EXPRESSION OF PSA (PROSTATE SPECIFIC ANTIGEN) IN BREAST LESIONS AT A TERTIARY CARE TEACHING HOSPITAL IN CHENGALPET DISTRICT

Dr. Jainab Zubetha. Z[1], Dr. Priyanka.P[2], Dr. Govindarajan.R[3], Dr. Revathishree. R[4]

[1]Junior Resident, Department of Pathology, Shri Sathya Sai Medical College & Research Institute, (Sri Balaji Vidyapeeth University (DU), Chennai campus), Ammapettai, Nellikuppam Post, Chengalpattu District, Tamilnadu, 603108, India , zainabzubetha@gmail.com

[2]Professor, Department of Pathology, Shri Sathya Sai Medical College & Research Institute, (Sri Balaji Vidyapeeth University (DU), Chennai campus), Ammapettai, Nellikuppam Post, Chengalpattu District Tamilnadu, 603108, India., PRIYANKA05.@GMAIL.COM

[3]Professor & Head, Department of Pathology, Shri Sathya Sai Medical College & Research Institute, (Sri Balaji Vidyapeeth University (DU), Chennai campus), Ammapettai, Nellikuppam Post, Chengalpattu District Tamilnadu, 603108, India gjhospital@yahoo.com

[4]Professor, Department of Pathology, Shri Sathya Sai Medical College & Research Institute, (Sri Balaji Vidyapeeth University (DU), Chennai campus), Ammapettai, Nellikuppam Post, Chengalpattu District Tamilnadu, 603108, India , mail2rrevathi@gmail.com

Abstract: Prostate-Specific Antigen (PSA) is a long-known biomarker of prostate disease but recent results indicate that it is also present in breast tissue and could be diagnostic and prognostic in breast tumors. The study compared the expression of PSA between benign and malignant lesions of the breast and its correlation with some clinicopathological parameters. A cross-sectional, observational, study was done on a total of 94 formalin-fixed, paraffin-embedded, breast tissue specimens of female patients in a tertiary care teaching hospital. A histopathologic analysis and the use of immunohistochemical staining of PSA were carried out. PSA expression was compared by grading based on the intensity of the stain, and the relationship with age, size of tumour, histological type, pathological stage and histological grade were compared using descriptive statistics, Spearman rank correlation and Chi-square test. The most common staining pattern was medium PSA expression (2+). Notable inverse linear relationships between the expression of PSA and the age of patients, the size of tumours, and the histology of tumours were observed. Increased PSA expression was found in fibroadenomas and most well differentiated invasive ductal carcinomas, whereas decreased or missing PSA expressions were found in malignant and poorly differentiated tumours. PSA expression and pathological stage were not alleviated by any statistically significant correlation. PSA expression had also shown considerable correlations with positive clinicopathological features and thus PSA could have been used in conjunction with immunohistochemical biomarkers as an auxiliary to differentiate benign and malignant breast lesions and tumour differentiation. It is proposed that larger multicentre studies are necessary to further provide proof of its diagnostic and prognostic value.

Keywords: Prostate-Specific Antigen (PSA); Breast Lesions; Immunohistochemistry; Breast Carcinoma; Biomarker.

I. INTRODUCTION

Breast lesions do form a wide range of benign and malignant disorders, which are one of the most prevalent pathological conditions in women all over the world. Although most of the breast masses are benign (e.g., fibroadenoma), breast carcinoma has been refuted as the most prevalent cancer-causing condition in women in

terms of morbidity and mortality [1]. Early detection and proper distinction between benign and malignant lesions of the breast are critical towards identifying the proper treatment plans to ensure that more patients have good outcomes. Traditional methods of diagnosis, such as histopathological analysis, and immunohistochemistry have significantly contributed to the improvement of the diagnosis, but the requirement to find other biomarkers capable of enhancing pragmatic IVC and managing patients in a personalized manner remains. Prostate specific antigen (PSA) or kallikrein-related peptidase 3 (KLK3) is traditionally considered to be a highly specific biomarker of prostate disease [2]. However, a growing body of research shows that PSA progressively is found to have an expression in a variety of non-prostate tissues, such as normal and neoplastic breast tissue. It seems to be controlled by steroid hormones like androgens and progesterone in its expression in the breast, indicating that it might have a role in breast tissue differentiation and can be involved in tumor biology. Past studies have indicated that an elevated or higher level of PSA expression is common in benign breast lesions and well-differentiated breast carcinomas, and lower levels are related to more aggressive tumor features [3]. The above observations suggest that PSA can have diagnostic and prognostic value in the pathology of the breast. Although there has been increasing interest in PSA as a biomarker of breast lesions, there has been a lack of thorough research on its clinical implications especially in the Indian population. Local literature is required since biological behaviour and biomarker expression can be different in response to genetic, environmental and lifestyle influences. In this regard, this study assesses the immunohistochemical findings of PSA in benign and malignant lesions of the breast diagnosed in a tertiary care teaching hospital within Chengalpet District and the correlation between the clinical-pathological measure. This study will help fill the evidence gap by exploring the connection between PSA expression and breast lesion properties to determine the possible application of PSA as a diagnostic and prognostic biomarker in breast pathology.

