Original Article

Integrated Ultrasound and Cytological Assessment of Breast Cysts: A Cross-Sectional Diagnostic Study for Predicting Malignancy

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ABSTRACT

Objective: To evaluate the diagnostic performance of an integrated ultrasound and FNAC approach in differentiating benign and malignant breast cystic lesions

Study Design: Cross-sectional diagnostic study

Place and Duration of Study: This study was conducted at the Tertiary Care Hospitals in Mosul, Iraq, from January 2025 to December 2025.

Methodology: Women presenting with breast cystic lesions underwent ultrasound and FNAC evaluation. Histopathology served as the reference standard. Logistic regression and ROC curve analysis were performed to assess diagnostic performance.

Results: Complex cyst morphology, irregular margins, vascularity, and suspicious FNAC findings were significantly associated with malignancy ($p < 0.001$). The integrated model demonstrated superior diagnostic accuracy (AUC = 0.93) compared to ultrasound alone (AUC = 0.81). Sensitivity and specificity exceeded 90%.

Conclusion: The combined ultrasound–FNAC approach significantly enhances diagnostic accuracy and supports clinical decision-making in breast cyst evaluation.

Key Words: Breast cysts; Ultrasound; FNAC; Malignancy; Diagnostic accuracy.

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INTRODUCTION

Breast cystic lesions are common in clinical practice, particularly among women of reproductive age[1]. Although most are benign, a small proportion may contain atypical or malignant pathology, making accurate differentiation essential[2-4]. Ultrasonography is widely used because it is accessible, cost-effective, and effective in distinguishing cystic from solid lesions. Simple cysts typically show benign features, including anechoic content, thin walls, and posterior acoustic enhancement[5]. However, complicated or complex cysts with internal echoes, septations, mural nodules, or irregular margins may overlap with malignant features, limiting the diagnostic accuracy of ultrasound alone[6,7]. Fine-needle aspiration cytology (FNAC) provides complementary cytological assessment and is minimally invasive and inexpensive. Nevertheless, inadequate sampling, operator dependency, and interpretive variability may limit its diagnostic value[8]. Residual masses after aspiration may further raise concern for underlying malignancy[9].

Integrating ultrasound and cytological findings may improve diagnostic accuracy, yet standardized predictive models for breast cystic lesions remain limited[10]. Such an approach may be particularly valuable in resource-limited settings. Therefore, this study aimed to develop and evaluate a predictive model combining ultrasound features and FNAC findings to differentiate benign from malignant breast cystic lesions and identify key predictors of malignancy.

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METHODOLOGY

Study Design: A prospective observational diagnostic study was conducted to evaluate the clinical, ultrasonographic, and cytological characteristics of cystic breast lesions and to identify factors associated with malignancy. Histopathological examination, when available, was used as the reference standard for definitive diagnosis.

Place and Duration of the Study: The study was conducted at the radiology and breast clinics of tertiary care hospitals in Mosul, Iraq, over a 12-month period from January to December 2025. Eligible women presenting to the participating clinics during the study period were assessed for inclusion.

Study Population and Sampling: The study population comprised adult women presenting with breast lumps or lesions suspected to have a cystic component. A consecutive sampling technique was employed, whereby all eligible women presenting during the study period were invited to participate until the required sample was achieved.

Eligibility Criteria: Women aged 18 years or older were eligible if they had a breast lesion suggestive of a cystic nature on clinical examination or imaging, underwent breast ultrasonography, and had FNAC and/or histopathological confirmation. Women with a previously diagnosed breast malignancy, solid breast masses without cystic components, incomplete imaging or cytological/histopathological data, or those who declined participation were excluded.

Breast Ultrasonography: Breast ultrasonography was performed by experienced radiologists using a high-frequency linear transducer (7.5–12 MHz). Each lesion was systematically evaluated for size, laterality, number, cyst type, internal echoes, septations, wall characteristics, posterior acoustic features, and Doppler vascularity. Cystic lesions were classified as simple, complicated, or complex according to standard sonographic criteria. Based on the overall ultrasonographic appearance, lesions were further categorized as benign or suspicious for malignancy.

Fine-Needle Aspiration Cytology: Fine-needle aspiration cytology (FNAC) was performed under aseptic conditions using a 22–25-gauge needle, either with or without ultrasound guidance according to lesion characteristics and clinical requirements. Aspirated material was appropriately processed and examined by experienced cytopathologists. Cytological findings were categorized as benign, atypical, suspicious, or malignant. For aspirated cystic lesions, the presence or absence of a residual mass following aspiration was also documented.

