology negative for breast cancer, and (iv) False negative (FN) = patient with US not suspicious for breast cancer but histopathology positive for breast cancer.

Sensitivity, specificity, and accuracy were defined and calculated as: Sensitivity: The sensitivity of a test is its ability to identify disease cases correctly, calculated as: TP/TP+FN. Specificity: The specificity of a test is its ability to identify disease-free cases correctly, calculated as: TN/TN+FP. Accuracy: The accuracy of a test is its ability to differentiate disease and healthy cases correctly, calculated as: TP+TN/TP+TN+FP+FN.

Data were entered and descriptive analyses performed in IBM SPSS Statistics version 25.0. Point estimate at the 95% confidence interval was calculated, along with frequency and percentage for binary data and mean with standard deviation for continuous data.

RESULTS

The age of the 418 patients ranged from 13 to 75 years (mean=37.2±11.8). Being a national government hospital, patients attended the hospital from around the country (average distance travelled = 189 kms (±131 kms). Only about 15% of patients travelled less than 15 kms; 10% travelled between 322 and 597 kms.

Table 1: Breast Complaint that Prompted Ultrasonography, BPKMCH, 2022

Primary Complaint	No. of Cases	%
Axillary discharge sinus	1	23.9
Breast pain	223	53.3
Burning breast	2	4.7
Nipple discharge	23	5.5
Nipple erosion	1	2.4
Painful lump	108	25.8
Painless lump	60	14.3
Total	418	100.0

All patients underwent US to evaluate for breast carcinoma. The most-commonly reported complaints prompting US were breast pain, and painful lump (Table 1). Detailed US findings (Table 2) indicate 117 (27.9%) had a normal US. Fibroadenoma, invasive carcinoma, and prominent fibrofatty tissue were detected in approximately 10% each.

Among the 418 patients, 97 underwent histo or

Table 2: Ultrasonography Findings, BPKMCH, 2022

Findings	Cases	%
Axillary lymphadenopathy	31	7.4
Benign lesion	9	2.1
Breast abscess	9	2.1
Complex cyst	2	0.5
Cyst	15	3.5
Dense breast	5	1.2
Ductal carcinoma	7	1.6
Ductal ectasis	19	4.5
Fibroadenoma	45	10.6
Fibroadenosis	14	3.3
Fibrocystic changes	22	5.2
Galactocele	2	0.5
Hidradentis	4	0.9
Inflammatory carcinoma	1	0.2
Invasive carcinoma	40	9.6
Lipoma	8	1.9
Mastitis	27	6.5
Normal	117	27.9
Papillary neoplasm	1	0.2
Prominent fibrofatty tissue	40	9.5
Total	418	100.0

cytopathology (FNA or Tru-cut biopsy) test based on suspicious US or clinical findings; 52 were positive for breast carcinoma (12.4% of all 418 cases, 53.6% of biopsies). The most-common histopathological finding was invasive carcinoma (44.3% of biopsies) followed by fibroadenoma (19.6%) (Table 3). Of breast cancer cases, 82.6% were invasive breast cancer, 13.5% ductal carcinoma, and 3.9% inflammatory breast carcinoma.

Comparing US findings with histopathological reports, 45 were true positive (TP), 49 patients were true negative (TN), none were false positive (FP), and 3 were false negative (FN). The sensitivity, specificity, negative predictive value, positive predictive value, and accuracy of US to detect breast cancer were 94%, 100%, 93.7%, 100%, and 96.9%, respectively (Table 4).

Correlation between specific US findings and pathology interpretation is presented in Table 5. Among patients whose US findings were concerning for ductal carcinoma, invasive carcinoma, inflammatory carcinoma, or papillary neoplasm who underwent biopsy (49 cases), 50% demonstrated cancer. Among patients whose US indicated likely fibroadenoma (45 cases), 4.4% were positive for cancer. Similarly, among patients who whose US findings indicated axillary lymphadenopathy (31 cases), 3.2% were positive for cancer. Of the remaining 46.4% of biopsied patients whose US findings suggested a benign lesion, breast abscess, breast cyst, complex cyst, ductal ectasis, fibroadenosis, fibrocystic changes, lipoma, mastitis, or galactocele, none who underwent cytopathology or histopathology showed cancer.

Table 3: Summary of Histo or Cytopathology Findings, 97 Patients, BPKMCH, 2022

Findings	Cases	%
Benign breast disease	8	8.2
Breast abscess	3	3.1
Breast cyst	2	2.1
Ductal carcinoma	7	7.2
Ductal ectasia	2	2.1
Fat necrosis	1	1.0
Fibroadenoma	19	19.6
Galactocele	2	2.1
Inflammatory carcinoma	2	2.1
Invasive carcinoma	43	44.3
Lobule of adipocytes	1	1.0
Mastitis	7	7.2
Total	97	100.0

Table 4: Test Characteristics of Ultrasound Compared to Tissue Diagnosis (Gold Standard), BPKMCH, 2022

Test Characteristic	Cases	%
True Positive (TP)	45	46.4
True Negative (TN)	49	50.5
False Positive (FP)	0	0
False Negative (FN)	3	3.1
Sensitivity		94.0
Specificity		100.0
Positive Predictive Value		100.0
Negative Predictive Value		93.7
Accuracy		96.9

DISCUSSION

Breast cancer is the most-common cancer in women worldwide and a significant cause of mortality. Awareness of breast cancer, public attentiveness, and advances in breast imaging have positive impacts on recognition, screening, diagnostic evaluation, and prognosis. Prevention or early detection is the best solution for any carcinoma; improved quality of diagnostic imaging (and use thereof) is an important component of any comprehensive breast cancer detection program. This study re-demonstrates that breast ultrasonography is excellent at identifying lesions which are high-risk (based on radiographic features) for being malignant and distinguishing those from lesions likely to be benign,[12] including evaluation of axillary lymphadenopathy.[10] Relatively-inexpensive, non-radiating, and essentially-painless, breast US is an excellent tool both for screening patients with dense breast tissue and for evaluating lesions identified by symptoms or physical examination.