II. RELATED WORKS

Breast lesions are broad in spectrum of benign and malignant lesions and precise diagnostic and prognostic assessment is the key to successful treatment of a patient. Even though the traditional histopathological analysis is the gold standard in terms of diagnosing, more and more focus has been given to the immunohistochemical biomarkers which can enhance diagnostic accuracy and offer prognostic data. One of such biomarkers is prostate-specific antigen (PSA) which as a traditionally specific biomarker of the prostate tissue has turned out to be a potential biological behaviour belonging to breast lesions. The varied ways of expressing PSA in breast tissue and its clinical implications have been studied with references to its potential use in tumour differentiation and prognosis. The biochemical properties of PSA were initially determined by experiments indicating that PSA acts as a serine protease with a chymotrypsin-like enzyme activity. Akiyama et al. [15] established the enzymatic activity of human PSA and the biological activity of the same, and laid the groundwork to other investigations that have been conducted on its expression in other tissues other than prostate tissue. This finding prompted scientists to analyze the PSA in other glands that are responsive to hormones such as the breast.

Lai et al. [16] further supported the evidence available that indicated the expression of PSA in breast tissue by finding that the expression of PSA existed in breast cyst fluid and that the synthesis of this protein could be regulated by hormone levels. They found that the expression of PSA depends on steroid hormones, specifically the androgens and progesterone and suggested that PSA could contribute to hormone-dependent breast diseases. This observation provided a biological foundation towards assessing PSA as a biomarker that could be used in breast pathology. Later clinical studies were done to determine the correlation between the PSA expression and clinicopathological features of breast carcinoma. Mohammadizadeh et al. [17] indicated that invasive breast carcinoma had PSA expression and also showed that PSA correlates with favourable pathological features significantly. In their study it was proposed that better differentiated tumours have a higher PSA expression but poorly differentiated carcinoma have lower expression. This evidence lent strength to the hypothesis that PSA could be a marker of tumour differentiation and biological behaviour.

It is more recently that Bouaod et al. [18] conducted an extensive literature review of the prognostic value of PSA in breast cancer and came to the conclusion that PSA expression is often linked with desirable clinical outcomes. The authors emphasized that PSA-positive tumours tend to have a lower histological grade, smaller tumour size, and a better prognosis as compared to PSA-negative lesions. They postulated that PSA can be used as an adjunctive biomarker that can guide clinicians in the risk-stratification and treatment-planning. Besides the expression of tissue, personnel have examined the PSA levels in the circadian of individuals with breast cancer. Giai et al. [19] measured the serum PSA levels and revealed that female breast cancer patients had detectable PSA levels. Despite the fact that serum PSA was not found to be useful in diagnostics over expression compared to tissue immunohistochemistry, the study validated the idea that PSA production is not restricted to prostate tissue and that it may have a larger biological role in breast disease.

Normal breast physiology and structure is also important to understand PSA expression. Classical anatomic and histologic sources define the breast as a hormonally sensitive system with epithelial and stromal components

that changes continuously in terms of morphology during the course of life [20,21]. Then, the texts on diagnostic pathology also underline that interpretation of immunohistochemical markers should never be performed without conventional histopathology as there is a need to gain a precise diagnosis [22]. Menstrual changes also may affect biomarker expression due to physiological changes that happen during the menstrual cycle. Other researches have shown periodic changes in the histology of the breast [23], the expression of epidermal growth factor receptor [24], the expression of anti-apoptotic proteins including Bcl-2 [25]. Moreover, Guinebretiere et al. [26] further highlighted that differentiating normal physiological changes and pathological changes are basic in the types of breast pathology. Altogether, these studies present a solid scientific groundwork to examine the PSA expression as a candidate diagnostic and prognostic biomarker of both benign and malignant lesions of the breast.

III. METHODOLOGY

3.1 Study Design

The current research adopted an observational cross-sectional study design with the aim of assessing the Prostate-Specific Antigen (PSA) expression in breast lesions as well as establishing its relationship with various clinicopathological parameters. The cross sectional design was deemed suitable owing to the fact that it allowed the ID of PSA expression in archived breast tissue samples which were obtained within a specified time frame with no form of intervention and follow up [4]. In the study the aim of establishing the patterns of PSA immunohistochemical expression in benign and malignant breast lesions and the association of this expression with patient age, tumour size, histological type, pathological stage and tumour grade were undertaken. Routinely processed formalin-fixed, paraffin-embedded (FFPE) tissue blocks that were present in the Department of Pathology were used, and thus minimized the exposure of patients to risks but permitted full histopathological examination [5].

