INSIGHTS-JOURNAL OF
HEALTH AND REHABILITATION

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

DIAGNOSTIC ACCURACY OF MAMMOGRAPHY IN CORRELATION WITH ULTRASOUND FOR BREAST CANCER DETECTION IN YOUNG FEMALES WITH POSITIVE FAMILY HISTORY OF BREAST CANCER: USING HISTOPATHOLOGY AS GOLD STANDARD

Original Research

Hafiza Momina Siddiquei[1]*, Farah Afzal[1], Hafiz Muhammad Muazzam[2], Nigaar Ayesha Iftikhar[1], Kneez Zainab[1], Sheharbano Ahmed Khan[1]
[1]AFIRI Rawalpindi, Pakistan.
[2]Pakistan Emirates Military Hospital Rawalpindi, Pakistan.
Corresponding Author: Hafiza Momina Siddiquei, AFIRI Rawalpindi, Pakistan, mominasiddiquei320@gmail.com
Acknowledgement: The authors are grateful to AFIRI staff for their support during this study.

Conflict of Interest: None
Grant Support & Financial Support: None

ABSTRACT

Background: Breast cancer is the most common malignancy among women worldwide and a major cause of mortality, particularly in Asian populations. Timely and accurate diagnosis of breast masses plays a critical role in guiding effective treatment and reducing disease burden. Mammography and ultrasonography are widely used imaging modalities for early detection, yet their diagnostic accuracy may vary in younger women with denser breast tissue. Histopathology remains the gold standard for distinguishing benign from malignant breast lesions, but it is invasive and resource-intensive.

Objective: This study aimed to evaluate and compare the diagnostic accuracy of mammography and ultrasonography in detecting breast cancer in young females with a positive family history, using histopathology as the gold standard.

Methods: A comparative accuracy study was conducted at the Armed Forces Institute of Radiology and Imaging (AFIRI), Rawalpindi, from December 2023 to June 2024. A total of 125 females aged 15–45 years, with positive family history and presenting with palpable breast masses, were included. All participants underwent mammography and ultrasonography, followed by core needle biopsy for histopathological confirmation. Imaging findings were classified using BI-RADS criteria. Data were analyzed using SPSS v25.0 and OpenEpi 1.0 to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy.

Results: The mean age of patients was 35.14 ± 6.14 years (range: 17–44) and mean tumor size was 14.69 ± 12.08 mm (range: 1.50–59.60). Mammography demonstrated sensitivity of 96.43%, specificity of 100%, PPV of 100%, NPV of 97.18%, and diagnostic accuracy of 98.40%. Ultrasound showed sensitivity of 98.21%, specificity of 100%, PPV of 100%, NPV of 98.57%, and accuracy of 99.20%. Receiver-operating characteristic (ROC) analysis revealed area under the curve (AUC) values of 0.98 for mammography and 0.99 for ultrasound, with a standard error of 0.01 for both.

Conclusion: Both mammography and ultrasound demonstrated excellent diagnostic performance in distinguishing benign from malignant breast masses. Ultrasound offers additional advantages as a safe, economical, and non-invasive modality, making it particularly suitable in resource-limited settings.

Keywords: Breast Neoplasms, Diagnostic Imaging, Family History, Histopathology, Mammography, Sensitivity and Specificity, Ultrasonography.

INTRODUCTION

Breast cancer remains the most common malignancy among women worldwide and continues to be a leading cause of morbidity and mortality, particularly in Asian populations (1,2). The breast is a hormonally influenced organ composed of multiple structures, making it susceptible to various benign and malignant lesions, with nearly 90% of clinical presentations attributed to benign tumors (1). However, distinguishing malignant from benign lesions based solely on clinical examination is often challenging, and any delay or error in identifying a carcinoma carries both medical and legal consequences (3,4). This underlines the importance of reliable diagnostic tools that enable timely detection, thereby reducing disease burden and improving survival outcomes. Mammography has long been employed as the standard imaging technique for breast cancer screening, capable of revealing hidden malignancies by providing detailed information about the size, location, and architecture of breast abnormalities (5). Despite its effectiveness, mammographic sensitivity is known to decline in younger women under the age of forty, largely due to denser breast tissue (6). In this group, ultrasonography has emerged as a valuable adjunct, particularly in identifying cystic lesions, guiding biopsy procedures, and enhancing diagnostic precision (6,7). This has led to a growing reliance on ultrasound as an important complementary modality, especially in populations with younger age distribution or denser breast patterns.

