

Association of Serum Prostate-Specific Antigen Levels with Gleason Grade Groups in Prostatic Adenocarcinoma

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DOI: <https://doi.org/10.5281/zenodo.21943565>

Article Received: 20 July 2026, Accepted: 05 August 2026, Online First: 15 August 2026

ABSTRACT

Background: Prostatic adenocarcinoma is a common malignancy in elderly men. Serum prostate-specific antigen (PSA) is widely used in the clinical evaluation of prostatic disease, while Gleason grading and International Society of Urological Pathology (ISUP) Grade Groups provide histological assessment of tumour aggressiveness. Correlating serum PSA with Grade Group may aid clinicopathological risk stratification. **Objective:** To evaluate the association between pre-treatment serum PSA levels and Gleason Grade Groups in patients aged more than 70 years with histologically confirmed prostatic adenocarcinoma. **Materials and Methods:** A hospital-based observational cross-sectional study was conducted at Mata Chanan Devi Hospital, Janakpuri, New Delhi, over three months from January to March 2026. Sixty consecutive histologically confirmed cases of acinar adenocarcinoma of the prostate in patients aged >70 years were included. Clinical symptoms, pre-treatment serum total PSA, Gleason score and ISUP Grade Group were recorded. Differences in PSA across Grade Groups were assessed and Spearman rank correlation was used to evaluate the relationship between PSA and Grade Group. **Results:** The mean age was 76.9 ± 4.2 years (range 71–89 years). Increased urinary frequency was the commonest symptom (81.7%), followed by nocturia (76.7%), urgency (68.3%), poor urinary stream (61.7%), hesitancy (55.0%) and dysuria (46.7%). Grade Groups 1–5 comprised 7 (11.7%), 11 (18.3%), 14 (23.3%), 15 (25.0%) and 13 (21.7%) cases, respectively. Median PSA increased progressively from 10.6 ng/mL in Grade Group 1 to 79.2 ng/mL in Grade Group 5. Serum PSA showed a strong positive correlation with increasing Grade Group (Spearman $\rho=0.66$, $p<0.001$). **Conclusion:** Serum PSA levels increased significantly with increasing Gleason Grade Group. Markedly elevated PSA values were concentrated in Grade Groups 4 and 5. PSA is useful as a complementary marker but should be interpreted with histopathological grade rather than used independently.

Keywords: Prostatic adenocarcinoma; prostate-specific antigen; PSA; Gleason score; ISUP Grade Group; histopathology; prostate cancer.

INTRODUCTION

Prostatic adenocarcinoma is predominantly a malignancy of older men and exhibits considerable biological heterogeneity. While some tumours follow an indolent course, others demonstrate rapid local progression and metastatic potential. Accurate assessment of tumour grade is therefore essential for prognostication and treatment planning.

The Gleason grading system is based primarily on the architectural pattern of prostatic adenocarcinoma. Contemporary practice incorporates the five-tier ISUP

Grade Group system: Grade Group 1 corresponds to Gleason score 3+3=6; Grade Group 2 to 3+4=7; Grade Group 3 to 4+3=7; Grade Group 4 to Gleason score 8; and Grade Group 5 to Gleason scores 9–10. This grouping improves clinical interpretation and communicates increasing tumour aggressiveness more clearly.

Serum PSA is a widely used biomarker in the evaluation of prostatic disease. Although PSA is organ-associated rather than cancer-specific and can be elevated in benign prostatic hyperplasia, prostatitis, urinary retention and

after instrumentation, increasing PSA in a patient with established carcinoma often reflects increasing tumour burden and disruption of normal glandular architecture. Clinically, elderly patients with prostate carcinoma may present with lower urinary tract symptoms such as frequency, urgency, nocturia, dysuria, hesitancy, poor urinary stream and incomplete bladder emptying. These complaints overlap considerably with benign prostatic disease, making combined clinical, biochemical and histopathological assessment important. The present study was undertaken to determine the association between serum PSA concentration and Gleason Grade Groups in histologically confirmed prostatic adenocarcinoma among patients aged more than 70 years at a tertiary hospital in New Delhi.