3.2 Study Setting

The study was carried out, in the mechanisms of the Department of Pathology, Shri Sathya Sai Medical College and Research Institute, Chengalpet District, Tamil Nadu, within the diversity of the Histopathology and Immunohistochemistry laboratory. The facility is a teaching tertiary care hospital which receives a significant number of breast biopsy and surgical specimens in a year. Such an environment allowed the opportunity to see a variety of benign and malignant lesions of the breast available to immunohistochemical testing. The analysis was conducted in a period of 18 months whereby the archived breast tissue specimens that had been diagnosed between July 2024 and January 2026 were retrieved in the department records and evaluated in detail [6].

3.3 Study Population and Sample Size

The research sample involved patients with breast lesions visiting the study center and diagnosed with this condition and subjected to MISP or perioperative lipectomy. The benign and malignant lesions were considered to enable a comparison of the PSA expression in various pathological conditions.

The estimation of the sample size was made on an already realized study where there was a prevalence of Grade I and Grade II breast tumours of 44.4%. The minimum sample size was estimated using the formula $n = 4pq/l^2$ as about 82 participants. Doing this with an allowance of 10 percent of non-response or unusable specimens brought the necessary sample size to about 90 cases. In the end, sufficient 94 tissue samples of the breast were available, and should be referred to during the final analysis which is more than the minimum requirement calculated and enhances the statistical dependability of the final results [7].

Table 1. Study Population Characteristics

Variable	Description
Study design	Observational cross-sectional study
Study centre	Department of Pathology, Shri Sathya Sai Medical College and Research Institute
Study period	18 months (July 2024–January 2026)

Study population	Female patients with breast lesions
Final sample size	94 breast tissue specimens
Tissue type	Formalin-fixed paraffin-embedded (FFPE) tissue blocks

3.4 Eligibility Criteria

All age groups of females who have been diagnosed by histological confirmation of breast lesions were included. The specimens used in the study comprised of biopsy and mastectomy of both benign lesions like fibroadenoma and fibrocystic disease and malignant lesions like ductal carcinoma in situ (DCIS), invasive ductal carcinoma (IDC), lobular carcinoma in situ (LCIS), and invasive lobular carcinoma (ILC).

Patients receiving neoadjuvant chemotherapy prior to surgery were not included since they might change tumour morphology and biomarker expression with the treatment. Participation was also not allowed in male breast lesions, pregnant women and patients who had not been willing and/or could not be asked to give an informed consent. These criteria provided consistency in the study population but also minimized other confounding factors that could affect the expressing of PSA [8].

3.5 Data Collection Procedure

Demographic and clinical data were taken directly through a pathology report, and the hospital records supplied the relevant data. Data taken was patient age, clinical presentation, tumour size, pathological diagnosis, tumour subtype and lymph node status, pathological stage and tumour grade. Additional reproductive history, family history of breast cancer as well as radiological investigations available e.g. mammography, breast ultrasonography, and computed tomography were reviewed where suitable [9].

FFPE tissue blocks of eligible breast lesions were located by means of unique histopathology numbers archived. All specimens were previously fixed in 10% neutral buffered formalin followed by standard tissue processing and paraffin embedding procedures that are standard to the department. Microscopic examination and immunohistochemical analysis were performed on representative tissue sections taken out of each block.

3.6 Histopathological Examination

With a rotary microtome, paraffin blocks were cut in 4 0m slices. Hematoxylin and Eosin (H&E) staining of tissue sections were carried out according to regular laboratory protocols. All the slides were examined using the light microscopy under the eyes of experienced pathologists to confirm the histopathological diagnosis and categorize lesions as benign or malignant before immunohistochemical staining was done. Routine pathological examinations were used to grade invasive breast cancers in a histological manner whereas pathological staging was identified by use of the TNM classification system [10]. These histopathological results acted as reference standard in assessing the associations between tumour characteristics and the PSA expression.

3.7 Immunohistochemical Analysis

Additional 4mm sections of paraffin blocks were immunohistochemically stained with the antibodies of Prostate-Specific Antigen (PSA). Normal immunohistochemical procedures were used during the entire process of specimen preparation, antigen recovery, antibody use, visualization and microscopic examination.

PSA expression was measured in epithelial tumour cells, mainly using cytoplasmic and cytoplasmic-membranous staining patterns. The intensity of staining was scored on a four-point ordinal scale that included 0 + (negative), 1 + (weak), 2 + (moderate), and 3 + (strong) staining. The percentage of positively stained cells was also estimated and a composite score of both staining intensity and the percentage of positive tumour cells was computed [11]. The consistency and quality control of the assessment process was guaranteed by independent microscopic evaluation.