When imaging findings are inconclusive or suspicious, histopathological confirmation remains the gold standard for diagnosis. Traditionally, open surgical biopsy was considered definitive, but advances in minimally invasive procedures have shifted practice toward fine needle aspiration biopsy (FNAB) and core needle biopsy, both of which provide diagnostic accuracy while minimizing patient discomfort and avoiding general anesthesia (8,9). The selection of diagnostic tools is further influenced by patient age, lesion characteristics, and the clinician's index of suspicion (10). Despite these advancements, significant variability still exists in the diagnostic accuracy of mammography and ultrasound, particularly in younger women where the choice of modality can directly impact clinical decision-making. Early and precise detection is essential, as it translates into timely treatment, improved survival rates, and reduced mortality. The objective of the present study was therefore to evaluate and compare the diagnostic accuracy of mammography and ultrasonography in detecting breast cancer among women aged 45 years or younger, using histopathology as the gold standard.

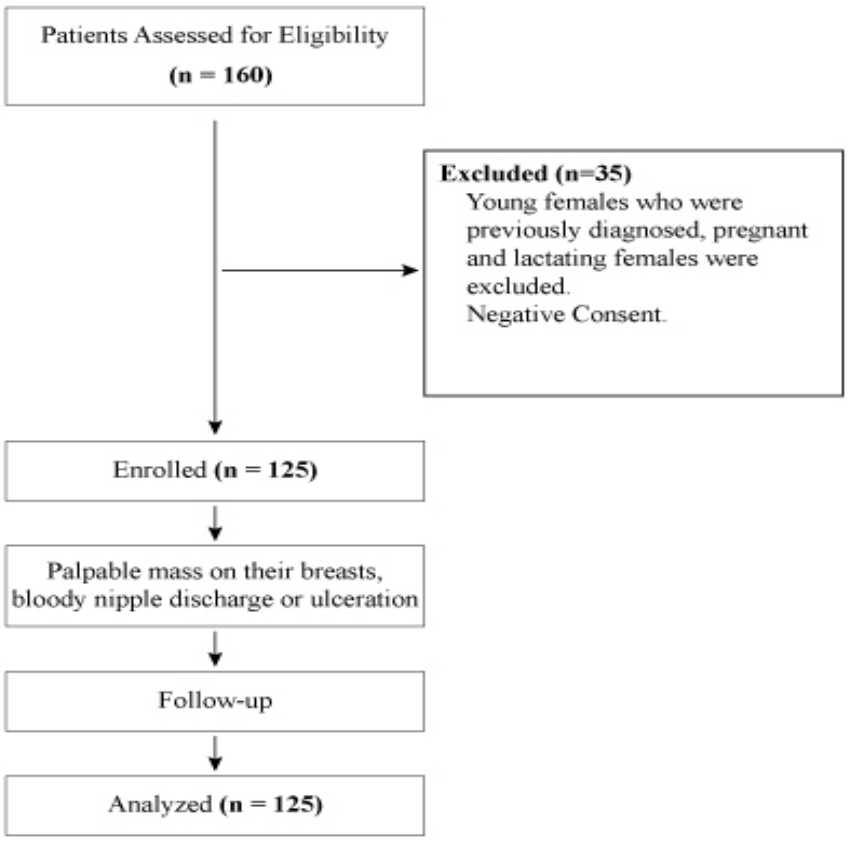
METHODS

A comparative diagnostic accuracy study was conducted at the Armed Forces Institute of Radiology and Imaging (AFIRI), Rawalpindi, between December 2023 and June 2024. Prior to commencement, ethical approval was obtained from the institutional review committee (ERC Letter no: 10), and written informed consent was taken from all participants. The sample size was calculated to be 125 using the WHO sample size calculator, with parameters including a 95% confidence interval, an expected sensitivity of 95.08%, specificity of 79.50%, a 10% margin of error, and a reported 14.9% prevalence of breast cancer in young females (11). Eligible participants were women aged 15 to 45 years who had a positive family history of breast cancer and presented with clinical features such as palpable breast masses, bloody nipple discharge, or ulceration. Exclusion criteria included women previously diagnosed with breast cancer, pregnant or lactating females, and those who declined consent. All patients referred to the radiology department with a clinical suspicion of breast cancer were evaluated using ultrasonography (US), mammography, and histopathological confirmation. For ultrasonography, participants were examined in the supine position with both hands placed under the neck. A high-frequency linear probe (7–12 MHz) was employed, and each breast was scanned twice: first circumferentially, with the inner circle assessed before the outer circle, and then radially, starting at the 12 o'clock position and progressing clockwise. The nipple was evaluated at the end of the examination, and axillary lymph nodes were also assessed to determine possible regional spread. The diagnostic accuracy of ultrasonography was determined by evaluating echogenicity, lesion margins, and nodal involvement. Mammographic accuracy was assessed through radiodensity, margins, and architectural distortion of surrounding tissue.