Histopathological Reference Standard: Histopathological examination of biopsy or surgically excised specimens was considered the reference standard for definitive diagnosis. Based on histopathological findings, lesions were classified as benign or malignant. Histopathological results were subsequently compared with ultrasonographic and cytological findings to assess their diagnostic performance.

Outcome Measures: The primary outcome was the presence of malignancy among cystic breast lesions. Secondary outcomes included the identification of ultrasonographic and cytological characteristics significantly associated with malignancy and the evaluation of the diagnostic performance of ultrasonography, FNAC, and the integrated diagnostic model.

Statistical Analysis: Data was analyzed using IBM SPSS Statistics version 28.0. Continuous and categorical variables were summarized as mean ± SD and frequencies with percentages, respectively. Associations with malignancy were assessed using Chi-square or Fisher's exact tests, followed by multivariable logistic regression to identify independent predictors, reported as adjusted odds ratios (AORs) with 95% CIs. Diagnostic performance was evaluated using sensitivity, specificity, PPV, NPV, and ROC analysis with AUC. A two-sided $p<0.05$ was considered statistically significant.

RESULTS

Participant and Clinical Characteristics: A total of 120 women with breast cystic lesions were included in the study. The mean age of the participants was 41.8 ± 11.6 years, with 74 (61.7%) aged 40 years or older and 46 (38.3%) aged younger than 40 years. Regarding lesion laterality, 52 (43.3%) lesions involved the right breast, 48 (40.0%) involved the left breast, and 20 (16.7%) were bilateral. Most participants had a single cystic lesion (66.7%), whereas 33.3% had multiple lesions. The mean cyst size was 18.6 ± 7.9 mm (Table No. 1).

Ultrasound Characteristics According to Histopathological Diagnosis: Histopathology identified 96 (80.0%) benign and 24 (20.0%) malignant lesions. Simple cysts were more frequent among benign lesions (60.4% vs. 8.3%), whereas complex cysts were more common among malignant lesions (66.7% vs. 18.8%; $p<0.001$). Malignant lesions also showed significantly higher frequencies of internal echoes (75.0% vs. 22.9%), septations (62.5% vs. 14.6%), irregular margins (70.8% vs. 10.4%), and Doppler vascularity (79.2% vs. 12.5%). All associations were statistically significant ($p<0.001$) (Table No. 2).

FNAC Findings According to Histopathological Diagnosis: FNAC findings showed a clear distribution according to the final histopathological diagnosis. Among the 96 histopathologically benign lesions, FNAC classified 72 as benign, 16 as atypical, 6 as suspicious, and 2 as malignant. In contrast, among the 24 histopathologically malignant lesions, only 2 were classified as benign by FNAC, while 4 were atypical, 8 were suspicious, and 10 were classified as malignant. Thus, suspicious and malignant cytological findings occurred predominantly among histopathologically

confirmed malignant lesions, demonstrating substantial agreement between FNAC findings and the definitive diagnosis (Table No. 3).

Independent Predictors of Malignancy: Multivariable logistic regression analysis identified several independent predictors of malignancy. Complex cyst morphology was associated with approximately a fivefold increase in the odds of malignancy (AOR = 4.8; 95% CI: 2.1–10.9; $p < 0.001$). Lesions with irregular margins had 5.6 times higher odds of malignancy (AOR = 5.6; 95% CI: 2.4–13.1; $p < 0.001$), while the presence of Doppler vascularity was associated with 6.9-fold greater odds (AOR = 6.9; 95% CI: 3.0–15.8; $p < 0.001$).

The strongest independent predictor was a suspicious or malignant FNAC result, which was associated with a 12.5-fold increase in the odds of histopathological confirmed malignancy (AOR = 12.5; 95% CI: 5.2–29.8; $p < 0.001$). These findings indicate that cytological findings provided the greatest independent contribution to malignancy prediction, followed by Doppler vascularity, irregular margins, and complex cyst morphology (Table No. 4).

