International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Research Article

Diagnostic Utility Of Serum Psa In Differentiating Benign And Malignant Breast Lesions: A Prospective Study

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OPEN ACCESS

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Received: 16-09-2025
Accepted: 29-09-2025
Available online: 14-10-2025

ABSTRACT

Background: Prostate-specific antigen (PSA), though primarily utilized as a biomarker in the detection and monitoring of prostate cancer, has been increasingly recognized for its expression in non-prostatic tissues, including the breast. Recent studies suggest that PSA may be secreted by both normal and malignant breast epithelial cells under hormonal regulation. This study investigates the diagnostic utility of serum total PSA levels in distinguishing between benign and malignant breast lesions.

Methods: This prospective observational study was conducted at Rajarajeshwari Medical College between June 2024 and June 2025. Fifty female patients presenting with breast lumps were enrolled. Serum total PSA (T-PSA) levels were measured, and histopathological examination served as the diagnostic gold standard. Clinical, imaging, and biochemical correlations were also assessed.

Results: Of 50 patients, 20 (40%) were diagnosed with malignant lesions and 30 (60%) with benign pathology. Mean T-PSA was significantly higher in malignant cases (3.38 ± 1.04 ng/mL) compared to benign (2.17 ± 0.74 ng/mL; $p = 0.018$). A T-PSA cutoff of >2.75 ng/mL yielded a sensitivity of 76.6%, specificity of 80%, and AUC of 0.79. Estradiol levels were significantly lower in malignancy ($p = 0.001$), and biochemical abnormalities in glucose, LDL, urea, and creatinine were notable.

Conclusion: Serum PSA levels, particularly T-PSA >2.75 ng/mL demonstrate moderate diagnostic accuracy in differentiating malignant from benign breast lesions. PSA may serve as a cost-effective adjunct biomarker in the diagnostic algorithm, especially in resource-limited settings or when histopathology is delayed.

Keywords: *Breast cancer, PSA, Prostate-specific antigen, Tumor markers, Benign breast disease, Free PSA.*

INTRODUCTION

Breast cancer remains one of the most prevalent malignancies among women worldwide, contributing significantly to cancer-related morbidity and mortality. Early diagnosis remains pivotal for favorable outcomes, yet challenges persist in low-resource settings due to delayed presentation, limited access to imaging, and histopathological bottlenecks [1, 2].

Prostate-specific antigen (PSA), traditionally used in the diagnosis and monitoring of prostate cancer, has been observed in extraprostatic tissues including the breast [3]. Studies have demonstrated that PSA is secreted in trace amounts by normal and malignant breast epithelial cells, and its expression may be modulated by steroid hormone activity. Given the hormone-responsive nature of many breast tumors, PSA has emerged as a candidate biomarker for breast disease stratification [4-6].

Recent evidence suggests that elevated levels of serum total and free PSA may correlate with malignant breast pathology, though its diagnostic utility remains underexplored [4-9]. The advantage of PSA lies in its availability, low cost, and ease

of testing, making it a potential adjunct diagnostic marker, especially in settings where access to advanced diagnostics is constrained. This study was undertaken to evaluate the role of serum total PSA in differentiating malignant from benign breast lesions and to establish a practical cutoff value that could assist in early clinical decision-making.

AIMS AND OBJECTIVES

The primary aim of this study was to evaluate the diagnostic utility of serum prostate-specific antigen (PSA) levels as a biomarker for differentiating between benign and malignant breast lesions in female patients. The primary objective was to measure and compare serum total PSA (T-PSA) levels between patients with histopathologically confirmed malignant breast lesions and those with benign breast pathology. Secondary objectives included establishing an optimal cutoff value for serum total PSA to discriminate between benign and malignant lesions, determining diagnostic accuracy parameters including sensitivity, specificity, positive predictive value, negative predictive value through ROC curve analysis, and evaluating correlations between PSA levels and clinical parameters such as age, menopausal status, and biochemical markers including estradiol, lipid profile, and renal function tests.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based prospective observational study was conducted in the Department of General Surgery at Rajarajeshwari Medical College and Hospital, Bengaluru, from June 2024 to June 2025. The study protocol was approved by the institutional ethics committee, and all participants provided written informed consent before enrollment.

Study Population and Sample Size

A total of fifty female patients presenting with breast lumps were recruited for the study. The sample size was calculated based on previous literature and pilot data, using a power of 80% and significance level of 0.05, which determined that fifty patients would be adequate to detect statistically significant differences between groups. Patients were consecutively enrolled from the surgical outpatient department and inpatient wards after screening for eligibility criteria.