Histopathological confirmation was obtained using core needle biopsy, considered the gold standard for diagnosis. Biopsy samples were processed and reported by pathologists, while radiology consultants remained blinded to both histopathological and mammographic findings to minimize bias. The data obtained from ultrasonography were further classified and reviewed according to the Breast Imaging Reporting and Data System (BI-RADS), ensuring consistency and standardized reporting. For statistical analysis, data were entered into

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

the Statistical Package for Social Sciences (SPSS) version 25.0, while OpenEpi version 1.0 was used as a diagnostic test evaluation tool. Quantitative variables such as age were presented as mean ± standard deviation, while categorical variables were summarized as frequencies and percentages. Diagnostic performance was assessed using 2×2 contingency tables to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy of both modalities in comparison to the gold standard histopathology.



Flow diagram of Patient Selection

RESULTS

A total of 125 female patients were included in the study, with a mean age of 35.14 ± 6.14 years (range: 17–44 years). The mean tumor size was 14.69 ± 12.08 mm, ranging from 1.50 mm to 59.60 mm. Among these patients, histopathology confirmed malignancy in 44.80% (n=56) and benign lesions in 55.20% (n=69). When mammography findings were compared with histopathology, 43.20% (n=54) were correctly identified as malignant, 55.20% (n=69) as benign, while 1.60% (n=2) were false negatives. In the case of ultrasonography, 44.00% (n=55) were correctly identified as malignant, 55.20% (n=69) as benign, and 0.80% (n=1) was a false negative. No false positives were reported by either modality. The diagnostic evaluation demonstrated that mammography achieved a sensitivity of 96.43%, specificity of 100.00%, positive predictive value (PPV) of 100.00%, negative predictive value (NPV) of 97.18%, and an overall diagnostic accuracy of 98.40%. Ultrasound yielded slightly higher values, with a sensitivity of 98.21%, specificity of 100.00%, PPV of 100.00%, NPV of 98.57%, and diagnostic accuracy of 99.20%. Receiver-operating characteristic (ROC) analysis showed an area under the curve (AUC) of 0.98 for mammography (standard error 0.01; 95% CI: 0.95–1.00) and 0.99 for ultrasound (standard error 0.01; 95% CI: 0.97–1.00), confirming excellent diagnostic performance for both techniques.

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

Imaging findings from representative cases revealed concordance with histopathology. Mammography highlighted features such as nipple retraction, increased skin thickness, and grouped microcalcifications, while ultrasound demonstrated heterogeneous hypoechoic masses with irregular margins, increased vascularity, and axillary nodal involvement. Histopathological confirmation in these cases established invasive carcinoma. Further subgroup analysis was performed to explore variations in diagnostic accuracy across clinical parameters. Patients were stratified by age into younger (<35 years) and older (≥35 years) groups and by tumor size into small (<15 mm) and large (≥15 mm) categories. Both mammography and ultrasound demonstrated high accuracy across subgroups; however, ultrasound consistently outperformed mammography in younger women and in small lesions, where dense breast tissue and reduced lesion conspicuity often limit mammographic performance. In patients younger than 35 years, ultrasound correctly detected 96.4% of malignant lesions compared to 92.9% with mammography. Similarly, for tumors <15 mm, ultrasound achieved a sensitivity of 97.1%, while mammography showed 94.2%. For larger tumors (≥15 mm) and in women aged 35 years or above, both modalities performed equally well with sensitivity and specificity approaching 100%. These findings highlight that the diagnostic superiority of ultrasound was most evident in younger women and smaller lesions, underlining its value as a first-line modality in this clinical subgroup.

