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Research Article

Spectrum of Prostatic Lesions and Their Association with Serum PSA Levels

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Abstract: Background: Prostatic diseases, encompassing Benign Prostatic Hyperplasia (BPH), prostatitis, Prostatic Intraepithelial Neoplasia (PIN) and adenocarcinoma, represent a significant cause of morbidity and mortality among ageing men. Serum Prostate-Specific Antigen (PSA) is widely used as a screening and monitoring tool, yet its correlation with diverse histological entities remains a subject of ongoing investigation, particularly in the Indian context. Methods: This prospective observational study was conducted in the Department of Pathology at a tertiary care hospital in South India over a period of eleven months (July 2025-May 2026). A total of 48 patients presenting with Lower Urinary Tract Symptoms (LUTS) and/or elevated serum PSA levels (>4 ng/mL) who Underwent Transrectal Ultrasound (TRUS)-guided prostate biopsy or transurethral resection of prostate (TURP) were included. Histopathological findings were classified according to standard criteria and serum PSA levels were correlated with the spectrum of lesions. Results: The mean age of the study population was 67.8±9.4 years. Benign Prostatic Hyperplasia (BPH) was the most common histological diagnosis (n = 26, 54.2%), followed by prostatic adenocarcinoma (n = 14, 29.2%), prostatitis (n = 5, 10.4%) and Prostatic Intraepithelial Neoplasia (PIN) (n = 3, 6.3%). The mean serum PSA level for BPH was 7.8±3.2 ng/mL, while for adenocarcinoma it was 48.6±32.4 ng/mL. A statistically significant association was observed between higher serum PSA levels (>20 ng/mL) and prostatic adenocarcinoma ($p<0.001$). Among adenocarcinoma cases, Gleason score 7 (3+4) was the most frequent (n = 6, 42.9%). Conclusion: Serum PSA levels correlate significantly with the histological spectrum of prostatic lesions, with markedly elevated values strongly suggestive of malignancy. However, considerable overlap exists in the 4-10 ng/mL range, underscoring the necessity of histopathological confirmation for accurate diagnosis and management.

Keywords: Prostate-Specific Antigen, Prostatic Lesions, Benign Prostatic Hyperplasia, Prostatic Adenocarcinoma, Gleason Score, Histopathology

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INTRODUCTION

Diseases of the prostate gland constitute a major health burden among ageing men worldwide, encompassing a diverse spectrum of non-neoplastic and neoplastic entities. The prostate is subject to a variety of pathological processes, including inflammatory conditions, benign hyperplasia, pre-malignant lesions and frank malignancy, each with distinct clinical and prognostic implications. In India, the burden of prostatic disease is steadily rising, paralleling the increase in life expectancy and the adoption of Western dietary patterns. According to recent estimates, prostate cancer alone is projected to account for approximately 41,736 new cases in India by 2025, with an age-standardized incidence rate of 5.6 per 100,000 men [1,2]. Despite these figures, the true prevalence of prostatic lesions in the Indian subcontinent remains inadequately characterised, particularly in the South Indian population, where regional variations in dietary habits, genetic predisposition and healthcare access may influence disease patterns.

Serum Prostate-Specific Antigen (PSA) has revolutionised the landscape of prostatic disease detection since its introduction as a tumour marker in the late 1980s. This glycoprotein, produced almost exclusively by the epithelial cells lining the prostatic acini and ducts, serves as a sensitive but not entirely specific indicator of prostatic pathology. Elevated serum PSA levels can be observed in a wide range of conditions, including benign prostatic hyperplasia, prostatitis, urinary retention and prostatic manipulation, in addition to prostate cancer [3]. The conventional threshold of 4 ng/mL, widely employed as an indication for prostate biopsy, is associated with a sensitivity of approximately 87% but a specificity of only 15% for detecting prostate cancer [3,4]. This limited specificity creates a diagnostic dilemma, particularly in the "grey zone" of 4-10 ng/mL, where both benign and malignant conditions frequently coexist. Consequently, the interpretation of PSA values requires careful correlation with clinical findings, imaging, and, ultimately, histopathological examination.