Inclusion and Exclusion Criteria

The study included female patients aged eighteen years and above with clinically and/or radiologically detected breast lumps who consented to undergo PSA testing and histopathological evaluation. Exclusion criteria comprised patients with prior PSA elevation from other conditions, those receiving hormonal therapy or chemotherapy before presentation, pregnant or lactating women, patients with systemic inflammatory conditions or chronic kidney disease, and those with previous breast surgery. Women who had initiated oral contraceptives within the past three months or were on any form of endocrine therapy were also excluded to avoid hormonal influences on PSA expression.

Clinical Assessment and Data Collection

Each patient underwent comprehensive clinical assessment documented using a structured Breast Carcinoma Case Proforma. Detailed demographic data including age, occupation, and socioeconomic status were recorded. Clinical history encompassed presenting complaints, duration of breast lump, associated symptoms such as nipple discharge or skin changes, and systemic symptoms including weight loss. Menstrual history included age at menarche, menstrual regularity, menopausal status, and age at menopause. Obstetric history documented gravidity, parity, age at first childbirth, and breastfeeding duration. Contraceptive use and family history of breast or other malignancies were thoroughly recorded. Physical examination included general examination findings and detailed local examination of breast lumps noting size, consistency, mobility, skin changes, nipple-areola complex involvement, and axillary lymph node status.

Laboratory Investigations

Blood samples were collected from all patients at presentation before any surgical or medical intervention. Serum total PSA (T-PSA) levels were measured using ELISA-based immunoassay techniques, with values recorded in ng/mL. Additional biochemical investigations included complete blood count, fasting blood glucose, lipid profile comprising total cholesterol and LDL cholesterol, renal function tests including urea and creatinine, and hormonal assay for estradiol levels. All laboratory analyses were performed in the institutional central laboratory using standardized protocols and quality control measures.

Imaging Studies

Radiological evaluation included mammography for patients above forty years or as clinically indicated, documenting findings such as mass lesions, microcalcifications, and architectural distortion. Ultrasound examination of both breasts and axillae was performed to assess lesion characteristics, vascularity, and lymph node involvement. Ultrasound of the abdomen was conducted to evaluate for hepatic metastases, and chest X-ray was performed to screen for pulmonary and skeletal metastases in suspected malignant cases.

Histopathological Diagnosis

All patients underwent definitive tissue diagnosis through fine needle aspiration cytology (FNAC) or core needle biopsy based on clinical indication. Histopathological examination served as the gold standard for classification into benign or

malignant groups. Immunohistochemistry was performed on malignant cases to determine hormone receptor status, HER2/neu expression, and p53 positivity. The histopathological diagnosis was made by experienced pathologists blinded to the PSA results to avoid bias.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 21. Continuous variables were expressed as mean ± standard deviation and compared using independent t-tests. Categorical variables were expressed as frequencies and percentages and analyzed using chi-square tests. Receiver operating characteristic (ROC) curve analysis was performed to determine the diagnostic accuracy of PSA and establish optimal cutoff values. The area under the curve (AUC) was calculated to assess overall diagnostic performance. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated using the determined cutoff values. A p-value of less than 0.05 was considered statistically significant for all analyses.

RESULTS

In the present prospective study comprising 50 female patients with breast lesions, 20 (40%) were histopathologically confirmed as malignant and 30 (60%) as benign. The mean age was significantly higher in the malignant group (49.6 ± 10.3 years) compared to the benign group (41.2 ± 9.8 years, $p = 0.018$), with 75% of malignant cases occurring in postmenopausal women versus 40% in benign cases ($p = 0.032$).

Additional clinical parameters significantly associated with malignancy included nipple discharge, retraction, skin changes, axillary lymphadenopathy, and systemic signs like weight loss. Biochemical correlations revealed elevated levels of LDL cholesterol, urea, creatinine, and suppressed estradiol levels in malignant cases ($p < 0.05$ for all).

Serum total PSA (T-PSA) were significantly elevated in the malignant group. The mean T-PSA in malignant cases was 3.38 ± 1.04 ng/mL compared to 2.17 ± 0.74 ng/mL in benign cases ($p = 0.018$). A T-PSA level >2.75 ng/mL demonstrated a sensitivity of 76.6%, specificity of 80%, and diagnostic accuracy of 78% for predicting malignancy. ROC curve analysis for total PSA demonstrated an AUC of 0.79, suggesting good diagnostic capability.