Aim and Objectives

Aim

- To determine the association of serum prostate-specific antigen levels with Gleason Grade Groups in prostatic adenocarcinoma.

Objectives

- To determine the distribution of Gleason scores and ISUP Grade Groups in histologically confirmed prostatic adenocarcinoma.
- To compare serum PSA levels across Gleason Grade Groups.
- To evaluate the correlation between serum PSA concentration and increasing Grade Group.
- To describe the age distribution and common lower urinary tract symptoms in the study population.
- To document representative histomorphological features of prostatic adenocarcinoma.

MATERIALS AND METHODS

Study Design

A hospital-based observational cross-sectional study was conducted.

Study Setting

The study was conducted at Mata Chanan Devi Hospital, Janakpuri, New Delhi, with histopathological evaluation performed in the Department of Pathology in collaboration with the Department of General Surgery and other concerned clinical services.

Study Duration

The study was conducted over a period of three months, from January 2026 to March 2026.

Study Population and Sample Size

A total of 60 consecutive histologically confirmed cases of prostatic adenocarcinoma in male patients aged more

than 70 years were included. Consecutive sampling was used during the study period until the target sample size was achieved.

Clinical Evaluation

Clinical details were recorded with emphasis on lower urinary tract symptoms, including increased frequency, urgency, nocturia, dysuria, hesitancy, poor urinary stream, straining during micturition, sensation of incomplete bladder emptying, urinary retention and hematuria. Constitutional symptoms and bone pain, where present, were also documented.

Serum PSA Estimation

Pre-treatment serum total PSA values were recorded in ng/mL. For categorical analysis, PSA levels were grouped as ≤ 10 ng/mL, 10.1–20 ng/mL, 20.1–50 ng/mL and > 50 ng/mL.

Histopathological Examination

Prostatic tissue obtained by core biopsy, transurethral resection and/or prostatectomy was fixed in 10% neutral-buffered formalin and processed routinely. Paraffin sections were stained with hematoxylin and eosin. Tumours were evaluated for glandular architecture, infiltrative growth, nuclear atypia, prominent nucleoli, poorly formed glands, fused glands, cribriform architecture and solid growth where present. Gleason scoring was performed and cases were assigned to ISUP Grade Groups 1–5.

Statistical Analysis

Continuous variables were summarized as mean $\pm$ standard deviation or median with interquartile range, as appropriate. Categorical variables were expressed as frequency and percentage. Differences in serum PSA across Grade Groups were assessed using the Kruskal-Wallis test. Spearman rank correlation was used to evaluate the relationship between serum PSA and Grade Group. Association between categorized PSA and Grade Group was assessed using an appropriate contingency-table test. A p-value < 0.05 was considered statistically significant.

Inclusion Criteria

- Male patients aged > 70 years.
- Histopathologically confirmed conventional/acinar adenocarcinoma of the prostate.
- Availability of pre-treatment serum total PSA.
- Adequate prostatic tissue for histological grading.
- Availability of relevant clinical information.

Exclusion Criteria

- Age ≤ 70 years.
- Inadequate or poorly preserved tissue for Gleason grading.
- Absence of documented pre-treatment serum PSA.
- Prior androgen-deprivation therapy, chemotherapy or radiotherapy before tissue sampling.
- Non-acinar primary prostatic malignancies.
- Metastatic tumours involving the prostate from another primary site.

RESULT

A total of 60 histologically confirmed cases were included. All patients were older than 70 years. The mean age was 76.9 ± 4.2 years, with an age range of 71–89 years. The largest proportion of patients was in the 75–79-year age group.