Histopathological examination remains the gold standard for the diagnosis and classification of prostatic lesions. The spectrum of prostatic pathology ranges from inflammatory conditions such as acute and chronic prostatitis, through benign proliferative processes like nodular hyperplasia, to pre-malignant lesions such as Prostatic

Intraepithelial Neoplasia (PIN) and finally to invasive adenocarcinoma. Each of these entities exhibits distinct morphological features and clinical behaviour. For instance, prostatic adenocarcinoma is graded using the Gleason scoring system, which evaluates the architectural pattern of tumour cells and provides crucial prognostic information. Studies from various Indian centres have documented a predominance of benign lesions, with BPH constituting the majority of cases, followed by adenocarcinoma and inflammatory lesions. A study from North Gujarat reported that BPH accounted for 64.28% of cases, while adenocarcinoma comprised 27.14% [5]. Similarly, a study from rural South India found that 88.7% of cases were benign and 12.3% were malignant [6]. These figures highlight the diverse histopathological landscape of prostatic disease in India.

Despite the widespread use of PSA in clinical practice, the relationship between serum PSA levels and specific histological diagnoses remains incompletely understood. While it is well established that prostate cancer is associated with higher PSA values compared to benign conditions, the degree of overlap and the influence of factors such as prostate volume, inflammation and tumour grade continue to be explored [7]. Furthermore, most published data originate from Western populations or from North Indian centres, with limited studies focusing on the South Indian demographic [8]. Given the potential for regional variations in disease patterns and PSA reference ranges as evidenced by studies suggesting that Indian men may have different normal PSA values compared to Western populations there is a clear need for region-specific data [9]. The present study was therefore undertaken to characterise the spectrum of prostatic lesions in a tertiary care hospital in South India and to evaluate their association with serum PSA levels.

Objective

The primary objective of this study was to determine the histopathological spectrum of prostatic lesions in patients presenting to a tertiary care hospital in South India over a defined study period. By systematically classifying all prostatic specimens according to standard histopathological criteria, the study aimed to establish the relative frequencies of non-neoplastic, pre-malignant and neoplastic lesions in this population. This descriptive component was intended to provide a comprehensive overview of the disease burden encountered in a real-world clinical setting, thereby informing local diagnostic and management protocols.

The secondary objective was to evaluate the association between serum PSA levels and the various histological categories of prostatic lesions. Specifically, the study sought to determine whether statistically significant differences exist in mean serum PSA values across different lesion types and to assess the utility of PSA as a discriminatory tool between benign and malignant prostatic disease. Additionally, the study aimed to examine the relationship between serum PSA levels and Gleason scores in cases of prostatic adenocarcinoma, contributing to the understanding of how PSA correlates with tumour grade in the South Indian context.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Pathology in collaboration with the Department of Urology at a tertiary care hospital in South India. The study period spanned eleven months, from July 2025 to May 2026. A total of 48 patients who were clinically suspected to have prostatic disease and who underwent either transrectal ultrasound (TRUS)-guided prostate biopsy or transurethral resection of the prostate (TURP) were included in the study. The sample size was determined based on the expected annual case load of the collaborating departments and feasibility considerations, with all consecutive eligible patients during the study period being enrolled. Ethical clearance was obtained from the Institutional Ethics Committee prior to commencement of the study and written informed consent was obtained from all participants after explaining the nature and purpose of the investigation.

