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Original Research Article

CORRELATION OF SERUM PSA LEVELS WITH GLEASON GRADING AND PERINEURAL INVASION IN PROSTATE CARCINOMA

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ABSTRACT

Background: Prostate carcinoma is a malignant neoplasm arising from the epithelial cells of the prostate gland, predominantly affecting older men. Serum prostate-specific antigen (PSA) serves as an important biochemical marker for screening and monitoring, while histopathological parameters such as the Gleason grade and perineural invasion (PNI) are key prognostic indicators. Understanding the correlation between these factors aids in predicting tumor aggressiveness and optimizing patient management, particularly in the Indian setting where prostate cancer incidence is steadily increasing. The aim is to evaluate the correlation between serum PSA levels, Gleason grading, and perineural invasion in cases of histologically confirmed prostate carcinoma.

Materials and Methods: This prospective study was conducted at a tertiary care center in India and included 62 patients with biopsy-proven prostate adenocarcinoma. Serum PSA levels were estimated using an enzyme-linked immunosorbent assay (ELISA). Histopathological evaluation was performed on hematoxylin and eosin–stained sections to determine Gleason score and assess for perineural invasion. Statistical analysis was conducted to determine the correlation between PSA, Gleason grade, and PNI, with $p < 0.05$ considered significant.

Results: The majority of patients (35.5%) had PSA > 50 ng/mL, and 51.6% showed high Gleason scores (8–10). Perineural invasion was observed in 54.8% of cases. A strong positive correlation was found between serum PSA and Gleason score ($r = +0.72$, $p < 0.001$). PSA > 20 ng/mL predicted high Gleason grade (≥ 7) with a sensitivity of 84.6%, specificity of 80%, and accuracy of 83.9%. For predicting PNI, the same cutoff showed sensitivity 84.9%, specificity 60.7%, and accuracy 74.2%.

Conclusion: Serum PSA levels show a significant positive correlation with both Gleason grade and perineural invasion, underscoring their combined value in assessing tumor aggressiveness. PSA > 20 ng/mL is a reliable threshold for identifying high-grade prostate carcinoma and PNI, though histopathological examination remains the gold standard for definitive diagnosis and prognostication.

Keywords: Prostate carcinoma, PSA, Gleason grading, Perineural invasion, Correlation, Prognosis.

INTRODUCTION

Prostate carcinoma is a malignancy arising from the epithelial cells of the prostate gland, typically seen in older men. Clinically, it may present with urinary symptoms (such as hesitancy, frequency, nocturia), or may be asymptomatic and only detected via screening tests such as the Prostate-specific antigen

(PSA). Histopathologic assessment (for example via the Gleason grade/Gleason score) and features such as perineural invasion are important prognostic markers.[1,2] With increasing life expectancy, changing lifestyle and dietary habits, as well as greater diagnostic awareness, prostate carcinoma represents a growing challenge in India.[3,4]

In India, the reported incidence of prostate cancer has historically been lower than that in Western countries, but data show a clear increasing trend. A review reported that the estimated age-adjusted incidence rate (AAR) of prostate cancer in the country as a whole was about 3.7 per 100,000 persons (from data around 2008) — though with considerable regional variation.[5] More recent data from 28 population-based cancer registries (PBCRs) for the period 2012–2016 found that in urban registries the AAR ranged as high as ~11.8 per 100,000 in Delhi, 10.9 per 100,000 in Kamrup Urban (Assam), and ~9.7 per 100,000 in Mumbai.[6] It has been estimated that prostate cancer accounted for 6.1% of all male cancer incidence in India in recent years.[7]

Projections suggest that new cases will continue to rise sharply: one study reported that current annual numbers (~33,000–42,000 new cases) may double to around ~71,000 per year by 2040 in India.[8] There is also a marked difference between urban and rural incidence rates, likely reflecting differing access to diagnosis, screening, lifestyle differences and registry coverage.[9,10]

Given the increasing incidence and the observed trend towards diagnosis at more advanced stages in India, understanding biomarkers (such as PSA) and their correlation with histopathological prognostic features (Gleason grading, perineural invasion) becomes particularly important in the Indian context. The local epidemiology emphasises the need for enhanced early detection and appropriate prognostication of prostate carcinoma in India.

MATERIALS AND METHODS

This prospective study was conducted in the Department of Pathology and Biochemistry at a tertiary care center in India over a defined study period. A total of 62 patients clinically and radiologically suspected of having carcinoma of the prostate and subsequently confirmed on histopathological examination were included in the study.

