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Original Article

Diagnostic Accuracy of Serum Prostate Specific Antigen (PSA ≥50ng/ml) in Estimating Aggressiveness of Adenocarcinoma of Prostate (Gleason Score ≥7)

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Abstract

Objective: To assess the diagnostic accuracy of serum PSA > or = 50ng/ml in estimating aggressiveness of adenocarcinoma of prostate (Gleason score 7 or more). An alternative to the Gleason score (GS), a new grading system for the diagnosis of prostate cancer was applied in this study based on the modified Gleason score grouping which included five Grade groups. The main objective of our study was to evaluate the diagnostic accuracy of PSA level ≥ 50 ng/ml for evaluation of the aggressiveness of adenocarcinoma prostate (GS ≥7) in patients with this tumor.

Methods: This descriptive, cross-sectional study was done at the Histopathology department of Shaikh Zayed Hospital, Lahore, from October 2024 to April 2025. Formalin fixed samples of 338 patients aged 40-70yrs with suspected prostate cancer were done. Pre-biopsy PSA levels were selected through non-probability, consecutive sampling. Eight needle core TRUS biopsies of each patient, received in separate containers fixed in formalin and submitted in separate blocks, were studied after Hematoxylin and Eosin staining. The Gleason score (GS) was calculated. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of PSA ≥ 50 ng/ml were used to calculate the aggressiveness of adenocarcinoma of prostate (GS ≥7). Demographic information was noted on predesigned proforma.

Results: Patients (Mean age=56.43+7.90 years) had a mean duration of 10.36+10.51 months for prostate cancer. Gleason score ≥ 7 was found in 99 (29.29%) and <7 in 239 (70.71%) patients. Serum PSA levels <50 ng/ml were found in 232 (68.64%) and ≥ 50 ng/ml in 106 (31.36%). On histopathology, PSA levels ≥ 50 ng/ml were 65.7% sensitive and 82.8% specific in diagnosing aggressiveness of adenocarcinoma. PSA levels Positive predictive value (PPV) was 61.3% and negative predictive value (NPV) was 85.3%.

Age stratification of two age groups 40-55 and 56-70 years showed sensitivity of PSA as 68.9% and 63.0% respectively, whereas the specificity as 80.2%. and 85.4% respectively. Duration stratification showed prostate cancer <6 months, sensitivity of PSA levels was 77.1%, and specificity was 82.2%.

Conclusion: The serum total PSA was found strongly correlated with tumor diagnosis and tumor aggressiveness. The sensitivity and specificity of serum PSA levels was 65.7% sensitive and 82.8% specific at a cut off value of 50 ng/ml. for diagnosing aggressiveness

Keywords: Prostate Specific antigen, Carcinoma, Gleason's score

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Introduction

Grading prostate cancer accurately is essential for understanding how aggressive the disease is and deciding on the best treatment plan.[1,2,3] The Gleason grading system, which remains the cornerstone of prostate cancer evaluation, is usually applied using low-power magnification of 4x objective.[4] In some cases, where the gland patterns are hard to distinguish, e.g. between tightly packed glands and fused ones, a closer look

with higher magnification of 10x objectives may be needed. To avoid confusion, Gleason scores are written as an equation like 4 + 3 = 7, with the first number showing the commoner pattern under the microscope.[5-7]

Over time, the Gleason system has gone through important updates. In the past, lower scores of 2 to 5 were used more often in needle biopsies, but we now know that these grades are not reliable and do not match what is later found during surgery.[9] Many of those earlier low-grade diagnoses likely missed the mark, partly because older studies did not have the benefit of modern tools like immunohistochemistry. Today, nearly all of what was once called Gleason pattern 2 would now be considered pattern 3.[9]

Pattern 3 cancers still form recognizable, well-structured glands and are usually easy to spot at low magnification.[6] Pattern 4, however, includes more concerning features like glands that are poorly formed, fused together, or have cribriform structures. These are now known to signal a more aggressive disease. In fact, cribriform glands, once considered less serious, are now clearly linked to worse outcomes, including cancer spreading beyond the prostate and even cancer-related deaths.[8]

Gleason pattern 5 is the most aggressive form. It appears as solid sheets, single cells, or structures with dead tissue inside. These cancers can be tricky to recognize, and they are often underestimated.[5] As grading has improved, we have become better at predicting from a biopsy how serious the cancer is.[11] However, beyond microscopic patterns, one of the most widely used blood tests, Prostate Specific Antigen (PSA), still has an important role in raising alarm[12]. Very high PSA levels may point to a more aggressive tumor, but exactly how reliable this signal is, remains a key question.[13,14] This study aims to explore whether PSA 50 ng/ml or higher can accurately predict prostate carcinoma of high grade, shown as Gleason score 7 or above, in men diagnosed with adenocarcinoma of the prostate. Understanding this relationship could help doctors catch aggressive cancer earlier and tailor treatment more effectively. Aim present study is to evaluate the diagnostic accuracy of PSA level ≥50 ng/ml in determining the aggressiveness of prostatic cancer (GS ≥7) in patients with adenocarcinoma.