Table No. 1. Demographic and Clinical Characteristics (n = 120)

Variable	Category	n (%)
Age (years)	Mean ± SD	41.8 ± 11.6
Age group	<40	46 (38.3)
	≥40	74 (61.7)
Laterality	Right	52 (43.3)
	Left	48 (40.0)
	Bilateral	20 (16.7)
Number of cysts	Single	80 (66.7)
	Multiple	40 (33.3)
Cyst size (mm)	Mean ± SD	18.6 ± 7.9

Table No. 2: Ultrasound Features vs Histopathological Outcome

Feature	Benign n=96	Malignant n=24	p-value
Simple cyst	58 (60.4%)	2 (8.3%)	<0.001
Complex cyst	18 (18.8%)	16 (66.7%)	<0.001
Internal echoes	22 (22.9%)	18 (75.0%)	<0.001
Septations	14 (14.6%)	15 (62.5%)	<0.001
Irregular margins	10 (10.4%)	17 (70.8%)	<0.001
Doppler vascularity	12 (12.5%)	19 (79.2%)	<0.001

Table No. 3: FNAC Results vs Histopathology

FNAC Category	Benign n=96	Malignant n=24
Benign	72	2
Atypical	16	4
Suspicious	6	8
Malignant	2	10

Table No. 4: Multivariate Logistic Regression Analysis

Variable	AOR	95% CI	p-value
Complex cyst	4.8	2.1–10.9	<0.001
Irregular margin	5.6	2.4–13.1	<0.001
Doppler vascularity	6.9	3.0–15.8	<0.001
Suspicious/Malignant FNAC	12.5	5.2–29.8	<0.001

Table No. 5: Diagnostic Accuracy of Models

Model	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC
Ultrasound alone	83.3	78.1	48.5	94.7	0.81
FNAC alone	87.5	90.6	70.0	96.7	0.89
Integrated model	**95.8**	**92.7**	**79.3**	**98.9**	**0.93**

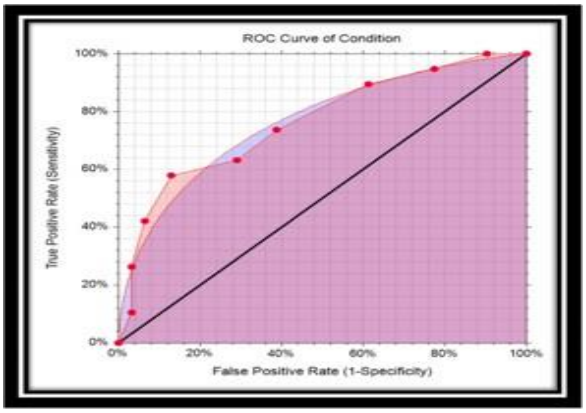


Figure No. 1: ROC Curve Analysis

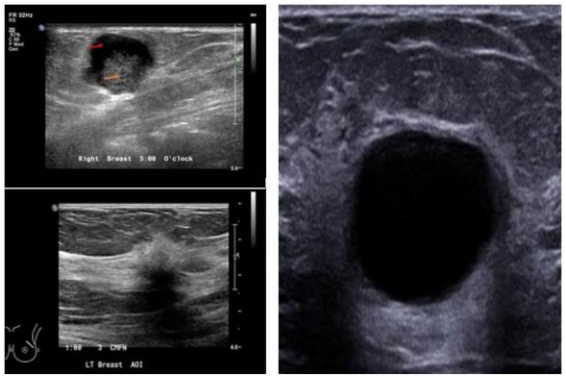


Figure No. 2: Ultrasound Examples (Clinical Relevance)

Diagnostic Performance of Ultrasound, FNAC, and the Integrated Model: The diagnostic performance of the three approaches demonstrated progressive improvement when ultrasonographic and cytological findings were combined. Ultrasound alone achieved a sensitivity of 83.3%, specifically of 78.1%, PPV of 48.5%, NPV of 94.7%, and AUC of 0.81. FNAC alone demonstrated better diagnostic performance, with a sensitivity of 87.5%, specificity of 90.6%, PPV of 70.0%, NPV of 96.7%, and AUC of 0.89.

The integrated ultrasound–FNAC model demonstrated the highest diagnostic performance, achieving a sensitivity of 95.8%, specificity of 92.7%, PPV of 79.3%, and NPV of 98.9%. ROC curve analysis yielded an AUC of 0.93, indicating excellent discrimination between benign and malignant lesions. Overall, the integrated model demonstrated superior diagnostic performance compared with either ultrasound or FNAC used independently (Table No. 5 and Figure No. 1).

