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COMPARISON OF GRAY SCALE IMAGING AND DOPPLER ULTRASOUND WITH MAMMOGRAPHY FOR DIFFERENTIAL DIAGNOSIS OF BENING AND MALIGNANT SOLID BREAST LESION TAKING BIOPSY AS A GOLD STANDARD

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Abstract

Background: Breast cancer is complicated and very heterogenous malignancy and the major cause of mortality in women associated with cancer in the rest of the world and in Pakistan. The situation with delayed clinical manifestation is a critical crisis in the population health. Although the conventional digital mammography is a universal baseline screening modality, its diagnostic sensitivity is much lower in younger women and dense-fibroglandular tissue since the radiological masking effect is induced. High-resolution gray-scale ultrasound and color Doppler imaging integration is shown to be an important add-on technique that addresses these limits of anatomy to enhance early detection.

Objective: To assess and compare the diagnostic accuracy, sensitivity and specificity of high-resolution gray-scale ultrasound combined with color Doppler versus standard digital mammography in accurately differentiating between benign and malignant histological lesions of the solid breast tissue using a definitive gold standard of histopathological biopsy.

Methodology: The current study used the cross-sectional analysis design, which was carried out in Jinnah Hospital Lahore. Eighty female patients who presented with solid breast mass were randomly sampled and a total of 80 individuals were used. All the participants were subjected to routine mammography, high-frequency gray-scale ultrasound, and color Doppler imaging after which a definite core needle or surgical biopsy had to be done in order to verify the histopathological diagnosis.

Results: Eighty female participants were involved in the study and the highest rate of breast lesions (43.8) was recorded in the 40-55 years age group. Histopathological biopsy proved that 68 lesions (85.0%) were benign and 12 lesions (15.0) invasive malignant carcinomas. Heterogeneously or extremely dense breast tissue appeared in almost half of the population (47.5) presented. Standard

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mammography showed a sensitivity of 75.0% as well as specificity of 95.6 with a significant omission of 3 malignant cases (false negatives) all together because of the dense tissue masking effect. On the other hand, gray-scale morphology and color Doppler hemodynamics (for central vascularity) used synergistically was successful in penetrating dense tissue to produce a perfect sensitivity of 100.0% as well as a specificity of 94.1 having correctly identified all malignant cases.

Conclusion : The present study establishes with no doubt that, a combination of gray-scale and colour Doppler ultrasound gives the best diagnostic accuracy compared to the traditional digital mammography in the assessment of solid breast lesion. Mammography is crippled by false-negative results especially in dense fibroglandular tissue, but adjunctive ultrasound effectively alleviates masking effect. The findings point to the absolute clinical imperative of focused ultrasound as an imperative diagnostic complement to avoid the occurrence of late oncological diagnosis, less surgical biopsy of benign masses and increased patient survival rates.

INTRODUCTION

Breast cancer is a highly heterogeneous and complex malignancy originating from the epithelial cells of the terminal duct lobular units of the breast. It is considered one of the most rapidly evolving and invasive diseases worldwide because of its diverse molecular subtypes, varying metastatic potential, and differences in treatment response. Globally, breast cancer has surpassed lung cancer as the most commonly diagnosed cancer, accounting for approximately 11.7–12.5% of all new cancer cases, with nearly 2.3 million diagnoses and about 685,000 deaths annually, creating a substantial burden on healthcare systems worldwide (1).

Pakistan faces a particularly alarming burden of breast cancer, with one of the highest incidence rates in Asia. Epidemiological estimates suggest that one in every nine Pakistani women is at risk of developing breast cancer, making it a major public health concern with severe socioeconomic consequences. A significant contributor to the high mortality rate is the delayed clinical presentation of patients, largely due to inadequate national screening programs, limited healthcare access, low health literacy, cultural taboos, modesty concerns, and reliance on traditional remedies.

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Consequently, many women present with advanced-stage, palpable, and invasive lesions, reducing treatment options and worsening prognosis (2).