Table 1. Age distribution of the study population

Age group (years)	n	Percentage
71–74	15	25.0%
75–79	23	38.3%
80–84	15	25.0%
≥ 85	7	11.7%
Total	60	100%

Lower urinary tract symptoms were the predominant presentation, and several patients reported more than one symptom.

Table 2. Clinical presentation of patients

Clinical symptom/sign	n	Percentage
Increased urinary frequency	49	81.7%
Nocturia	46	76.7%
Urgency	41	68.3%
Poor urinary stream	37	61.7%
Hesitancy	33	55.0%
Dysuria	28	46.7%
Incomplete bladder emptying	26	43.3%
Urinary retention	17	28.3%
Suprapubic discomfort	14	23.3%
Hematuria	10	16.7%
Constitutional symptoms/weight loss	8	13.3%
Bone pain	7	11.7%

Note: Multiple symptoms could occur in the same patient; therefore, percentages do not total 100%.

Distribution of Gleason Grade Groups

Grade Group 4 was the largest individual category, followed by Grade Groups 3 and 5. Grade Groups 3–5 together accounted for 42 of 60 cases (70.0%), indicating a predominance of intermediate- to high-grade disease.

Table 3. Distribution according to Gleason score and ISUP Grade Group

Gleason score	Grade Group	n	Percentage
3+3=6	1	7	11.7%
3+4=7	2	11	18.3%
4+3=7	3	14	23.3%
Score 8	4	15	25.0%
Scores 9–10	5	13	21.7%
Total		60	100%

Serum PSA Levels Across Grade Groups

Median serum PSA showed a progressive increase with increasing Grade Group.

Table 4. Serum PSA according to Gleason Grade Group

Grade Group	n	Median PSA (ng/mL)	Interquartile range (ng/mL)
1	7	10.6	8.3–14.2
2	11	16.8	12.5–23.1
3	14	28.1	20.4–40.2
4	15	49.0	34.7–70.1
5	13	79.2	56.1–113.4

The difference in serum PSA concentration across the five Grade Groups was statistically significant (Kruskal-Wallis $p < 0.001$).

Relationship Between PSA Category and Grade Group

Table 5. Distribution of serum PSA categories according to Grade Group

Serum PSA	GG1	GG2	GG3	GG4	GG5	Total
≤ 10 ng/mL	4	2	0	0	0	6
10.1–20 ng/mL	3	6	4	1	0	14
20.1–50 ng/mL	0	3	8	7	3	21
> 50 ng/mL	0	0	2	7	10	19
Total	7	11	14	15	13	60

Among 19 patients with PSA > 50 ng/mL, 17 (89.5%) belonged to Grade Groups 4 or 5. Conversely, all six patients with PSA ≤ 10 ng/mL belonged to Grade Groups 1 or 2. Categorized PSA was significantly associated with increasing Grade Group ($p < 0.001$).

Spearman rank analysis demonstrated a strong positive correlation between serum PSA concentration and Grade Group ($\rho = 0.66$; $p < 0.001$).

Histopathological Findings

The tumour sections showed irregular infiltrating acini within fibromuscular prostatic stroma. Malignant glands demonstrated variation in size and contour, loss of benign glandular organization, nuclear enlargement and conspicuous nucleoli. Lower-grade areas showed relatively discrete gland formation, while higher-grade foci showed increased architectural complexity with poorly formed and fused glands. Representative histomorphological findings are shown in Figure 1A–H.

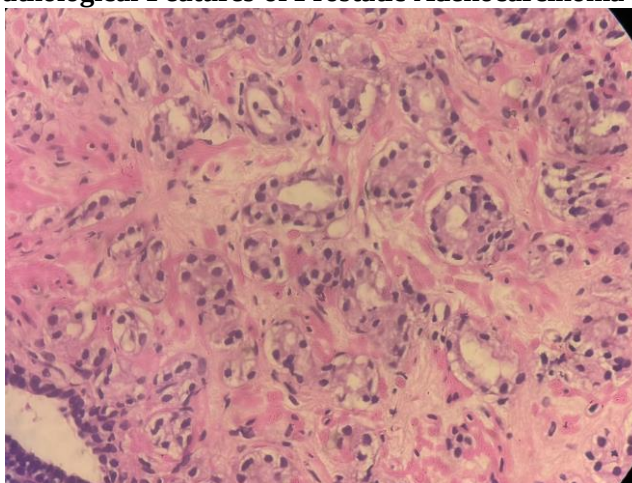
Figure 1. Representative Histopathological Features of Prostatic Adenocarcinoma