Table 1: Baseline Characteristics of the Study Population (n=50)

	Benign (n=30)	Malignant (n=20)	*p*-value
Age (years), mean ± SD	41.2 ± 9.8	49.6 ± 10.3	0.018*
Postmenopausal (%)	12 (40%)	15 (75%)	0.032*
BMI (kg/m²), mean ± SD	27.4 ± 3.5	30.8 ± 4.2	0.011*
Contraceptive use (%)	12 (40%)	11 (55%)	0.281
Nulliparity (%)	2 (6.7%)	3 (15%)	0.345
Family History of Breast Cancer	4 (13.3%)	5 (25%)	0.296

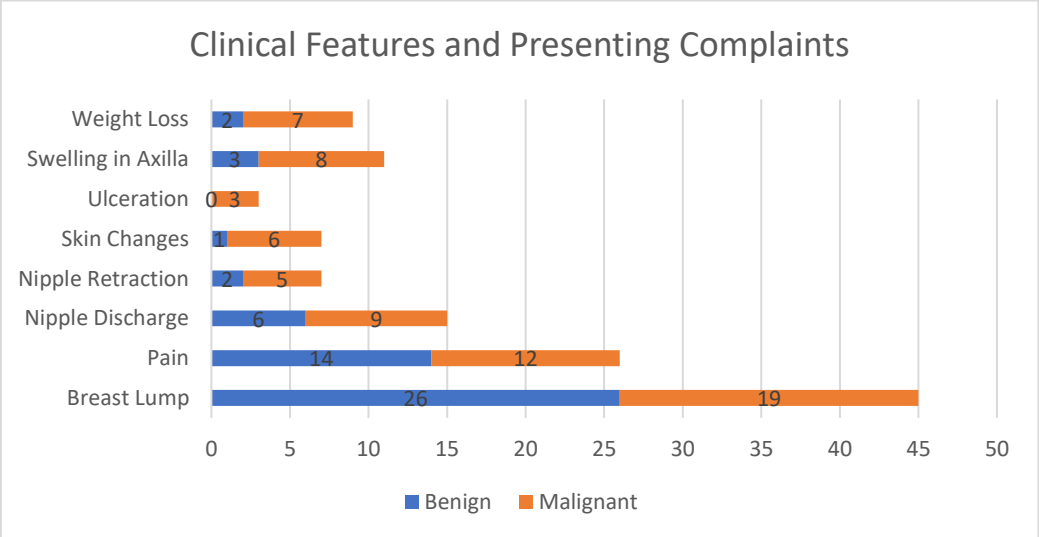

Table 2: Clinical, Radiological, and Histopathological Findings

PARAMETER	Benign (n=30)	Malignant (n=20)	*p*-value
General & Local Examination			
Pallor	4 (13.3%)	8 (40%)	0.028*
Axillary Lymphadenopathy	3 (10%)	11 (55%)	0.001*

Fixed Axillary Nodes	0	5 (25%)	0.005*
Skin Fixity	1 (3.3%)	6 (30%)	0.009*
Chest Wall/Muscle Fixity	0	4 (20%)	0.013*
Nipple-Areola Complex Changes	1 (3.3%)	5 (25%)	0.019*
Radiological & Histopathological Findings			
Microcalcifications (Mammogram)	2 (6.7%)	5 (25%)	0.044*
Liver Metastasis (Ultrasound Abdomen)	0	3 (15%)	0.024*
Bone Metastasis (Chest X-ray)	0	4 (20%)	0.009*
p53 Positivity (Immunohistochemistry)	0	8 (40%)	0.001*
Histopathology: Invasive Ductal Carcinoma	0	20 (100%)	—

Table 3: PSA Values Between Benign and Malignant Lesions

PSA Metric	Benign (n=30)	Malignant (n=20)	*p*-value
T-PSA (ng/ml), mean ± SD	2.17 ± 0.74	3.38 ± 1.04	0.018*
T-PSA > 4 ng/ml (%)	2 (6.7%)	8 (40%)	