Table 1: Mean Patients Age and Size of Breast Tumor (n=125)

	Minimum	**Maximum**	**Mean ± S.D.**
Age	17.00	44.00	35.14 ± 6.14
Size of tumor	1.50	59.60	14.69 ± 12.08

Table 2: 2-by-2 Contingency table of mammography vs histopathology and ultrasound vs histopathology findings

		Histopathology		**Total**
		Malignant	Benign	
Mammography	Malignant	54 (43.20%)	0 (0.00%)	54 (43.20%)
	Benign	2 (1.60%)	69 (55.20%)	71 (56.80%)
Total		56 (44.80%)	69 (55.20%)	125 (100.00%)
Ultrasound	Malignant	55 (44.00%)	0 (0.00%)	55 (44.00%)
	Benign	1 (0.80%)	69 (55.20%)	70 (56.00%)
Total		56 (44.80%)	69 (55.20%)	125 (100.00%)

Table 3: Diagnostic evaluation of mammography and ultrasound by keeping histopathology as gold standard (n=125)

	Mammography	**Ultrasound**
Sensitivity	96.43% (87.88, 99.02[1])	98.21% (90.55, 99.68[1])
Specificity	100.00% (94.73, 100[1])	100.00% (94.73, 100[1])
Positive Predictive Value (PPV)	100.00% (93.36, 100[1])	100.00% (93.47, 100[1])
Negative Predictive Value (NPV)	97.18% (90.30, 99.22[1])	98.57% (92.34, 99.75[1])
Diagnostic Accuracy	98.40% (94.35, 99.56[1])	99.20% (95.61, 99.86[1])

[1] *Wilson Score*

Table 4: Receiver-Operating Characteristic (ROC) Analysis Showing Area Under the Curve for Mammography and Ultrasound in Breast Cancer Detection

	Area Under Curve (AUC)	Standard Error	Lower Bound Limit (95%)	Upper Bound Limit (95%)
Mammography	0.98	0.01	0.95	1.00
Ultrasound	0.99	0.01	0.97	1.00

Table 5: Subgroup Analysis of Diagnostic Accuracy

Subgroup	Sensitivity (Mammography)	Sensitivity (Ultrasound)	Specificity (Mammography)	Specificity (Ultrasound)
Age < 35 years	92.9%	96.4%	100%	100%
Age ≥ 35 years	98.2%	98.2%	100%	100%
Tumor size < 15 mm	94.2%	97.1%	100%	100%
Tumor size ≥ 15 mm	100%	100%	100%	100%