Figure 1A. High-power H&E photomicrograph showing closely packed, irregular infiltrating prostatic glands within fibromuscular stroma. Tumour cells show nuclear enlargement and conspicuous nucleoli with intraluminal secretory material.

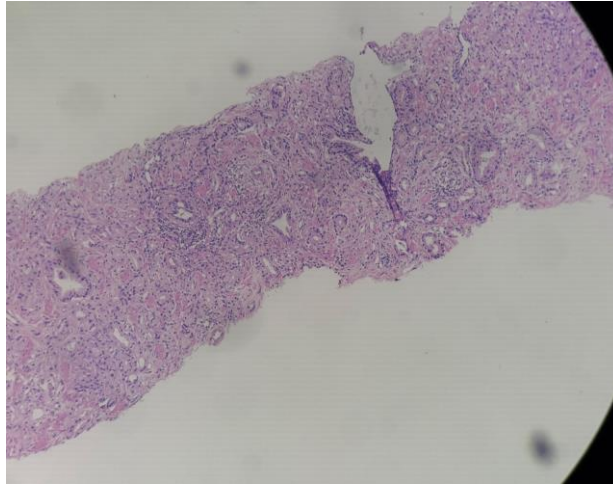


Figure 1B. Low-power H&E photomicrograph of a prostatic tissue core demonstrating multifocal infiltration by irregular neoplastic glands dispersed within fibromuscular stroma.

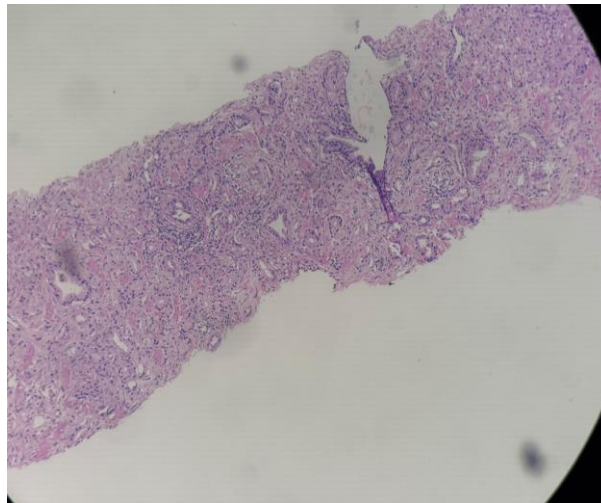


Figure 1C. Low-power H&E section showing extensive gland-forming prostatic adenocarcinoma in a core biopsy, with heterogeneous glandular architecture and infiltrative growth.

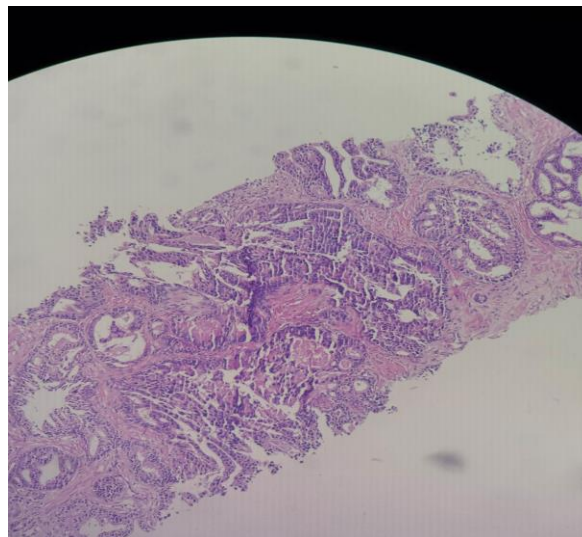


Figure 1D. H&E photomicrograph showing architecturally complex carcinoma with crowded, fused and irregular glandular structures, representing higher-grade architectural features.