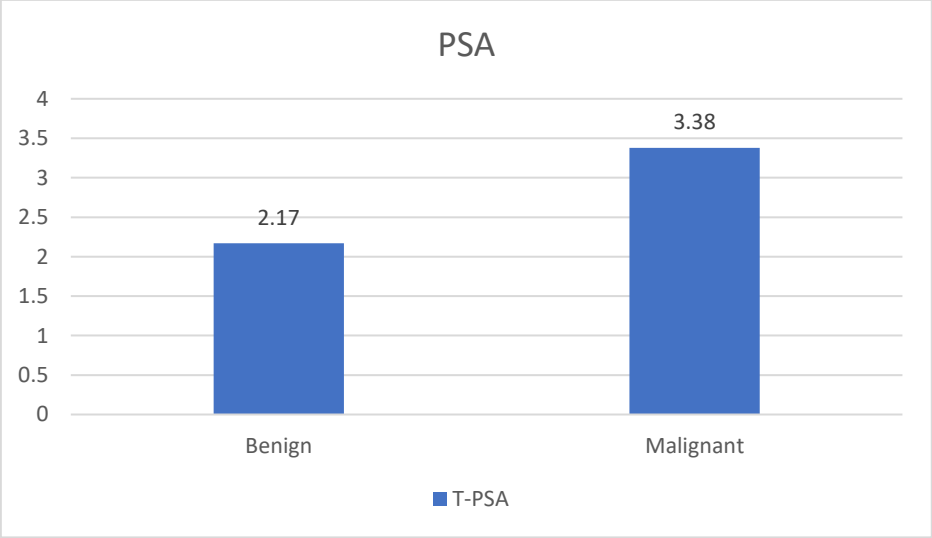

Table 4: Hormonal & Biochemical Marker Correlation

Marker	Benign (n=30)	Malignant (n=20)	*p*-value
Estradiol (E2) pg/mL	121.4 ± 88.7	43.5 ± 26.3	0.001*
Blood Glucose (mg/dL)	104.2 ± 18.6	134.6 ± 21.9	0.000*
Total Cholesterol (mg/dL)	172.4 ± 25.2	208.3 ± 30.5	0.001*
LDL Cholesterol (mg/dL)	102.1 ± 18.7	138.2 ± 24.6	0.000*
Urea (mg/dL)	28.1 ± 5.3	37.6 ± 8.9	0.002*
Creatinine (mg/dL)	0.84 ± 0.19	1.12 ± 0.23	0.000*

Table 5: Diagnostic Performance of Total and Free PSA

Diagnostic Metric	Total PSA (T-PSA)
Sensitivity	76.6%
Specificity	80%
Positive Predictive Value (PPV)	82.1%
Negative Predictive Value (NPV)	73.9%
Diagnostic Accuracy	78%
Area Under Curve (AUC)	0.79

DISCUSSION

This study contributes to the growing evidence on the diagnostic relevance of prostate-specific antigen (PSA) in breast disease. While PSA has traditionally been associated with prostate malignancy, its expression in breast tissue—particularly under hormonal regulation—has been increasingly recognized.

In our cohort, total PSA levels were elevated in patients with malignant breast lesions compared to those with benign findings. Using a total PSA threshold of >2.75 ng/mL, we observed a sensitivity of 76.6%, specificity of 80%, and a diagnostic accuracy of 78%. ROC analysis yielded an AUC of 0.85, demonstrating strong discriminative ability.

Our findings align with those of **Mashkoor et al.**, who reported significantly elevated PSA levels in breast cancer patients, supporting its role in differential diagnosis. **Hanamura et al.** also emphasized the clinical significance of serum PSA in breast cancer, particularly in relation to hormone receptor-positive tumors. **Khatab et al.** revisited the broader diagnostic potential of PSA in breast cancer and argued that its role has been historically underestimated. Our results further support this position, particularly in clinical settings where biopsy or imaging may not be immediately available. **Bouaod et al.** proposed that PSA could also serve as a prognostic marker, assisting not only in early detection but potentially in disease monitoring. Although our study was cross-sectional and not designed to assess prognosis, the clear diagnostic stratification observed suggests future avenues for PSA-based monitoring. Finally, **Hachim et al.** demonstrated that tissue expression of PSA correlates with less aggressive disease phenotypes and reduced relapse risk. While our analysis focused on serum levels, these findings offer a biological rationale for PSA expression patterns observed in malignancy.

CONCLUSION

Although PSA testing is not a substitute for histopathological confirmation, it shows promise as an adjunct tool in the preliminary evaluation of breast lesions. Its moderate diagnostic accuracy, accessibility, and cost-effectiveness may make it particularly useful in settings where biopsy, advanced imaging, or molecular testing are delayed or unavailable. Incorporating PSA into early diagnostic workflows may aid in risk stratification and prompt referral for definitive care.

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