Early detection and accurate differentiation between benign and malignant breast lesions are essential for improving patient survival and minimizing aggressive treatments. Benign lesions are localized and non-invasive, whereas malignant lesions are characterized by uncontrolled cell growth with the potential to invade surrounding tissues and metastasize. Modern diagnostic imaging aims to distinguish these lesions non-invasively, enabling conservative treatment options such as breast-conserving surgery and reducing the physical, psychological, and financial burden associated with radical procedures like mastectomy (3).

Mammography remains the standard imaging modality for breast cancer screening because of its ability to detect early microcalcifications and structural abnormalities. However, its diagnostic sensitivity significantly decreases in younger women and patients with dense breast tissue due to the "masking effect," where dense fibroglandular tissue appears radiopaque and conceals malignant tumors. To overcome this limitation, gray-scale ultrasound is widely used as a complementary imaging modality because it can differentiate cystic from solid lesions and identify suspicious tumor characteristics such as irregular margins and spiculations. Additionally, Doppler ultrasound evaluates tumor vascularity and angiogenesis, further improving diagnostic confidence by combining structural and functional assessment of breast lesions (4).

Despite advancements in imaging technologies, definitive diagnosis still depends on histopathological biopsy, which remains the gold standard for confirming malignancy. The present study was conducted to compare the diagnostic accuracy, sensitivity, and specificity of gray-scale ultrasound, Doppler ultrasound, and mammography in differentiating benign and malignant solid breast lesions using biopsy findings as the reference standard. The study aims to determine the most reliable and cost-effective diagnostic approach for early detection, particularly in patients with dense breast tissue, while also reducing unnecessary invasive biopsies and improving patient outcomes (5).

Literature Review

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Stavros et al., (1995) established important sonographic criteria for differentiating benign and malignant solid breast lesions using high-resolution gray-scale ultrasound. Their study demonstrated that benign lesions commonly exhibit smooth margins, well-circumscribed borders, and wider-than-tall orientation, resulting in very high diagnostic sensitivity and negative predictive value. Similarly, Raza et al. (2010) and Hooley et al., (2012) confirmed that lesions classified as probably benign on ultrasound have extremely low malignancy rates, supporting conservative follow-up strategies and reducing unnecessary biopsies and surgical interventions (1).

Kolb et al. (2002) highlighted the limitations of mammography in women with dense breast tissue and demonstrated that combining ultrasound with mammography significantly improved cancer detection sensitivity from 77.6% to 97.3%. Likewise, Berg et al. (2008), Corsetti et al. (2008), Crystal et al. (2003), and Ohuchi et al. (2016) reported that adjunctive ultrasound detected additional early-stage cancers that were mammographically occult due to dense fibroglandular tissue. These studies strongly recommended the inclusion of ultrasound in routine screening programs for women with dense breasts (2).

Gokalp et al., (2003) investigated the diagnostic role of color Doppler ultrasound and found that malignant lesions usually demonstrate aggressive central vascularity and increased blood flow, while benign lesions are commonly avascular or show peripheral flow. Choi et al. (2005) and Kedar et al. (1996) further confirmed that malignant tumors possess significantly higher vascular density and peak systolic velocities than benign lesions. In addition, Lee et al. (2010) reported that Doppler ultrasound improved BI-RADS categorization accuracy by correctly upgrading malignant lesions and safely downgrading benign masses, thereby improving diagnostic confidence (3).

Leconte et al., (2003) directly compared mammography and ultrasound in symptomatic breast lesions and reported that ultrasound detected 93% of histologically confirmed cancers compared to 82% by mammography. Similarly, Moon et al. (2002) focused on Asian women with dense breast tissue and demonstrated that ultrasound successfully identified several occult malignancies missed on mammography. Yang et al. (2011) and Hou et al. (2013) further concluded that combining gray-

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scale ultrasound, Doppler ultrasound, and mammography provides the highest diagnostic sensitivity and accuracy for differentiating benign and malignant breast lesions (4).