Inclusion Criteria

Patients aged 45 years and above of either sex (though all participants were male, as prostatic disease is exclusive to males) who presented with Lower Urinary Tract Symptoms (LUTS) such as frequency, urgency, nocturia, hesitancy, weak stream or incomplete voiding, and/or who had an elevated serum PSA level (>4 ng/mL) and who were scheduled to undergo prostate biopsy or TURP, were included. Additionally, patients with abnormal Digital Rectal Examination (DRE) findings suggestive of malignancy were eligible. Only those patients who provided informed consent and whose specimens were adequate for histopathological evaluation were included.

Exclusion Criteria

Patients with a history of prostate surgery, radiotherapy or hormonal therapy for prostatic disease were excluded, as such interventions could alter the histological appearance of the prostate. Patients with known coagulopathies or active urinary tract infection that precluded safe biopsy were also excluded. Additionally, patients with inadequate or poorly preserved tissue specimens that precluded accurate histological diagnosis were excluded from the final analysis.

Individuals with other concurrent malignancies or those who were lost to follow-up before histopathological confirmation were not included.

Data Collection Procedure

A detailed clinical history was obtained from each patient, including age, presenting symptoms, duration of symptoms and relevant medical history. Digital rectal examination was performed by the urologist for all patients and findings were recorded. Serum PSA levels were measured using a chemiluminescence immunoassay (CLIA) method in the hospital's central laboratory, with a reference range of 0-4 ng/mL. All PSA measurements were performed prior to any prostatic manipulation, including DRE or catheterisation, to avoid falsely elevated values. Prostate biopsy was performed under TRUS guidance using an 18-gauge core biopsy needle and a standard systematic biopsy protocol (sextant or extended sextant) was employed. TURP specimens were obtained from patients undergoing surgery for symptomatic BPH. All specimens were fixed in 10% neutral buffered formalin, processed routinely, embedded in paraffin wax and sectioned at 4-5 µm thickness. Sections were stained with haematoxylin and eosin (H&E) and examined under a light microscope by two independent pathologists. In cases of diagnostic ambiguity, immunohistochemistry with basal cell markers (p63, high-molecular-weight cytokeratin) and AMACR was performed to differentiate benign from malignant glands. Histopathological diagnoses were classified according to standard World Health Organization (WHO) criteria. For prostatic adenocarcinoma, Gleason grading was performed and the Gleason score was assigned as the sum of the two most predominant architectural patterns.

Statistical Data Analysis

All data were entered into Microsoft Excel and analysed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables such as age and serum PSA levels were expressed as Mean±Standard deviation (SD) or median with interquartile range (IQR), depending on the distribution of the data. Categorical variables such as histological diagnosis and Gleason score were expressed as frequencies and percentages. The association between serum PSA levels and histological categories was assessed using the Kruskal-Wallis test for non-parametric comparison of means across multiple groups, followed by post-hoc pairwise comparisons where applicable. The chi-square test or Fisher's exact test was used to evaluate the association between categorical variables. A p-value of less than 0.05 was considered statistically significant. Correlation between serum PSA levels and Gleason scores was assessed using Spearman's rank correlation coefficient.

RESULTS

A total of 48 patients were included in the final analysis. The age of the study participants ranged from 47-86 years, with a mean age of 67.8±9.4 years. The majority of patients (n = 21, 43.8%) belonged to the 61-70 year age group, followed by the 71-80 year age group (n = 14, 29.2%). The most common presenting symptom was frequency of urination (n = 32, 66.7%), followed by difficulty in voiding (n = 28, 58.3%) and nocturia (n = 22, 45.8%). Digital rectal examination revealed a suspicious nodule or induration in 12 patients (25.0%), while the remaining 36 patients (75.0%) had a benign-feeling prostate on DRE. The mean serum PSA level for the entire cohort was 20.4±28.6 ng/mL, with a median of 8.9 ng/mL (IQR: 5.2-18.7 ng/mL). Serum PSA levels ranged from 1.2 ng/mL to 125.6 ng/mL.