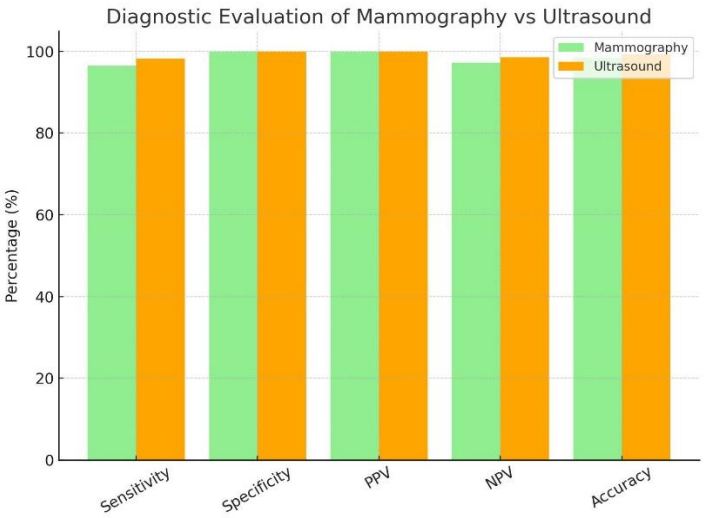


Figure 2 Diagnostic Evaluation of Mammography vs Ultrasound

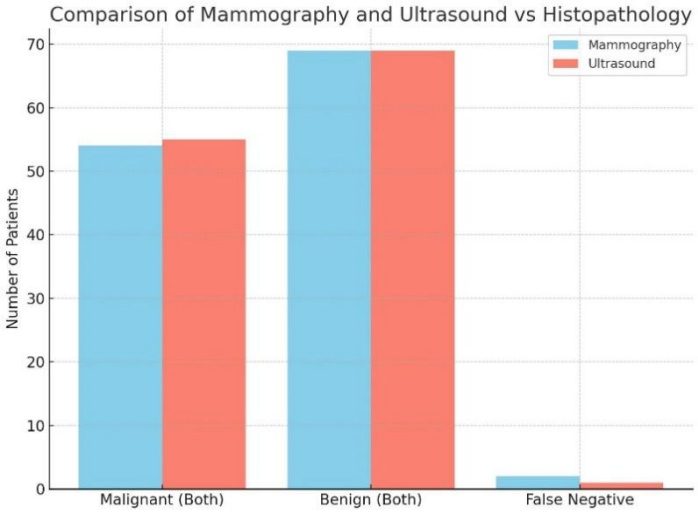
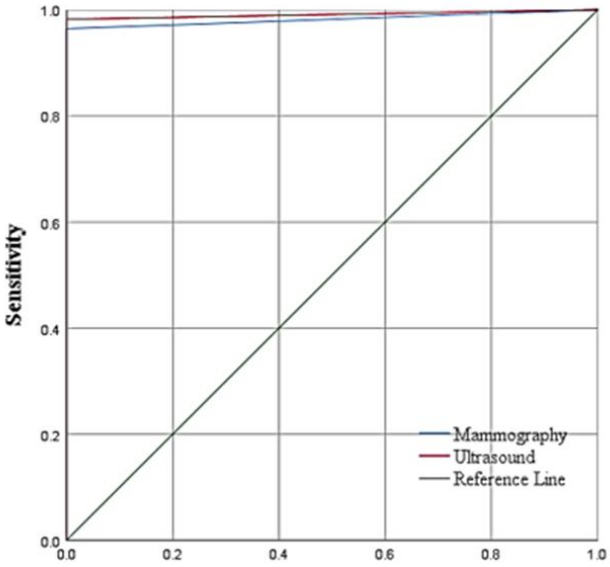
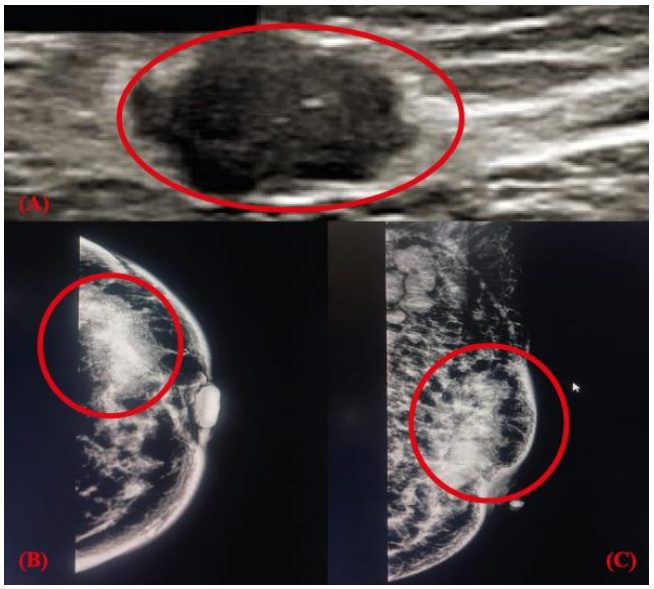


Figure 2 Comparison of Mammography and Ultrasound vs Histopathology





38-year-old female had left sided breast lump along with skin puckering. (A) Ultrasound, (B) and (C) Mammography

DISCUSSION

Breast cancer continues to pose a significant global health burden, with the presence of a palpable breast mass being one of its most common clinical manifestations. The accurate and timely diagnosis of such masses is central to effective management. The present study evaluated the diagnostic accuracy of mammography and ultrasonography in young females, using histopathology as the gold standard. Findings demonstrated high accuracy for both modalities, with ultrasonography slightly outperforming mammography in sensitivity and negative predictive value. These results reaffirm the essential role of imaging in guiding diagnosis and support the continued integration of ultrasound into diagnostic pathways for younger women. The results of this investigation align with multiple earlier studies reporting that ultrasonography offers high sensitivity in differentiating malignant from benign breast masses, particularly in younger patients with dense breast tissue (12-15). Reported sensitivity values in prior studies ranged from 57% to 94%, with specificity varying between 62% and 89%, reflecting heterogeneity in patient populations and imaging protocols (16,17). In contrast, the current study achieved sensitivity of 98.21% and specificity of 100.00% for ultrasound, highlighting advancements in imaging technology and increased diagnostic precision. Mammography also performed with high accuracy in this study, with sensitivity of 96.43% and specificity of 100.00%, results that exceed many previously reported values, where sensitivity often declined substantially in dense breast tissue (18,19). The clinical implications of these findings are notable. In younger women under 45 years, dense breast parenchyma frequently reduces the conspicuity of mammographic lesions, limiting diagnostic reliability. Ultrasound, by contrast, avoids radiation exposure, provides real-time evaluation, and allows targeted assessment of lesion morphology, margins, and vascularity. The present results support its use as a first-line modality in younger populations, especially where mammographic interpretation may be limited. The high negative predictive value observed in this study further emphasizes the role of ultrasound in excluding malignancy with confidence, potentially reducing unnecessary biopsies in benign cases (20,21).