Table 2. Variables and Statistical Analysis

Variable	Measurement	Statistical Method

Age	Years	Mean ± SD, Spearman correlation
Tumour size	Centimetres	Mean ± SD, Spearman correlation
Histological type	Benign/Malignant	Frequency (%), Chi-square test
Histological grade	Grade I–III	Spearman correlation
Pathological stage	TNM Stage	Spearman correlation
PSA expression	0+, 1+, 2+, 3+	Frequency (%), Correlation analysis

3.8 Outcome Variables

The main outcome measure was PSA immunohistochemical expression whose data were categorized into four levels of staining intensity. Patient age, tumour size, histological type, tumour grade, pathological stage and lymph node status were the secondary outcome variables. These variables were chosen since there was some evidence in the past that these might indicate a relationship with PSA expression and breast tumour behaviour [12]. The study sought to find out the significant difference in expressed PSA between benign and malignant lesions and the increasing moderate or decreasing moderate expressions and the shared prognostic indicators.

3.9 Statistical Analysis

All the data collected were imported to Microsoft Excel after which they were transferred to Statistical Package of the Social Sciences (SPSS) Version 16.0 in order to be analyzed. The data on demographic and clinicopathological features was summarized by descriptive statistics. The presentation of continuous variables (age and tumour size) was in the form of mean potential standard deviation and the presentation of categorical variables was in the form of frequencies and percentages.

As the change in PSA expression was an ordinal variable and that the normality was not met the Spearman rank correlation coefficient was used to test the relationships between PSA expression and the continuous or ordinal variables including age, tumour size, tumour grade, and pathological stage [13]. The Chi-square test was used to analyze associations between PSA expression and histological type. The p-value of less than 0.05 was considered the statistical significance, and two-tailed tests were used during the analysis.

3.10 Ethical Considerations

The study was approved by the Institute Ethics Committee in terms of ethics prior to the start of the study. The research was conducted in accordance with principles of research formulated in the Indian Council of Medical Research (ICMR) National Ethical Guidelines to Biomedical Research and Health Research Involving Human participants (2018). The participants who provided informed consent had to do it in writing and then they could gain access to clinical information [14].

Patient confidentiality was ensured through the use of unique identification for the different patients and also by excluding the personal identifiers in the analysis of the data. Only the research team had access to medical records, and the electronic data were secured by the use of password-protected systems [27]. Because the research involved the use of archived tissue samples without any other invasive measures, there was a low risk to the respondents yet the study conformed to the expected ethical standards of conducting biomedical research.

IV. RESULTS AND ANALYSIS

4.1 Overview of the Study Population

The study incorporates 94 female patients with the diagnosis of breast lesions. It involved both benign and malignant lesions of the breast to study the immunohistochemical expression of Prostate-Specific Antigen (PSA) which then correlates with the clinicopathological traits. The participants of the study were mostly of age, with a mean of 33.65 ± 10.04 years, which implies that breast lesions had an impact on the women at a relatively large age range. The mean tumour size was 4.36 ± 1.06 cm and this indicator indicated that the majority of the lesions

could be detected at the time of presentation [28]. These baselines features served to offer a suitable model to assess the relationship between PSA expression and pathological observations.

Table 1. Demographic and Clinical Characteristics of the Study Population (n = 94)

Variable	Value
Total participants	94
Mean age (years)	33.65 ± 10.04
Mean tumour size (cm)	4.36 ± 1.06
Study population	Female patients
Breast lesions analysed	Benign and malignant

4.2 Histopathological Characteristics

The histopathological analysis showed that the most common breast lesion was fibroadenoma with 66 cases (70.2) and invasive ductal carcinoma (IDC), 28 cases (29.8). The high rates are due to the dominance of fibroadenoma because of the increased number of benign lesions experienced in the normal pathological practice.

Within the 28 cases of invasive ductal carcinoma, Grade II tumours were the most prevalent with 57.1 per cent of the malignant lesions. The proportion of Grade III tumours were 25.0, and Grade I lesions were 17.9. This frequency suggests that moderately differentiated carcinomas were more often than well-differentiated tumours or poorly differentiated tumours [29].

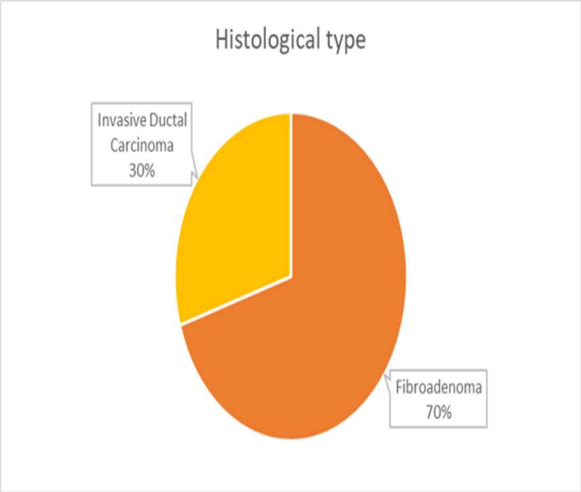

Figure 1: “Distribution of histological types among the study participants”

Staging showed that Stage IIA was the most typical stage of disease at diagnosis with 53.6% of invasive ductal carcinoma cases. Stage IIB was 21.4, Stage IIIA (17.9), and Stage IIIB (7.1). The fact that the majority of the disease was of Stage II implies that a lot of patients had presented with localised disease before it advanced to higher stages.