Inclusion Criteria

Patients with histologically confirmed adenocarcinoma of the prostate.

Patients for whom serum PSA levels were available prior to biopsy or surgical intervention.

Exclusion Criteria

Patients who had received prior hormonal therapy, radiotherapy, or chemotherapy for prostate malignancy.

Patients with incomplete clinical or laboratory data.

Sample Collection and Processing

Blood samples were collected from all patients prior to any treatment, and serum PSA levels were estimated using an enzyme-linked immunosorbent assay (ELISA) method following standard protocol.

Prostatic tissue samples obtained through transrectal ultrasound-guided core biopsy, transurethral resection of the prostate (TURP), or radical prostatectomy were fixed in 10% neutral buffered formalin, processed routinely, and embedded in paraffin. Sections of 4–5 µm thickness were stained with hematoxylin and eosin (H&E) for histopathological evaluation.

Histopathological Examination

Each case was examined for:

Histological type (based on WHO classification)

Gleason grading and scoring, according to the International Society of Urological Pathology (ISUP) 2014 modified Gleason system.

Presence or absence of perineural invasion (PNI) in tumor sections.

Statistical Analysis

The relationship between serum PSA levels, Gleason score, and perineural invasion was analyzed using standard statistical methods. Correlation between PSA and Gleason score was assessed using the Pearson correlation coefficient, and association between categorical variables (e.g., PSA category vs. PNI) was tested using the Chi-square test. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 62 histopathologically confirmed cases of prostate adenocarcinoma were included in this study. The findings were analyzed in relation to serum PSA levels, Gleason grading, and perineural invasion.

Table 1: Distribution of patients according to serum PSA levels

Serum PSA level (ng/mL)	Number of patients (n = 62)	Percentage (%)
< 10	8	12.9
10 – 20	14	22.6
20 – 50	18	29
> 50	22	35.5

Most patients (35.5%) presented with serum PSA levels above 50 ng/mL, indicating late detection and advanced disease presentation in the study population.

Table 2: Distribution of cases according to Gleason score

Gleason score	Number of patients	Percentage (%)
≤ 6 (Well-differentiated)	10	16.1
7 (Moderately differentiated)	20	32.3
8–10 (Poorly differentiated)	32	51.6

More than half of the patients (51.6%) showed a high Gleason score (8–10), reflecting predominance of poorly differentiated carcinomas in this cohort.

Table 3. Correlation between serum PSA level and Gleason score

Serum PSA (ng/mL)	≤ 6	7	8–10	Total
< 10	6	2	0	8
10 – 20	3	9	2	14
20 – 50	1	6	11	18
> 50	0	3	19	22
Total	10	20	32	62

A strong positive correlation was observed between serum PSA levels and Gleason score ($r = +0.72$, $p < 0.001$), suggesting that higher PSA values were associated with higher-grade tumors.

Table 4: Association between perineural invasion and serum PSA level

Serum PSA (ng/mL)	PNI Present	PNI Absent	Total
< 10	1	7	8
10 – 20	4	10	14
20 – 50	11	7	18
> 50	18	4	22
Total	34 (54.8%)	28 (45.2%)	62

Perineural invasion was present in 54.8% of cases and showed a significant association with higher PSA levels ($p < 0.05$).

Table 5. Correlation between Gleason score and perineural invasion

Gleason score	PNI Present	PNI Absent	Total
≤ 6	2	8	10
7	8	12	20
8–10	24	8	32

A statistically significant association was found between high Gleason score and presence of perineural invasion ($p < 0.01$), indicating that poorly differentiated tumors were more likely to show PNI.

-PSA > 20 ng/mL is considered high (test positive). Gleason score ≥ 7 or PNI present is considered disease positive (clinically significant carcinoma).

Table 6: Diagnostic validity of the tests

PSA (>20 ng/mL)	Gleason ≥7 (Positive)	Gleason ≤6 (Negative)	Total
Positive (≥20)	44	2	46
Negative (≤20)	8	8	16
Total	52	10	62

Sensitivity - 84.6%
Specificity- 80.0%
Positive predictive value- 95.7%
Negative predictive value- 50.0%
Accuracy- 83.9%
Serum PSA >20 ng/mL showed high sensitivity (84.6%) and specificity (80%) for predicting high-grade (Gleason ≥7) carcinoma. The high PPV (95.7%) indicates that most patients with high PSA truly had aggressive disease. However, the lower NPV (50%) suggests that a low PSA does not completely rule out malignancy, emphasizing the need for histopathological confirmation.

Table 7: calculations for PSA vs PNI presence.