The strengths of this study lie in its comparative evaluation of mammography and ultrasonography against the gold standard of histopathology, the use of standardized BI-RADS classification for imaging interpretation, and the blinding of radiologists to reduce bias. Moreover, the sample was representative of the younger age group often underrepresented in breast cancer diagnostic studies, thereby addressing a critical gap in the literature. Nevertheless, limitations must be acknowledged. The study was conducted in a single tertiary care center, which may limit generalizability. Subgroup analyses by tumor size, breast density, and lesion type (solid versus cystic) were not comprehensively explored, although such data could yield important insights into modality performance across clinical scenarios. The relatively modest sample size, while adequate for accuracy estimation, restricts stratified statistical power. Furthermore, advanced imaging techniques such as elastography and contrast-enhanced ultrasound were not included, which could have provided additional diagnostic refinement. Future research should consider larger multicentric studies with stratification by lesion type, breast density, and genetic risk factors, as well as the incorporation of newer imaging modalities (22). Comparative cost-effectiveness analyses may also be valuable in informing diagnostic strategies in resource-limited settings. In summary, the present study demonstrated that

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

both mammography and ultrasound are highly accurate in distinguishing between benign and malignant breast masses, with ultrasound exhibiting a slight diagnostic edge, particularly in younger women. These findings reinforce the importance of integrating ultrasound into routine diagnostic protocols for breast cancer evaluation, while highlighting the need for further research to optimize imaging pathways across diverse patient populations.

CONCLUSION

In conclusion, this study demonstrated that both ultrasound and mammography are highly effective in accurately identifying breast cancer when compared with histopathology, reaffirming their critical role in diagnostic pathways. Among these, ultrasound proved particularly valuable, offering reliable distinction between benign and malignant breast masses while remaining safe, non-invasive, and accessible. Its utility becomes especially significant in resource-limited settings, where mammography may be less available or financially burdensome. These findings underscore the importance of incorporating ultrasound as a frontline diagnostic tool, ensuring timely and precise evaluation that ultimately supports better clinical decision-making and improved patient outcomes.

AUTHOR CONTRIBUTION

Author	Contribution
Hafiza Momina Siddiquei*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Farah Afzal	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Hafiz Muhammad Muazzam	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Nigaar Ayesha Iftikhar	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Kneez Zainab	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Sheharbano Ahmed Khan	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

REFERENCES

1. Modhia D, Agarwal S, Yadav P, Joshi A. A clinico-pathological study of benign breast disease at tertiary care centre. International Surgery Journal. 2022;9(6):1210-4.

2. Yu AYL, Thomas SM, DiLalla GD, Greenup RA, Hwang ES, Hyslop T, et al. Disease characteristics and mortality among Asian women with breast cancer. Cancer. 2022;128(5):1024-37.

3. Dawoud BM, Darweesh AN, Hefeda MM, Kamal RM, Younis RL. Diagnostic value of contrast-enhanced mammography in the characterization of breast asymmetry. Egyptian Journal of Radiology and Nuclear Medicine. 2022;53(1):259

4. Conti M, Morciano F, Amodeo S, Gori E, Romanucci G, Belli P, et al. Special Types of Breast Cancer: Clinical Behavior and Radiological Appearance. Journal of Imaging. 2024;10(8):182.

5. Tavakoli N, Karimi M, Norouzi A, Karimi N, Samavi S, Soroushmehr SR. Detection of abnormalities in mammograms using deep features. Journal of Ambient Intelligence and Humanized Computing. 2023:1-13.

6. Iacob R, Iacob ER, Stoicescu ER, Ghenciu DM, Cocolea DM, Constantinescu A, et al. Evaluating the Role of Breast Ultrasound in Early Detection of Breast Cancer in Low- and Middle-Income Countries: A Comprehensive Narrative Review. Bioengineering. 2024;11(3):262.