DISCUSSION

This study evaluated the diagnostic performance of an integrated ultrasound and cytological approach in differentiating benign and malignant breast cystic lesions. The findings demonstrated that combining ultrasound features with FNAC significantly improves diagnostic accuracy, achieving excellent discrimination (AUC = 0.93), with sensitivity and specificity exceeding 90%. These results support the growing evidence that multimodal diagnostic strategies provide superior clinical value compared to single-modality assessment[11-12].

The overall malignancy rate observed in this study (20%) is consistent with previous reports indicating that the majority of breast cystic lesions are benign, with malignancy rates typically ranging between 15% and 25% in complex cyst categories. Importantly, our findings confirmed that complex cyst morphology, internal echoes, septations, irregular margins, and vascularity were strongly associated with malignancy. Similar associations have been reported in recent imaging studies, where ultrasound-based classification systems such as BI-RADS demonstrated strong predictive capability in distinguishing benign from malignant lesions[13-15].

Ultrasound alone in the present study showed good diagnostic performance (AUC ≈ 0.81), which aligns with recent evidence indicating that ultrasonography achieves diagnostic accuracy around 80–86% with high negative predictive value, particularly in dense breast tissue 29-31. However, ultrasound remains limited in differentiating complicated and complex cysts due to overlapping imaging characteristics. This limitation highlights the need for adjunctive diagnostic tools.

FNAC demonstrated high diagnostic accuracy in this study, consistent with recent literature reporting accuracy rates between 71% and 96%, depending on lesion characteristics and operator expertise. Other contemporary studies have also reported FNAC sensitivity exceeding 90% with strong correlation to histopathology, reinforcing its role as a reliable and minimally invasive diagnostic tool 34. However, FNAC is known to have limitations in borderline or atypical lesions, where false negative or indeterminate results may occur[16-18].

A key finding of this study is the superior performance of the integrated ultrasound–FNAC model, which significantly outperformed either modality alone. This finding is consistent with recent studies emphasizing that combining imaging modalities with cytological or histopathological assessment enhances diagnostic accuracy. For example, a 2025 study reported that combined imaging approaches achieved diagnostic accuracy exceeding 93%, compared to lower performance when modalities were used independently 36-38. Similarly, multimodal ultrasound techniques (e.g., combining conventional ultrasound with elastography or contrast-enhanced imaging) have been shown to significantly improve sensitivity and overall diagnostic performance[19].

The strong predictive value of FNAC observed in the multivariate model (AOR = 12.5) highlights its critical role in confirming malignancy, particularly when ultrasound findings are inconclusive. Moreover, the identification of residual mass after aspiration as a clinically relevant indicator further strengthens the diagnostic pathway, as persistent lesions may warrant closer evaluation and possible biopsy.

From a clinical perspective, the findings of this study have important implications, particularly in resource-limited settings such as Iraq. The integrated approach provides a cost-effective and accessible diagnostic strategy, reducing reliance on more invasive procedures such as core needle biopsy while maintaining high diagnostic accuracy. This aligns with global recommendations advocating stepwise diagnostic evaluation using imaging and minimally invasive techniques[20].

Furthermore, the development of a predictive model offers a structured framework for risk stratification, supporting clinicians in decision-making and potentially reducing unnecessary biopsies in benign cases. This is particularly relevant given the increasing emphasis on personalized and evidence-based breast cancer diagnostics[21-22].

Limitations: Despite its strengths, this study has some limitations. The cross-sectional design limits causal inference, and the sample size, although adequate, may not fully capture all variations of breast cystic lesions. Additionally, FNAC interpretation may be subject to operator variability, and not all cases may have undergone uniform histopathological confirmation. Future multicenter and longitudinal studies are recommended to validate the predictive model.

CONCLUSION

This study demonstrates that combining ultrasound with fine-needle aspiration cytology (FNAC) improves the differentiation of benign and malignant breast cystic lesions. Complex morphology, irregular margins, Doppler vascularity, suspicious cytology, and residual masses after aspiration were important predictors of malignancy. This integrated approach provides high diagnostic accuracy while remaining minimally invasive, cost-effective, and suitable for resource-limited settings, supporting better risk stratification and timely clinical management.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Zinah Akram Hussein, Dina Akram Hussein
Drafting or Revising Critically:	Zinah Akram Hussein, Radhwan Hussein Ibrahim
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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