Table 2. Histopathological Characteristics

Characteristic	Frequency	Percentage (%)

Histological Type		
Fibroadenoma	66	70.2
Invasive ductal carcinoma	28	29.8
Histological Grade (IDC only)		
Grade I	5	17.9
Grade II	16	57.1
Grade III	7	25.0
Pathological Stage (IDC only)		
Stage IIA	15	53.6
Stage IIB	6	21.4
Stage IIIA	5	17.9
Stage IIIB	2	7.1

4.3 Distribution of PSA Immunohistochemical Expression

Immunohistochemistry analysis revealed that there was a variation in PSA levels in the examined breast lesions. The most common staining intensity was moderate (2+) found in 35 cases (37.2%). There were 21 patients (22.3) with strong PSA expression (3+), 19 with negative (0+) staining and 19 with weakly positive (1+) staining.

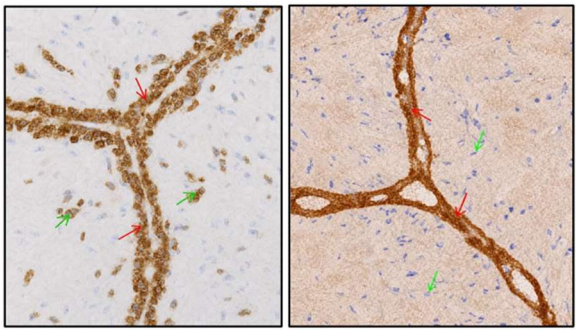

Figure 2: Immunohistochemical marker PSA showing strong cytoplasmic positive staining in Fibroadenoma (DAB, 40X).

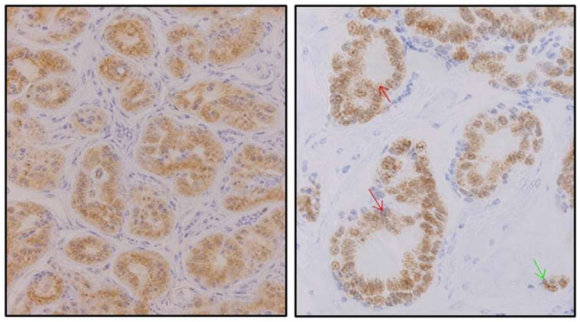

Figure 3: Immunohistochemical marker PSA showing moderate cytoplasmic positive staining in fibroadenoma with pericanalicular pattern (DAB, 10X and 40X respectively).

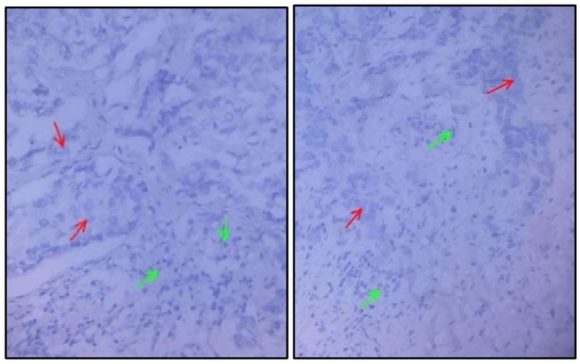

Figure 4: Immunohistochemical marker PSA showing negative staining in Invasive ductal carcinoma, NOS (Grade 3) (DAB, 10X).

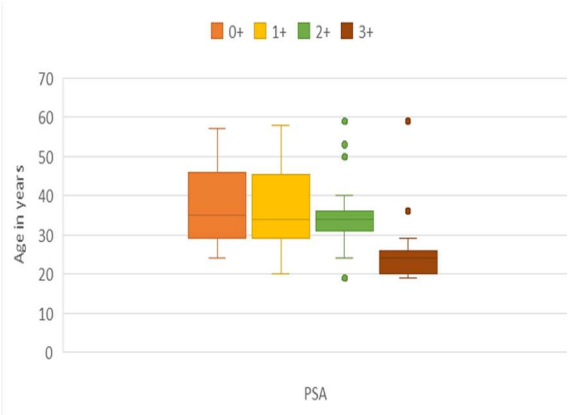

Figure 5: "Relationship between PSA expression and age"

All in all, about 80 percent lesions of the breast showed evidence of some level of PSA positivity and it is evidence of the fact that PSA expression is relatively high in the tissues of the breast. Nonetheless, the degree of expression differed significantly in individual lesions, indicating differences in biological behaviour across breast pathologies. This variability was taken as the foundation of the further correlation analyses with age, tumour size, histological type, the pathological stage, and tumour grade [30].