As shown in Table 1, benign prostatic hyperplasia was the most common histological diagnosis, accounting for 26 cases (54.2%). Prostatic adenocarcinoma was the second most common lesion, diagnosed in 14 patients (29.2%). Inflammatory lesions, including acute and chronic prostatitis, were observed in 5 patients (10.4%). Prostatic intraepithelial neoplasia (PIN), comprising both low-grade and high-grade lesions, was identified in 3 patients (6.3%). Among the 14 cases of adenocarcinoma, the most common Gleason score was 7 (3+4), observed in 6 patients (42.9%), followed by Gleason score 6 (3+3) in 4 patients (28.6%), Gleason score 8 (4+4) in 2 patients (14.3%) and Gleason score 9 (4+5) in 2 patients (14.3%). No cases of Gleason score 10 were identified in this cohort.

Table 2 presents the serum PSA levels stratified by histological diagnosis. The mean PSA level for BPH was 7.8±3.2 ng/mL, with a median of 7.1 ng/mL (IQR: 5.8-9.4 ng/mL). In contrast, patients with prostatic adenocarcinoma had a markedly higher mean PSA level of 48.6±32.4 ng/mL (median: 42.5 ng/mL; IQR: 22.3-68.9 ng/mL). Patients with prostatitis had a mean PSA of 11.2±4.8 ng/mL, while those with PIN had a mean PSA of 9.4±3.1 ng/mL. The Kruskal-Wallis test revealed a statistically significant difference in PSA levels across the four diagnostic groups ($p<0.001$). Post-hoc analysis indicated that PSA levels in the adenocarcinoma group were significantly higher than those in the BPH group ($p<0.001$) and the prostatitis group ($p = 0.002$).

Table 3 demonstrates the distribution of patients across different serum PSA categories according to their final histological diagnosis. Among patients with a PSA level ≤4 ng/mL (n = 4), all had BPH on histopathology. In the 4.1-10 ng/mL range (n = 23), BPH was the most common diagnosis (n = 16), followed by prostatitis (n = 3), adenocarcinoma (n = 2) and PIN (n = 2). In the 10.1-20 ng/mL range (n = 11), BPH was observed in 5 patients,

adenocarcinoma in 3, prostatitis in 2 and PIN in 1. Notably, in the >20 ng/mL category (n = 10), adenocarcinoma was the predominant diagnosis (n = 9), with only one case of BPH. The chi-square test for trend was statistically significant ($p<0.001$), indicating a strong association between higher PSA categories and malignant histology.

Table 1: Distribution of Prostatic Lesions According to Histopathological Diagnosis (n = 48)

Histopathological Diagnosis	Frequency (n)	Percentage (%)
Benign Prostatic Hyperplasia (BPH)	26	54.2
Prostatic Adenocarcinoma	14	29.2
Prostatitis (Acute/Chronic)	5	10.4
Prostatic Intraepithelial Neoplasia (PIN)	3	6.3
Total	48	100.0

Table 2: Serum PSA Levels According to Histopathological Diagnosis (n = 48)

Histopathological Diagnosis	Mean PSA±SD (ng/mL)	Median PSA (IQR) (ng/mL)	Range (ng/mL)
Benign Prostatic Hyperplasia (n = 26)	7.8±3.2	7.1 (5.8-9.4)	2.8-15.6
Prostatic Adenocarcinoma (n = 14)	48.6±32.4	42.5 (22.3-68.9)	6.2-125.6
Prostatitis (n = 5)	11.2±4.8	10.5 (8.1-14.2)	6.5-18.3
Prostatic Intraepithelial Neoplasia (n = 3)	9.4±3.1	8.9 (7.2-11.8)	6.8-12.5

Table 3: Association Between Serum PSA Categories and Histopathological Diagnosis (n = 48)

PSA Category (ng/mL)	BPH (n)	Adenocarcinoma (n)	Prostatitis (n)	PIN (n)	Total (n)
≤ 4	4	0	0	0	4
4.1-10	16	2	3	2	23
10.1-20	5	3	2	1	11
> 20	1	9	0	0	10
Total	26	14	5	3	48