PSA (>20 ng/mL)	PNI Present	PNI Absent	Total
Positive (>20)	29	11	40
Negative (≤20)	5	17	22
Total	34	28	62

Sensitivity -84.9%
Specificity -60.7%
Positive Predictive Value- 72.5%
Negative Predictive Value- 77.3%
Accuracy- 74.2%
A PSA > 20 ng/mL showed high sensitivity (84.9%) but moderate specificity (60.7%) for predicting perineural invasion.
The PPV (72.5%) and NPV (77.3%) indicate that elevated PSA levels moderately predict PNI presence, though histopathological confirmation remains essential. Overall accuracy (74.2%) demonstrates a fair diagnostic performance of PSA in anticipating PNI.

DISCUSSION

Prostate carcinoma is one of the most common malignancies affecting men worldwide, and its incidence in India is rising steadily, particularly in

urban areas. Accurate assessment of disease aggressiveness is crucial for appropriate management. In this study, we evaluated the correlation of serum PSA levels with Gleason grading and perineural invasion (PNI) in 62 histologically confirmed cases of prostate adenocarcinoma.

In our study, the majority of patients (35.5%) presented with serum PSA levels >50 ng/mL, and over half (51.6%) had a high Gleason score (8–10), suggesting late-stage disease at presentation. A strong positive correlation ($r = +0.72$, $p < 0.001$) was found between serum PSA levels and Gleason score, indicating that PSA increases with tumor dedifferentiation. These findings are consistent with those of Bostwick et al. (1998), who demonstrated that higher PSA levels are significantly associated with poorly differentiated adenocarcinomas. Similarly, Thompson et al,[11] in the New England Journal of Medicine reported that PSA levels correlate positively with tumor volume and grade, serving as an independent prognostic marker. Shah et al,[12] in their Indian cohort also found that patients with PSA > 20 ng/mL were more likely to have Gleason score ≥ 7.Our results agree with Dey et al. 13who observed a significant linear relationship between serum PSA and Gleason score in a study of 80 Indian patients. They suggested that PSA reflects tumor aggressiveness and can serve as a guide for biopsy targeting and prognosis prediction.

Perineural invasion is recognized as an adverse prognostic feature, associated with higher rates of extracapsular extension and biochemical recurrence. In our study, PNI was observed in 54.8% of cases, with a clear association between higher PSA values and PNI positivity ($p < 0.05$). Patients with PSA > 20 ng/mL demonstrated an 84.9% sensitivity and 60.7% specificity for predicting PNI, indicating PSA's moderate predictive value for tumor aggressiveness. These observations are in concordance with Samaratunga et al,[14] and Mete et al,[15] who reported that PNI correlates with both serum PSA and Gleason grade, representing a marker of biological aggressiveness. Egevad et al,[16] also showed that the presence of PNI is more frequent in tumors with higher Gleason scores and elevated PSA levels, emphasizing its role as a histopathological indicator of poor prognosis.

We observed a significant association between high Gleason score (≥8) and presence of PNI ($p < 0.01$). This finding parallels that of Nguyen et al,[17] who found that PNI was present in 68% of patients with Gleason ≥8. Kumar et al,[18] in an Indian study also demonstrated that PNI positivity was more frequent in high-grade tumors, concluding that PNI could serve as an adjunct prognostic parameter.

Using a PSA cutoff of 20 ng/mL to predict high-grade carcinoma (Gleason ≥ 7), our study demonstrated Sensitivity of 84.6%, Specificity of 80.0%, PPV of 95.7% and Accuracy of 83.9%. These diagnostic indices closely resemble those reported by Shah et al,[12] confirming PSA's high sensitivity in detecting clinically significant carcinoma. However, its lower NPV (50%) indicates that low PSA does not entirely rule out aggressive disease, as noted by Thompson et al.[11]

Indian literature, including studies by Mandal et al,[19] and Ramanathan et al,[20] has shown that most patients present with PSA levels >20 ng/mL and high Gleason scores. These studies, along with our findings, emphasize the delay in diagnosis and lack of early screening in India, underscoring the need for greater awareness and regular PSA monitoring in high-risk populations.

CONCLUSION

Our study demonstrates that serum PSA levels correlate significantly with both Gleason grading and perineural invasion, validating its role as a reliable biomarker for assessing tumor aggressiveness. PSA > 20 ng/mL shows high sensitivity for detecting high-grade prostate carcinoma and PNI, supporting its continued use as a valuable screening and prognostic tool. However, PSA alone cannot replace histopathological evaluation, which remains the gold standard for diagnosis and grading.

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