Table 3. Distribution of PSA Expression

PSA Expression	Frequency	Percentage (%)
0+ (Negative)	19	20.2

1+ (Weak)	19	20.2
2+ (Moderate)	35	37.2
3+ (Strong)	21	22.3
Total	**94**	**100.0**

4.4 Association Between PSA Expression and Clinicopathological Parameters

The association between PSA expression and the age of the patient was assessed by the use of the Spearman rank correlation analysis. The inverse relationship was statistically significant ($\rho = -0.428$, $p < 0.001$) meaning that an increased PSA expression was related to younger patients. Ages gradually dropped with growing PSA positivity, whereby the average age of PSA-negative cases was 37.11 years and that of cases with strong expression (3+) was 25.43 years. These would indicate that higher levels of PSA are commoner in younger women who present with breast lesions.

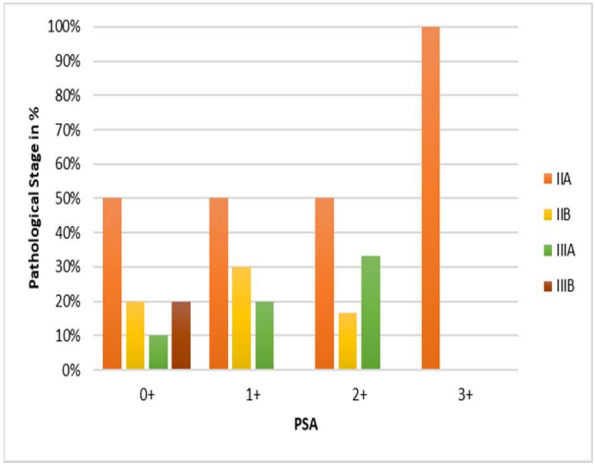

Figure 6: "PSA expression across pathological stages"

The same negative correlation was noted between PSA and Tumour size. The result of the statistical analysis indicated significant negative correlation (= 0.332, p = 0.001) and the decrease in tumour size was due to increasing intensity of PSA staining. The mean tumour size in PSA-negative lesions was the largest (4.96 + 1.15 cm) and the strong positive lesions were the smallest in average size (3.86 + 0.90 cm). This direction shows that higher PSA levels correlate with smaller breast lesions indicating that there is a relationship between low PSA positivity and lower tumour aggressiveness.

Table 4. Correlation Between PSA Expression, Age and Tumour Size

Variable	Statistical Test	Correlation (ρ)	p-value	Interpretation
Age	Spearman's correlation	-0.428	<0.001	Significant inverse association
Tumour size	Spearman's correlation	-0.332	0.001	Significant inverse association

4.5 Association Between PSA Expression and Histopathological Variables

The level of PSA expression by histological type revealed a statistically significant correlation (2 = 16.280, p = 0.001). The decreased PSA expression (0 + and 1 +) was more common in invasive ductal carcinoma and moderate and high PSA positivity (2 + and 3 +) were more common in fibroadenoma. Over nine tenths of all

lesions that expressed high levels of PSA were benign fibroadenomas, which contributes to the possible utility of PSA as an immunohistochemical detection of benign versus malignant breast lesions. The PSA expression was not statistically significantly associated with the pathological stage among invasive ductal carcinoma cases (0.151, p = 0.444). The distribution of PSA staining across the entire spectrum of tumour stages did not reveal any pattern, suggesting that pathological stage alone does not seem to have any impact on PSA expression of invasive breast carcinoma.

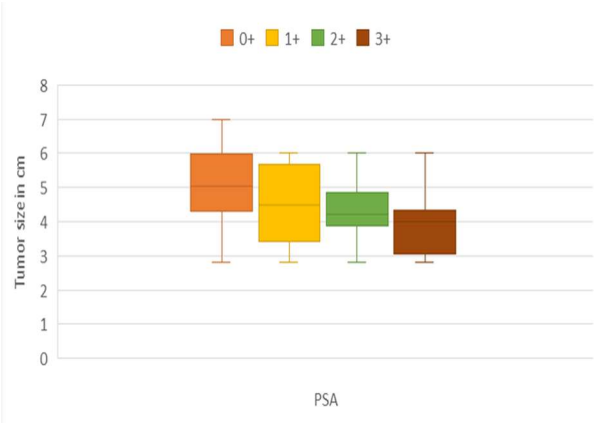

Figure 7: "PSA expression in relation to tumor size"

On the other hand, PSA expression had a strong negative correlation with histological grade (rho = -0.560, p = 0.002). The tumours with a PSA-negative phenotype were mainly Grade III lesions, with only Grade I and Grade II carcinomas displaying strong PSA expression. The Grade III tumours are not found in strongly positive cases, which implies that increased PSA expression correlates with improved tumour differentiation and witnessing less aggressive biological characteristics. These results support the possible prognostic value of PSA in breast carcinoma as they suggest that a decreasing expression level is correlated with the rising histologic severity.