US out-performs mammography in some patients (i.e., those with dense breast tissue).[9] Breast magnetic resonance imaging (MRI) can be a valuable supplement to mammography and US, particularly among women with dense breasts.[16] Several studies report MRI provides considerable increased detection in high-risk women than mammography or US. However, the use of MRI remains controversial because of the disadvantage of more false-positive results, which lead to unnecessary biopsy, high cost, and lack of availability.[17]

Early detection of breast cancer yields the best prognosis. However, pillars of early detection programs (e.g., awareness of breast cancer, breast self-examination) maybe inadequately-performed in developing countries. A systematic meta-analysis in Nepal demonstrated women's overall knowledge of breast self-examination was poor (only 27% of 1,910 subjects).[18] Expanding use of US in developing countries might be an effective component of a program to increase early breast cancer detection.

Our study findings showed the prevalence of breast cancer among patients who underwent US evaluation for symptoms or physical examination findings was high (12.4%). The sensitivity, specificity, negative predictive value, positive predictive value, and accuracy of US to detect breast cancer were 94%, 100%, 93.7%, 100%, and 96.9%, respectively. These values, which were higher than in previous studies, may be due to differences in prevalence between populations, advancement in technology and software, or selection bias regarding who was referred for US and sent for FNA or biopsy.

Table 5: Summary of Histopathology or Cytopathology Findings of Patients who Underwent Fine Needle Aspiration (FNA) or Biopsy, BPKMCH, 2022

Ultrasound Findings	Biopsy Performed (%, Cases)	Cancer Detected† (%, Cases)	Cancer Detected‡ (%, Cases)
Axillary lymphadenopathy	9.4 (2/31)	50.0 (1/2)	3.2 (1/31)
Benign lesion	44.4 (4/9)	0	0
Breast abscess	55.6 (5/9)	0	0
Complex cyst	50.0 (1/2)	0	0
Cyst	20.0 (3/15)	0	0
Dense breast	0 (0/5)	0	0
Ductal carcinoma	100.0 (7/7)	100.0 (7/7)	100.0 (7/7)
Ductal ectasis	5.3 (1/19)	0	0
Fibroadenoma	48.9 (22/45)	9.1 (2/22)	4.4 (2/45)
Fibroadenosis	7.1 (1/14)	0	0
Fibrocystic changes	4.5 (1/22)	0	0
Galactocele	100.0 (2/2)	0 (0/2)	0
Hidradentis	0 (0/4)	0	0
Inflammatory carcinoma	100.0 (1/1)	100.0 (1/1)	100.0 (1/1)
Invasive carcinoma	100.0 (40/40)	100.0 (40/40)	100.0 (40/40)
Lipoma	12.5 (1/8)	0 (0/1)	0
Mastitis	18.5 (5/27)	0 (0/5)	0
Normal	0 (0/117)	0	0
Papillary neoplasm	100.0 (1/1)	100.0 (1/1)	100.0 (1/1)
Prominent fibrofatty tissue	0 (0/40)	0	0
Total No. of Cases	97	52	52

†Among cases who were biopsied. ‡Among all biopsied and non-biopsied cases.
Note: Among 97 patients who underwent biopsy, some cases had FNA, while other highly-suspicious cases underwent biopsy.

LIMITATIONS

The data for the study came from a single referral hospital, so findings might not be generalizable, particularly as there was likely selection bias as to which patients attended the hospital (e.g., patients with more-concerning symptoms and signs may have been referred here; higher-income patients may have travelled to the hospital). Second, we did not perform multivariate or regression analysis to determine whether US test characteristics (e.g., sensitivity) varied by patient characteristics (e.g., age, prior access to health care). Such analyses should be considered in future studies.

CONCLUSION

Among patients in our study who underwent breast US in the diagnostic work-up of breast symptoms or signs, the prevalence of breast carcinoma was greater than in previous studies. Sensitivity, specificity, negative predictive value, positive predictive value, and accuracy of US to detect breast cancer were high. As breast US does not use radiation and is relatively-inexpensive and pain-free, its use should be encouraged and expanded, especially in low-resource environments and in young women with dense breast tissue.

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ABBREVIATIONS

BPKMCH	B.P. Koirala Memorial Cancer Hospital
FN	False Negative
FNA	Fine Needle Aspiration
FP	False Positive
MRI	Magnetic Resonance Imaging
SPSS	Statistical Package for the Social Sciences
TN	True Negative
TP	True Positive

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Authors' Contributions SG - study conceptualization, data acquisition, literature search, manuscript preparation; SKM - literature search; NS - clinical service, data acquisition, data review; GDA - clinical service, data acquisition, data review; AKY - study conceptualization, study design, manuscript preparation; MR – review, data interpretation, writing and editing. All reviewed the final version of the paper.
Ethics Approval and Consent to Participate Informed consent was obtained from the patient, and the patient identity was concealed.
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