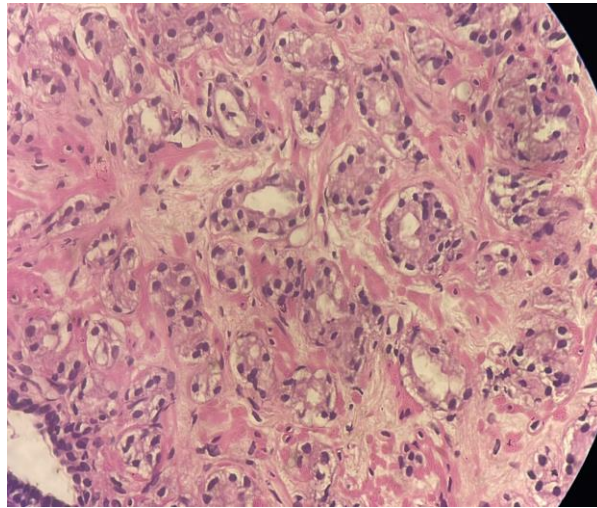


Figure 1E. High-power H&E photomicrograph demonstrating infiltrative malignant acini separated by fibromuscular stroma, with enlarged atypical nuclei and prominent nucleoli.

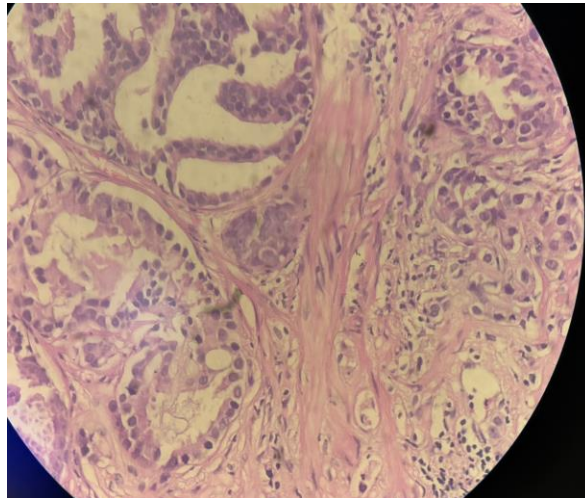


Figure 1F. H&E photomicrograph showing heterogeneous adenocarcinoma composed of irregular glandular structures with variable gland formation within dense fibromuscular stroma.

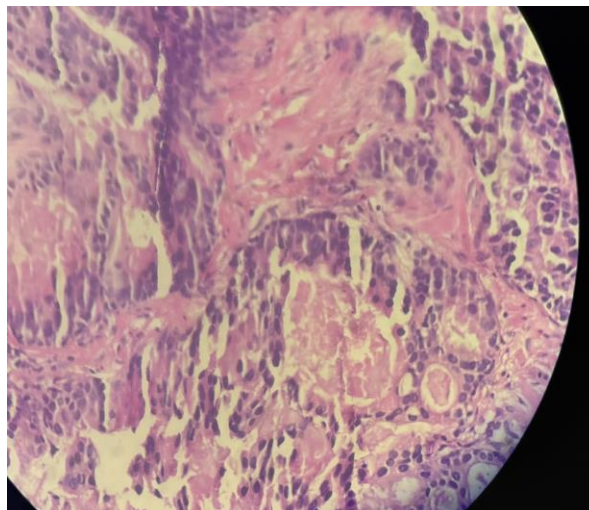


Figure 1G. High-power H&E section demonstrating crowded and focally poorly formed/fused malignant glands with eosinophilic luminal secretions and cytological atypia.