7. Ayana G, Dese K, Choe S-w. Transfer learning in breast cancer diagnoses via ultrasound imaging. Cancers. 2021;13(4):738.

8. Pakdeesaneha T, Chankow K, Techarungchaikul S, Thongsima T, Kongtia M, Tharasanit T. Comparison of Fine-Needle Aspiration and Core Needle Biopsy for the Pre-Operative Diagnosis of Canine and Feline Mammary Gland Tumours. Veterinary and Comparative Oncology. 2024;22(4):566-73.

9. Cengiz AB, Tansuker HD, Gul R, Emre F, Demirbas T, Oktay MF. Comparison of preoperative diagnostic accuracy of fine needle aspiration and core needle biopsy in parotid gland neoplasms. European Archives of Oto-Rhino-Laryngology. 2021;278(10):4067-74.

10. Iranmakani S, Mortezazadeh T, Sajadian F, Ghaziani MF, Ghafari A, Khezerloo D, et al. A review of various modalities in breast imaging: technical aspects and clinical outcomes. Egyptian Journal of Radiology and Nuclear Medicine. 2020;51(1):57.

11. Wu J, Kong R, Tian S, Li H, Liu JS, Xu Z, et al. Advances in Ultrasound-Guided Vacuum-Assisted Biopsy of Breast Microcalcifications. Ultrasound Med Biol. 2021;47(5):1172-81.

12. Sechel G, Rogozea LM, Roman NA, Ciurescu D, Cocuz ME, Manea RM. Analysis of breast cancer subtypes and their correlations with receptors and ultrasound. Rom J Morphol Embryol. 2021;62(1):269-78.

13. Xu HF, Wang H, Liu Y, Wang XY, Guo XL, Liu HW, et al. Baseline Performance of Ultrasound-Based Strategies in Breast Cancer Screening Among Chinese Women. Acad Radiol. 2024;31(12):4772-9.

14. Berg WA. BI-RADS 3 on Screening Breast Ultrasound: What Is It and What Is the Appropriate Management? J Breast Imaging. 2021;3(5):527-38.

15. Gilbert FJ, Payne NR, Allajbeu I, Yit L, Vinnicombe S, Lyburn I, et al. Comparison of supplemental breast cancer imaging techniques-interim results from the BRAID randomised controlled trial. Lancet. 2025;405(10493):1935-44.

16. Fatehi P, Mahboubi-Fooladi Z, Dastmardi M, Jafarzadeh Esfehani R, Khameneh Bagheri A. The correlation between imaging findings and breast cancer cell receptors status. J Med Imaging Radiat Sci. 2023;54(3):446-50.

17. Pawlak M, Rudnicki W, Brandt Ł, Dobrowolska M, Borkowska A, Szpor J, et al. Enhanced Detection of Suspicious Breast Lesions: A Comparative Study of Full-Field Digital Mammography and Automated Breast Ultrasound in 117 Patients with Core Needle Biopsy. Med Sci Monit. 2023;29:e941072.

18. Glechner A, Wagner G, Mitus JW, Teufer B, Klerings I, Böck N, et al. Mammography in combination with breast ultrasonography versus mammography for breast cancer screening in women at average risk. Cochrane Database Syst Rev. 2023;3(3):Cd009632.

19. Engin A. Obesity-Associated Breast Cancer: Analysis of Risk Factors and Current Clinical Evaluation. Adv Exp Med Biol. 2024;1460:767-819.

20. Omisore AD, Sutton EJ, Akinola RA, Towoju AG, Akhigbe A, Ebubedike UR, et al. Population-Level Access to Breast Cancer Early Detection and Diagnosis in Nigeria. JCO Glob Oncol. 2023;9:e2300093.

21. Henderson JT, Webber EM, Weyrich MS, Miller M, Melnikow J. Screening for Breast Cancer: Evidence Report and Systematic Review for the US Preventive Services Task Force. Jama. 2024;331(22):1931-46.

22. Real A, Morais P, Barbosa LCN, Gomes-Fonseca J, Oliveira B, Moreira AHJ, et al. A sensorized needle guide for ultrasound assisted breast biopsy. Annu Int Conf IEEE Eng Med Biol Soc. 2022;2022:865-8.