Table 5. Summary of Associations Between PSA Expression and Clinicopathological Parameters

Variable	Statistical Test	Result	p-value	Interpretation
Age	Spearman's correlation	$\rho = -0.428$	<0.001	Significant inverse association
Tumour size	Spearman's correlation	$\rho = -0.332$	0.001	Significant inverse association
Histological type	Chi-square	$\chi^2 = 16.280$	0.001	Significant association
Pathological stage	Spearman's correlation	$\rho = -0.151$	0.444	No significant association
Histological grade	Spearman's correlation	$\rho = -0.560$	0.002	Significant inverse association

4.6 Overall Interpretation of Findings

The results statistically show that, PSA expression in various lesions in the breast is heterogeneous and correlates with a variety of good clinicopathological factors. The increase of PSA was also found to be constant in younger patients, smaller tumours and benign histological lesions and low grade invasion carcinomas. In contrast, lower or no PSA expression could be more often detected in tumours that were malign- or poorly differentiated. The relationships with tumour grade and histological type observed regardless of pathological stage, though not significantly so, indicated that PSA can be a useful adjunctive biomarker immunohistochemically in breast pathology. Taken together, the findings suggest that PSA expression holds potential diagnostic/prognostic biomarker by helping to differentiate between benign and malignant breast lesions and revealing tumour differentiation.

V. CONCLUSION

The current research determined the expression of Prostate-Specific Antigen (PSA), an immunohistochemical manufacturer, in benign and malignant lesions of the breast as well as the connection of this expression with the chosen clinicopathological features. The results revealed that a large percentage of breast lesions expressed PSA and moderate and high expression was mainly found in benign fibroadenomas and well-differentiated invasive ductal cancers. On the other hand, the lack or low level of PSA expression was more commonly attributed to malign lesions with high histological grades. Statistical manipulation also showed that PSA expression had significant negative correlations with the patient age, tumour size and histological grade, which shows that the higher the PSA expression, the better it is in terms of pathological characteristics. Nonetheless, there was no significant correlation mechanism between PSA expression and pathological stage. These results indicate that PSA could be clinically useful as an adjunctive immunohistochemical stain to discriminate benign and malignant lesions in the breast and evaluate differentiation of tumours. PSA cannot substitute the known diagnostic and prognostic biomarkers; however, it can be used to complement the information about tumour biology and disease behaviour because of its expression pattern. On the whole, the paper illustrates the possible prognostics value of PSA as a supplementary biomarker tool in breast pathology and demonstrates the necessity of larger multicentre studies and a variety of patient groups and prolonged follow-up to further confirm its diagnostic, prognostic, and possible treatment value in breast cancer management.

REFERENCE

[1] Goldhirsch A, Wood W, Gelber R, Coates A, Thürlimann B, Senn HJ, et al. Progress and promise: highlights of the international expert consensus on the primary therapy of early breast cancer 2007. Annals of oncology. 2007; 18 (7): 1133 –44.

[2] Diamandis EP. Prostate-specific antigen: its usefulness in clinical medicine. Trends in Endocrinology & Metabolism. 1998; 9(8): 310 – 6. Yousef GM, Diamandis EP. The new human tissue kallikrein gene family: structure, function, and association to disease. Endocrine reviews. 2001; 22 (2):184 – 204 .

[3] Yu H, Diamandis EP, Levesque M, Giai M, Roagna R, Ponzone R, et al. Prostate specific antigen in breast cancer, benign breast disease and normal breast tissue. Breast cancer research and treatment. 1996; 40 (2):171 – 8.

[4] Yu H, Giai M, Diamandis EP, Katsaros D, Sutherland DJ, Levesque MA, et al. Prostate-specific antigen is a new favorable prognostic indicator for women with breast cancer. Cancer research. 1995; 55(10):2104 –10.

[5] Diamandis EP, Yu H. Nonprostatic sources of prostate -specific antigen. Urologic Clinics of North America. 1997;24(2):275 –82.

[6] Sarkar S, Mandal M. Breast cancer: classification based on molecular etiology influencing prognosis and prediction. Breast Cancer-Focusing Tumor Microenvironment, Stem cells and Metastasis. 2011.

[7] Mannello F, Gazzanelli G. Prostate-specific antigen (PSA/ hK3): a further player in the field of breast cancer diagnostics? Breast Cancer Research. 2001; 3(4):238.

[8] Narița D, Anghel A, Motoc M. Prostate- specific antigen may serve as a pathological predictor in breast cancer. R om J Morphol Embryol. 2008; 49 (2):173 – 80.

[9] Killian CS, Corral DA, Kawinski E, Constantine R. Mitogenic response of osteoblast cells to prostate-specific antigen suggests an activation of latent TGF-β and a proteolytic modulation of cell adhesion receptor s. Biochemical and biophysical research communications. 1993; 192(2):940 – 7.

[10] Cleutjens KB, van der Korput HA, van Eekelen CC, van Rooij HC, Faber PW, Trapman J. An androgen response element in a far upstream enhancer region is essential for high, androgen-regulated activity of the prostate-specific antigen promoter. Molecular endocrinology. 1997;11(2):148 –61.