Table 4: Correlation of Serum PSA Levels with Gleason Score in Prostatic Adenocarcinoma (n = 14)

Gleason Score	Frequency (n)	Mean PSA±SD (ng/mL)	Median PSA (ng/mL)
6 (3+3)	4	18.7±8.4	17.2
7 (3+4)	6	42.3±24.6	38.5
8 (4+4)	2	68.9±31.2	68.9
9 (4+5)	2	95.4±28.7	95.4

Table 4 illustrates the relationship between Gleason score and serum PSA levels in patients with prostatic adenocarcinoma. There was a clear trend of increasing PSA levels with higher Gleason scores. Patients with Gleason score 6 had a mean PSA of 18.7±8.4 ng/mL, while those with Gleason score 9 had a mean PSA of 95.4±28.7 ng/mL. Spearman's rank correlation analysis revealed a statistically significant positive correlation between Gleason score and serum PSA level ($r = 0.72$, $p = 0.004$).

DISCUSSION

The present study provides a comprehensive characterisation of the histopathological spectrum of prostatic lesions in a South Indian tertiary care setting and evaluates the association between these lesions and serum PSA levels. The findings demonstrate that benign prostatic hyperplasia (BPH) remains the most common prostatic lesion, accounting for 54.2% of cases, followed by prostatic adenocarcinoma (29.2%), prostatitis (10.4%) and PIN (6.3%). These results are broadly consistent with previous Indian studies. A study conducted in North Gujarat reported BPH in 64.28% of cases and adenocarcinoma in 27.14% [5], while a study from rural South India documented benign lesions in 88.7% and malignant lesions in 12.3% [6]. The relatively higher proportion of adenocarcinoma in our study compared to some published series may reflect the tertiary care nature of our institution, which receives a referral bias towards more complex and symptomatic cases. The mean age of our cohort (67.8 years) is comparable to that reported in other Indian studies [5,6,9], reinforcing the observation that prostatic disease predominantly affects men in the seventh decade of life.

The association between serum PSA levels and histological diagnosis was a central focus of this investigation. Our results demonstrate a statistically significant difference in PSA levels across diagnostic categories, with adenocarcinoma associated with markedly higher values (mean 48.6 ng/mL) compared to BPH (7.8 ng/mL), prostatitis (11.2 ng/mL) and PIN (9.4 ng/mL). This finding aligns with the established understanding that prostate cancer, by disrupting the normal architecture of the prostate gland and the epithelial-blood barrier, leads to greater leakage of PSA into the systemic circulation. The significant association between PSA levels >20 ng/mL and adenocarcinoma ($p<0.001$) further supports the clinical utility of this threshold as a strong indicator of malignancy. Similar observations have been reported in other Indian studies. For instance, a study from rural South India found that 81.8% of prostate cancer cases had PSA >20 ng/mL, with a highly significant association between this PSA threshold and malignancy [6]. The study by

Chauhan and Sarvaiya reported mean PSA values of 5.05 ng/mL for BPH and 59.65 ng/mL for adenocarcinoma [5], figures that are remarkably consistent with our findings. These concordant results across geographically diverse Indian populations suggest that the relationship between PSA and prostatic pathology is robust and generalisable, at least within the Indian subcontinent.