Methods

It was a descriptive, cross-sectional study conducted in the Histopathology department of Shaikh Zayed Hospital Lahore, from October 2024 to April 2025. Sample size for this study was calculated by taking expected prevalence of prostate cancer 10.5%,[5] sensitivity 66.7%[10] with precision level of 13%, and specificity 79.5%[10] with precision level of 13%. The calculated sample size was 338 patients. Non-probability, consecutive sampling was used to collect samples

Sample fixed in formalin for histopathological diagnosis of adenocarcinoma of prostate. Selected samples were of patients who visited the hospital for pre-biopsy PSA level, aged between 40-70 years. Small inadequate biopsies and samples of prostate hyperplasia on histopathological reporting were excluded.

Data Collection Procedure: After the hospital's ethical committee approved it, 338 biopsies with suspicion of prostate adenocarcinoma were sent to the histopathology department of the hospital to be included in this study. Transrectal ultrasound guided needle core biopsy tissues were used to diagnose prostatic adenocarcinoma. The cores were received in separate containers fixed in formalin. Eight needle cores were submitted in separate blocks and processed as per protocol and were studied after Hematoxylin and Eosin staining. Gleason scores (GS) were calculated for all patient biopsies. We calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of PSA ≥ 50 ng/ml to diagnose the aggressiveness of adenocarcinoma of prostate (GS ≥7). Sensitivity and specificity were calculated according to the formula given in the operational definitions. All the information was noted on a predesigned form.

Data analysis procedure: Software SPSS 20.0 was used to analyze the data we collected. For age and duration of disease, mean and standard deviation were calculated. For qualitative variables (PSA levels and GS score), frequency and percentages were calculated. To calculate sensitivity, specificity, positive predictive value and negative predictive values of PSA ≥50 ng/ml, contingency table of 2x2 was used for diagnosing aggressiveness of adenocarcinoma of prostate (GS ≥7). Stratification of confounder variables, e.g. age and duration of prostate cancer, was done, and the post-stratification 2×2 contingency table was also used.

Results

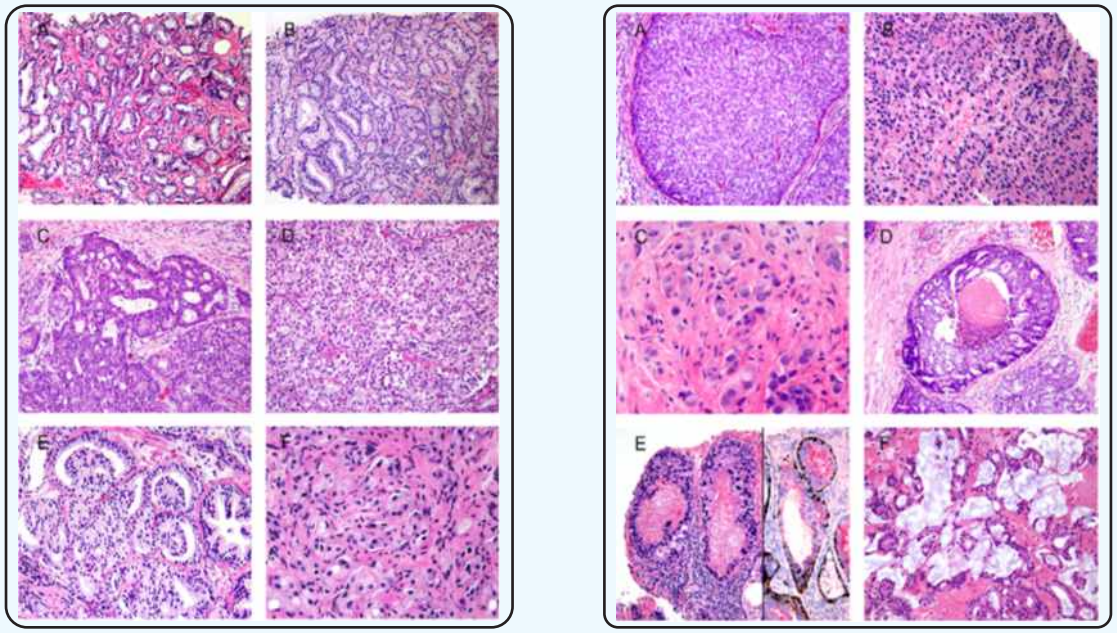
Iin this study, mean patient age was 56.43+7.90 years. The mean duration of prostate cancer was 10.36+10.51 months. Histological variants and grading of multiple scores with cancer are shown in figure 1. Maximum duration of cancer was 36 months Gleason score ≥ 7 was found in 99 (29.29%) patients and was < 7 in 239 (70.71%) patients as shown in figure 2.