[11] Webber MM, Waghray A, Bello D. Prostate -specific antigen, a serine protease, facilitates human prostate cancer cell invasion. Clinical cancer research: an official journal of the American Association for Cancer Research. 1995; 1(10):1089 – 94.
[12] Bodey B, Bodey Jr B, Kaiser H. Immunocytochemical detection of prostate specific antigen expression in human breast carcinoma cells. Anticancer research. 1997;17(4 A): 2577 –81.
[13] Foekens J, Diamandis E, Yu H, Look M, Gelder M, Van Putten W, et al. Expression of prostate-specific antigen (PSA) correlates with poor response to tamoxifen therapy in recurrent breast cancer. British journal of cancer. 1999;79 (5): 888–94.
[14] American Cancer Society. Breast Cancer Facts & Figures 2005 -2006 [Internet]. Atlanta, GA: American Cancer Society; 2005 [cited 2023 Aug 10]. Report No. Available from: https://www. cancer.org/ content/dam/ cancer-org/research/ cancer- facts-and-statistics/breast-cancer- facts-and-figures/breast- cancer- facts-and-figures-2005 -2006. pdf
[15] Akiyama K, Nakamura T, Iwanaga S, Hara M. The chymotrypsin -like activity of human prostate-specific antigen, γ-seminoprotein. FEBS letters. 1987;225(1 – 2):168– 72.
[16] Lai LC, Erbas H, Lennard TW, Peaston RT. Prostate-specific antigen in breast cyst fluid: Possible role of prostate- specific antigen in hormone-dependent breast cancer. International journal of cancer. 1996; 66(6): 743 – 6.
[17] Mohammadizadeh F, Ranaee M, Zavareh MHT, Faghihi M, Saremi M, Eftekhari M. The expression of prostate -specific antigen in invasive breast carcinoma and its relationship with routine clinicopathologic parameters. Advanced Biomedical Research. 2012;1(1):55.
[18] Bouaod W, Zakoko AM, Asif H, Hussain A, Malik N, Ray SD, et al. The potentiality of prostate-specific antigen as a prognostic biomarker in breast cancer. Cureus. 2023; 15(9).
[19] Giai M, Yu H, Roagna R, Ponzone R, Katsaros D, Levesque M, et al. Prostate-specific antigen in serum of women with breast cancer. British journal of cancer. 1995;72 (3): 728 –31
[20] Marieb EN, Brady PM, Mallatt JB. Human Anatomy, Global Edition. Pearson Education; 2016.
[21] Bobrysheva I, Kashchenko S. Histology, Cytology, Embryology: Textbook. Knowledge, Lugansk. 2011 .
[22] Lester SC, Hicks DG. Diagnostic pathology: breast, e -book: diagnostic pathology: breast, E Book. Elsevier Health Sciences; 2021.
[23] Vogel PM, Georgiade N, Fetter B, Vogel F, McCarty Jr K. The correlation of histologic changes in the human breast with the menstrual cycle. The American journal of pathology. 1981;104(1):23.
[24] Gompel A, Martin A, Simon P, Schöevaert D, Plu -Bureau G, Hugol D, et al. Epidermal growth factor receptor and c - erb B- 2 expression in normal breast tissue during the menstrual cycle. Breast cancer research and treatment. 1996;38 (2):227 –35.
[25] Sabourin J, Martin A, Baruch J, Truc J, Gompel A, Poitout P. bcl-2 expression in normal breast tissue during the menstrual cycle. International journal of cancer. 1994;59(1):1 –6.
[26] Guinebretière J, Menet E, Tardivon A, Cherel P, Vanel D. Normal and pathological breast, the histological basis. European journal of radiology. 2005; 54 (1):6 –14 .
[27] Walker R, Martin C. The aged breast. The Journal of Pathology: A Journal of the Pathological Society of Great Britain and Ireland. 2007; 211(2):232 – 40.
[28] Javed A, Lteif A. Development of the human breast. In: Vol. 27. Thieme Medical Publishers; 2013 . P. 005 –12.
[29] Hughes E. The development of the mammary gland: Arris and Gale Lecture, delivered at the Royal College of Surgeons of England on 25 th October, 1949 . Annals of the Royal College of Surgeons of England. 1950; 6(2):99 .
[30] Watson J, Sainsbury J, Dixon J. ABC of Breast Diseases Breast Reconstruction After Surgery. BMJ. 1995; 3(10): 117.
[31] Jolicoeur F. Intrauterine breast development and the mammary myoepithelial l ineage. Journal of mammary gland biology and neoplasia. 2005; 10 (3):199 – 210 .
[32] Sternlicht MD. Key stages in mammary gland development: the cues that regulate ductal branching morphogene sis. Breast Cancer Research. 2005; 8(1):201.
[33] Naccarato AG, Viacava P, Vignati S, Fanelli G, Bonadio AG, Montruccoli G, et al. Bio-morphological events in the development of the human female mammary gland from fetal age to puberty. Virchows Archiv. 2000; 436 (5): 431 –8.