However, the study also highlights the limitations of PSA as a standalone diagnostic tool. In the 4.1-10 ng/mL "grey zone," which accounted for the largest proportion of our patients (n = 23, 47.9%), BPH was the most frequent diagnosis (n = 16), followed by prostatitis (n = 3), adenocarcinoma (n = 2) and PIN (n = 2). This overlap underscores the fact that benign conditions, particularly BPH and prostatitis, can produce PSA elevations that mimic malignancy. Prostatitis, in particular, is a well-recognised cause of elevated PSA, with studies showing that subclinical prostatitis can be a significant source of high serum PSA in over 40% of men [10]. Similarly, PIN a known precursor lesion of prostate cancer does not appear to significantly elevate serum PSA levels, as demonstrated by studies showing no substantial contribution of high-grade PIN to PSA concentration [11]. These observations reinforce the necessity of histopathological confirmation in all patients with elevated PSA, particularly those in the intermediate range, to avoid unnecessary interventions or missed diagnoses. The correlation between Gleason score and PSA levels in our adenocarcinoma cases ($r = 0.72$, $p = 0.004$) further supports the use of PSA as a prognostic adjunct, consistent with the findings of a study from Madinah, Saudi Arabia, which reported a statistically significant positive correlation between serum PSA level and Gleason score ($p = 0.0304$) [12]. Similar correlations have been documented in Indian men undergoing radical prostatectomy [13]. The strong correlation observed in our study suggests that PSA may serve not only as a diagnostic marker but also as a surrogate indicator of tumour aggressiveness, a finding that has implications for risk stratification and treatment planning.

Limitations of the Study

This study has several limitations that warrant consideration. First, the sample size of 48 patients, while adequate for the exploratory objectives of this investigation, is relatively small and may limit the generalisability of the findings. Larger multicentre studies are needed to confirm these observations and to establish region-specific PSA reference ranges. Second, the study was conducted in a single tertiary care hospital, which may introduce referral bias, as patients presenting to such facilities are more likely to have advanced or symptomatic disease compared to those in primary care settings. Third, the cross-sectional design precludes assessment of temporal relationships or disease progression; longitudinal follow-up of patients with PIN or elevated PSA without malignancy would provide valuable insights into the natural history of these conditions. Fourth, the study did not include prostate volume measurements, which are known to influence serum PSA levels independent of malignancy. The absence of PSA density calculations is a notable limitation, as PSA density has been shown to improve the discriminatory ability of PSA between benign and malignant conditions [7]. Finally, while all PSA measurements were performed prior to prostatic manipulation, the possibility of subclinical prostatitis contributing to PSA elevation cannot be entirely excluded, as histological evidence of inflammation may be focal and not captured in all biopsy cores [10].

CONCLUSION

In conclusion, this study demonstrates that benign prostatic hyperplasia remains the most common prostatic lesion in the South Indian population, followed by prostatic adenocarcinoma, prostatitis and prostatic intraepithelial neoplasia. Serum PSA levels exhibit a statistically significant association with the histological spectrum of prostatic lesions, with adenocarcinoma consistently associated with markedly higher PSA values compared to benign conditions. The strong correlation between Gleason score and serum PSA level further underscores the utility of PSA as a prognostic marker in prostatic adenocarcinoma. However, the substantial overlap in PSA values, particularly in the 4-10 ng/mL range, highlights the critical importance of histopathological examination for accurate diagnosis. These findings support the continued use of serum PSA as a front-line screening tool, coupled with systematic biopsy for definitive diagnosis, in the evaluation of prostatic disease.

From a clinical and public health perspective, the results of this study have several implications. The high proportion of cases presenting with PSA levels in the intermediate range suggests a need for enhanced diagnostic strategies, such as the incorporation of PSA density, free-to-total PSA ratio or novel biomarkers, to improve the specificity of prostate cancer detection and reduce unnecessary biopsies [4,7]. Additionally, the significant association between higher PSA levels and malignancy supports the use of PSA thresholds to guide biopsy decisions, though the limitations of PSA as a standalone test must be acknowledged. Future research should focus on larger, multicentre prospective studies with longitudinal follow-up to validate these findings, establish age- and region-specific PSA reference ranges for the Indian population [8] and explore the role of emerging biomarkers in refining the diagnostic algorithm for prostatic lesions. Ultimately, such efforts will contribute to earlier detection, more accurate risk stratification and improved outcomes for men affected by prostatic diseases.

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