Serum PSA levels were <50 ng/ml in 232 (68.64%) patients and ≥ 50 ng/ml in 106 (31.36%) patients (Table 1). PSA levels ≥ 50 ng/ml were 65.7% sensitive and 82.8% specific in diagnosing the aggressiveness of adenocarcinoma while taking histopathological grading as a gold standard. Positive predictive value (PPV) of PSA levels was 61.3% and negative predictive value

(NPV) was 85.3% (Table 2). Age stratification was performed in patients of age 40-55 years of age, sensitivity of PSA was 68.9%, and specificity was 80.2%. and in patients having age 56-70 years, sensitivity of PSA was 63.0% and specificity of 85.4% (Table 2). Duration of disease stratification was also performed; hence in patients having duration of prostate cancer <6 months, sensitivity of PSA levels was 77.1% and specificity was 82.2%. While in patients having duration of cancer >6 months, sensitivity of PSA levels was 54.9% and specificity was 83.5% (Table 2).

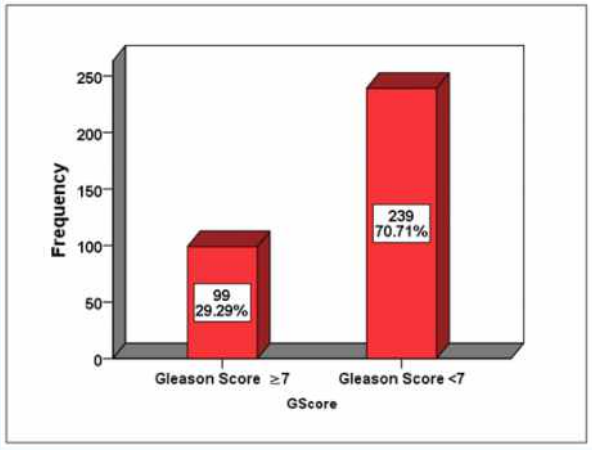
Figure 1A: Grade Group 1 (GS 3 + 3 = 6). b: Grade Group 2 with few foci of cribriform pattern (GS 3+4=7). c: Grade Group 4 with predominant cribriform glands (GS 4 + 4 = 8). d: Grade Group 4 closely packed glands with vacuolated cytoplasm (GS 4 + 4 = 8). e: Grade Group 4 with glomeruloid glands (GS 4 + 4 = 8) f: Grade Group 4 hyper nephroid cells (GS 4 + 4 = 8)

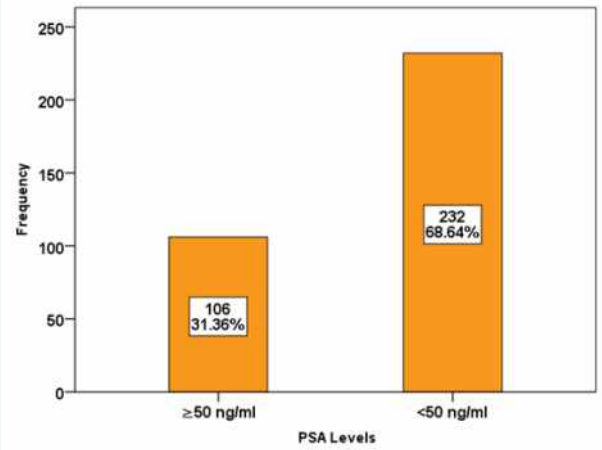
Figure 1B: Grade Group 5 (GS 5 + 5): A: reveals solid sheets of tumor cells. b. Shows cords of tumor cells, and c: individual cells. d: Grade Group 5 (GS 5 + 4) reveals cribriform patterns, glands and focal comedonecrosis. e: Intraductal adenocarcinoma with central necrosis (left); basal cells seen by p63 (right) and are also positive for racemase. f: Grade Group 2 (GS 3 + 4) mucinous adenocarcinoma shows mostly well-formed glands and few cribriform-pattern glands surrounded by mucin.