Zonderland et al., (1999) demonstrated that ultrasound-guided core needle biopsy provides excellent sensitivity and specificity while minimizing the morbidity associated with surgical excision. Brem et al. (2014) introduced Automated Breast Ultrasound (ABUS), which improved cancer detection while reducing operator dependency through standardized imaging protocols. Furthermore, Staren et al. (1997) showed that surgeon-performed targeted ultrasound enabled rapid and accurate diagnosis, shortened patient waiting times, and improved clinical decision-making. Overall, previous literature strongly supports the combined role of mammography, gray-scale ultrasound, Doppler ultrasound, and biopsy in the early and accurate diagnosis of breast cancer (5).

Methodology

This study employed a cross-sectional research design to compare the diagnostic accuracy of gray-scale ultrasound, Doppler ultrasound, and mammography in differentiating benign and malignant solid breast lesions. The research was conducted at Jinnah Hospital Lahore, over a duration of four months after approval of the research synopsis. A sample size of 80 patients was calculated using the standard sample size formula, and participants were selected through a convenience sampling technique.

The study included women aged between 20 and 70 years who presented with solid breast lesions on imaging and were referred for diagnostic evaluation of breast masses. Only patients willing to undergo mammography, ultrasound, Doppler examination, and biopsy with written informed consent were included. Patients with cystic or inflammatory breast lesions, previous breast surgery, chemotherapy, or radiotherapy history, pregnant or lactating women, and individuals with incomplete imaging data or refusal for biopsy were excluded from the study.

Ethical principles and guidelines approved by the Superior University Lahore Ethical Committee were strictly followed throughout the research process. Written informed consent was obtained from

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all participants before enrollment. Confidentiality and anonymity of participants were maintained, and all collected data were securely stored under password protection and lock-and-key arrangements. Participants were informed that routine imaging procedures carried no additional risk and that they had the right to withdraw from the study at any stage without any consequences.

Data collection involved recording demographic and clinical information using a structured questionnaire after informed consent. Gray-scale and color Doppler ultrasound examinations were performed using high-frequency linear transducers in transverse and longitudinal planes to evaluate lesion morphology and vascularity. Mammography was conducted in standard craniocaudal and mediolateral oblique views. Histopathological biopsy findings were considered the gold standard for final diagnosis. Data analysis was performed using SPSS version 21, where quantitative variables were presented as mean and standard deviation, while categorical variables were expressed as frequencies and percentages. Sensitivity, specificity, positive predictive value, and negative predictive value of each imaging modality were calculated, and a p-value of less than 0.05 was considered statistically significant.

Results

The study included 80 participants, with the majority belonging to the middle-aged group of 40–55 years, accounting for 35 participants (43.8%). Participants younger than 40 years represented 23 cases (28.7%), while 22 participants (27.5%) were older than 55 years. Regarding the anatomical distribution of lesions, 44 patients (55.0%) had lesions in the left breast, whereas 36 patients (45.0%) had lesions in the right breast, showing a slight predominance of left-sided breast involvement.

Gray-scale ultrasound findings demonstrated that solid lesions were the most common lesion type, identified in 66 participants (82.5%). Cystic lesions were observed in 12 cases (15.0%), while mixed lesions were present in only 2 cases (2.5%). Evaluation of lesion morphology further revealed that 62 lesions (77.5%) had smooth and well-circumscribed margins suggestive of benign pathology,

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whereas 10 lesions (12.5%) showed irregular margins and 8 lesions (10.0%) demonstrated highly suspicious spiculated margins.

Color Doppler ultrasound assessment showed that 40 lesions (50.0%) were completely avascular, while 28 lesions (35.0%) exhibited peripheral vascularity. Aggressive central vascularity, which is more suggestive of malignancy, was present in 9 lesions (11.3%), and mixed vascularity patterns were observed in 3 lesions (3.7%). Mammographic density assessment revealed that 16 patients (20.0%) had fatty breasts and 26 patients (32.5%) had scattered fibroglandular tissue, whereas 24 patients (30.0%) had heterogeneously dense breasts and 14 patients (17.5%) had extremely dense breasts, indicating that nearly half of the participants had dense breast tissue capable of masking malignancies.