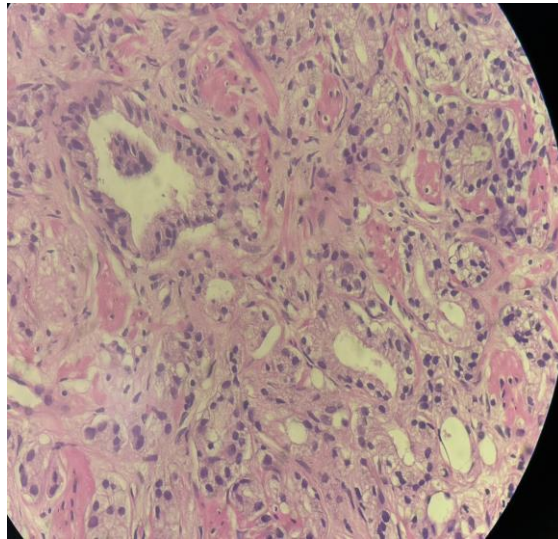


Figure 1H. High-power H&E photomicrograph demonstrating irregular infiltrating malignant glands with cytoplasmic vacuolation, nuclear atypia and stromal infiltration.

DISCUSSION

The present study evaluated the association between serum PSA concentration and Gleason Grade Group in elderly patients with histologically confirmed prostatic adenocarcinoma. A progressive increase in serum PSA was observed from Grade Group 1 through Grade Group 5, and serum PSA showed a strong positive correlation with increasing histological grade.

All patients were older than 70 years, with a mean age of 76.9 years. The concentration of cases in older age groups is consistent with the recognized age-related increase in clinically significant prostatic carcinoma. This age group also frequently has benign prostatic enlargement and other causes of lower urinary tract symptoms, which can complicate early clinical recognition of malignancy.

Lower urinary tract symptoms dominated the clinical presentation. Frequency was recorded in 81.7% of cases, nocturia in 76.7%, urgency in 68.3%, poor stream in 61.7%, hesitancy in 55.0% and dysuria in 46.7%. These findings highlight that patients may present with a mixture of storage and voiding symptoms. Because these complaints overlap with benign prostatic hyperplasia and inflammatory disorders, persistent or progressive symptoms in elderly men warrant appropriate clinical assessment rather than being presumed benign.

Grade Groups 3–5 represented 70.0% of the study population, indicating that a substantial proportion of patients had intermediate- to high-grade disease. A hospital-based series may preferentially include symptomatic individuals or patients with markedly abnormal PSA values, which can contribute to a higher proportion of clinically significant tumours.

Median PSA rose from 10.6 ng/mL in Grade Group 1 to 16.8 ng/mL in Grade Group 2, 28.1 ng/mL in Grade Group 3, 49.0 ng/mL in Grade Group 4 and 79.2 ng/mL

in Grade Group 5. The overall difference was statistically significant, and Spearman analysis demonstrated a strong positive correlation between PSA and Grade Group.

The biological relationship between PSA and tumour grade is complex. PSA level is influenced by tumour volume, residual benign prostate tissue, inflammation, urinary retention and disruption of normal glandular architecture. In addition, very poorly differentiated carcinomas may produce less PSA per unit tumour volume. Therefore, serum PSA cannot be regarded as a direct surrogate for histological grade in every individual patient.

Nevertheless, markedly elevated PSA values were concentrated in the higher Grade Groups in the present dataset. Of the patients with PSA >50 ng/mL, 89.5% belonged to Grade Groups 4 or 5. This pattern supports the clinical value of integrating PSA with tissue grade when estimating disease severity.

Histologically, the submitted sections demonstrated the expected spectrum of acinar adenocarcinoma, ranging from relatively well-formed infiltrating glands to more complex, poorly formed and fused glandular structures. The presence of architectural heterogeneity also emphasizes that Gleason grading should be based on examination of the complete tumour represented in the biopsy or resection specimen rather than isolated high-power fields.