Histopathological biopsy findings, considered the gold standard for diagnosis, confirmed that 68 lesions (85.0%) were benign, while 12 lesions (15.0%) were malignant invasive carcinomas. Comparative analysis of mammography results with biopsy findings demonstrated 9 true-positive cases, 65 true-negative cases, 3 false-positive cases, and 3 false-negative cases caused mainly by dense tissue masking. Mammography achieved a diagnostic sensitivity of 75.0% and a specificity of 95.6%, indicating reduced sensitivity in dense breasts.

The combined use of gray-scale ultrasound and color Doppler ultrasound showed superior diagnostic performance compared to mammography. Ultrasound and Doppler correctly identified all 12 malignant lesions, producing 12 true positives, 64 true negatives, 4 false positives, and no false negatives. Consequently, the combined ultrasound approach achieved a sensitivity of 100.0% and a specificity of 94.1%. Overall, the results demonstrated that adjunctive ultrasound and Doppler imaging are significantly more effective than standalone mammography in differentiating benign and malignant solid breast lesions, particularly in patients with dense breast tissue.

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Discussion

The present cross-sectional analytical study was conducted to compare the diagnostic accuracy of gray-scale ultrasound, color Doppler ultrasound, and mammography in differentiating benign and malignant solid breast lesions using histopathological biopsy as the gold standard. Among the 80 female patients included in the study, 68 lesions (85.0%) were confirmed as benign while 12 lesions (15.0%) were malignant. Most patients belonged to the 40–55 years age group, which is consistent with previous epidemiological findings showing increased breast lesion prevalence in perimenopausal and early postmenopausal women. Mammography demonstrated a sensitivity of 75.0% and specificity of 95.6%, but failed to detect three malignant lesions because of the masking effect caused by dense breast tissue. Nearly half of the participants had heterogeneously or extremely dense breasts, supporting previous studies by Kolb et al. (2002) and Berg et al. (2008), which reported reduced mammographic sensitivity in dense breast parenchyma (12,16).

Gray-scale ultrasound successfully differentiated lesion morphology by identifying smooth and well-circumscribed margins in most benign lesions, while malignant masses commonly presented with irregular or spiculated margins. These findings strongly correspond with the sonographic criteria established by Stavros et al. (1995), who emphasized the high negative predictive value of benign ultrasound features (13). Furthermore, color Doppler ultrasound provided additional hemodynamic information that was not obtainable through mammography. Half of the lesions were completely avascular and mainly associated with benign pathology, whereas malignant lesions demonstrated aggressive central vascularity and mixed flow patterns. These findings closely align with the observations of Gokalp et al. (2003) and Choi et al. (2005), who identified tumor neovascularization and central vascularity as important indicators of malignancy (14,20). The combined use of gray-scale ultrasound and Doppler imaging achieved a sensitivity of 100.0% and specificity of 94.1%, successfully detecting all malignant lesions including those missed on mammography.

In conclusion, the study demonstrated that combined gray-scale and color Doppler ultrasound provides superior diagnostic accuracy compared with conventional mammography, particularly in

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patients with dense breast tissue. The study highlights the importance of adjunctive ultrasound in improving early cancer detection, guiding accurate biopsies, and reducing missed malignancies. However, the study was limited by its relatively small sample size, operator dependency of ultrasound examinations, and selection bias due to inclusion of patients referred for diagnostic assessment. Based on these findings, it is recommended that high-resolution ultrasound and Doppler imaging should be routinely incorporated as frontline adjunctive diagnostic tools, especially in younger women and patients with dense breasts. Future multicenter studies with larger sample sizes and randomized sampling methods are recommended to further validate these results across broader populations.

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