PSA and Grade Group provide complementary information. PSA is a readily available biochemical marker reflecting, in part, the amount and biological activity of prostatic tissue, whereas the Grade Group provides a direct morphological assessment of tumour architecture and aggressiveness. Their combined interpretation is therefore more informative than either parameter alone.

Clinical Implications

- Persistent urinary frequency, urgency, nocturia, dysuria, hesitancy and poor urinary stream in elderly men should prompt appropriate prostatic evaluation.
- Markedly elevated PSA values should raise suspicion for clinically significant disease, while recognizing that PSA is not cancer-specific.
- A modest PSA concentration does not exclude aggressive carcinoma; histopathological confirmation and grading remain essential.
- Integrating serum PSA with Gleason score/ISUP Grade Group provides a practical clinicopathological framework for initial risk stratification.

Strengths of the Study

The present study has several strengths. First, all included cases were histologically confirmed prostatic acinar adenocarcinoma, ensuring accurate pathological diagnosis. Second, the study evaluated serum PSA levels in relation to the contemporary five-tier ISUP Grade Group classification, allowing direct assessment of the relationship between a commonly used serum biomarker and histological tumour grade. Third, consecutive sampling was used during the study period, reducing the possibility of selective case inclusion. The study also demonstrated a progressive increase in median serum PSA levels with increasing ISUP Grade Group, from 10.6 ng/mL in Grade Group 1 to 79.2 ng/mL in Grade Group 5. Furthermore, a strong positive correlation was observed between serum PSA levels and ISUP Grade Group (Spearman $\rho = 0.66$, $p < 0.001$), supporting the clinical relevance of PSA as a complementary marker of tumour aggressiveness.

Limitations

The study is limited by its single-centre design, relatively short three-month duration and modest sample size. Serum PSA may be affected by benign prostatic hyperplasia, prostatitis, urinary retention and recent instrumentation.

Future Directions

Future studies should include larger, multicentre patient populations with longer study periods to validate the observed association between serum PSA levels and ISUP Grade Groups. Prospective studies with long-term follow-up should assess whether baseline PSA levels and histological grade can predict clinically important outcomes such as biochemical recurrence, metastatic progression, treatment response, and disease-specific survival. Further research should also evaluate PSA together with other clinicopathological parameters, including tumour stage, tumour volume, prostate

volume, perineural invasion, lymphovascular invasion, and metastatic status. Multivariable analyses may help determine whether PSA independently predicts higher ISUP Grade Groups after adjustment for potential confounding factors. Future studies may also explore the combined value of PSA, imaging findings, biopsy characteristics, and emerging biomarkers for improved risk stratification and clinical decision-making in patients with prostatic adenocarcinoma.

CONCLUSION

Serum PSA showed a significant positive association with increasing Gleason Grade Group in prostatic adenocarcinoma among patients aged more than 70 years. Median PSA increased progressively from Grade Group 1 to Grade Group 5, and markedly elevated PSA values were concentrated in Grade Groups 4 and 5. Frequency, nocturia, urgency, poor urinary stream, hesitancy and dysuria were common presenting symptoms. Serum PSA should therefore be interpreted as a complementary marker alongside histopathological Gleason score and ISUP Grade Group rather than as a substitute for tissue diagnosis and grading.

Declarations

Consent for Publication

The manuscript contains no patient-identifying information. Histopathology images are presented without personal identifiers.

Conflict of Interest

The authors declare no conflict of interest.

Funding

No external funding was received for this study.

Data Availability

Study data may be made available by the corresponding author subject to institutional and ethical requirements.

Author Contributions

Dr Priyanka Dhingra: Conceptualization, histopathological evaluation, methodology, data interpretation, manuscript review. Dr Vivek Gautam: Clinical data collection, methodology, data interpretation, manuscript preparation and review.

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