IA *IIB*

Figure I. *Histological Variants and Grading of Multiple Scores with Cancer*





IIA. Severity of Adenocarcinoma *Figure IIB. PSA Levels.*

Figure II. *Frequency of Severity of Adenocarcinoma and PSA Levels According to Gleason Score*

Table 1: *Serum PSA Levels and Gleason Score in Adenocarcinoma of Prostate According to Age Groups.*

Age Group (Years)	PSA	Gleason Score		Total
		≥ 7	<7	
Overall	≥50 ng/ml	65	41	106
	<50 ng/ml	34	198	232
Total		99	239	338
40-55	≥50 ng/ml	31	23	54
	<50 ng/ml	14	93	107
Total		45	116	161
56-70	≥50 ng/ml	34	18	52
	<50 ng/ml	20	105	125
Total		54	123	177

Table 2: *Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of Serum PSA Levels (>50 ng/ml) in Diagnosing Aggressiveness of Adenocarcinoma of Prostate.*

Variables	Sen * (%)	Spe ** (%)	PPV (%)	NPV (%)
PSA ≥50 ng/ml	65.7	82.8	61.3	85.3
PSA <50 ng/ml				
Age 40 -50 years	68.9	80.2	57.4	86.9
Age 56 -70 Years	63.0	85.4	65.4	84
Duration of cancer < 6 months	77.1	82.2	63.8	89.8
Duration of cancer > 6 months	54.9	83.5	58.3	81.5

**: Sensitivity, **: Specificity, PPV: Positive Predictive value, NPV: Negative Predictive value*

Discussion

Presently, the tools which are acceptable for diagnosing prostatic cancer are: Digital Rectal examination (DRE) and PSA levels in serum.[14] PSA tests have been used by clinicians since 1986 and have resulted in changes with respect to diagnosing prostatic cancer early, facilitating earlier treatment. The global use of PSA screening has improved patient survival since an increased number of patients are diagnosed at an early stage.[15,16] Owing to higher detection of confined tumors at an early stage, the number of prostatic cancer patients with metastatic stage and associated complications has reduced by upto 25%. The advantage of PSA tests in serum cannot be ignored for early diagnosis, to monitor the treatment and determination of disease advancement.[18,19]

However, the disadvantages of testing PSA should not be overlooked. It increases the chance of overdiagnosis prompting unnecessary biopsy procedures which are negative owing to low specificity of PSA levels; hence, a limitation of this test. This occurs because PSA is prostate-disease specific rather than being specific for prostatic cancer. PSA can be raised by other conditions like prostatitis, benign prostate hyperplasia, prostatic manipulation and ejaculation within last 24 hours[17,19,20]. Generally, the PSA cutoff value is taken as 4.0 ng/mL. A lesser value increases the sensitivity but specificity is decreased leading to higher detection of prostatic cancers which are clinically silent. In patients having PSA between 4.0 and 10.0 ng/mL range, the mean positive predictive value for diagnosing prostatic cancer is 21% (range, 18%–25%).

In patients with PSA<4 ng/mL having unremarkable or an abnormal DRE, the incidence of prostatic cancer respectively ranges between 4% to 9% and 10% to 20%. Therefore, a significant number of cancers are missed with the above cutoff PSA value. However, when the PSA level is >4 ng/mL, in patients having unremarkable or an abnormal DRE, the incidence of prostatic cancer respectively ranges between 12% to 32% and 42% to 72%. Recent guidelines on prostate cancer have concluded that in patients having PSA > 50 ng/mL, risk of mortality is > 3.5-fold than patients with < 8 ng/mL level. If baseline PSA was >50 ng/mL in patients with adenocarcinoma, the risk of mortality was much higher.

In this study, the diagnostic accuracy of serum PSA levels in determining the severity of adenocarcinoma according to the Gleason score has been estimated. PSA levels ≥ 50 ng/ml is 65.7% sensitive and 82.8% specific in diagnosing the aggressiveness of adenocarcinoma while taking histopathological grading as a gold standard. Positive predictive value (PPV) of PSA levels is 61.3% and negative predictive value (NPV) is 85.3%.

Another study conducted by Kim SH, et al. found that at PSA ≥50 ng/mL, only ~47.8% of all prostate cancers were detected (sensitivity),but the specificity was very high (98.2%), meaning non-cancer cases were rarely falsely positive at this level. 21 Positive predictive value (PPV) was ~93.6%, indicating that most men with PSA ≥50 actually had prostate cancer on biopsy. Negative predictive value (NPV) was lower (~77.5%), because many cancers occur with PSA <50.

Our study is limited by the use of only serum PSA level for diagnosing prostatic cancer and determining its aggressiveness. Combining serum PSA with DRE and ultrasound/MRI can increase the sensitivity and specificity to diagnose prostatic cancer.[14,16,17]

Elevated serum PSA is accepted as an indicator for TRUSS biopsy in screened men and patients with symptoms of disease. If biopsy is malignant, the differentiation degree of the tumor sample is reported as GS

which is an indicator of how aggressive the cancer is, and what the prognosis may be. In third world countries without a stable system of health insurance, the patients who are mostly poor, have to bear the cost of diagnosis and treatment of disease; hence, the concerned doctor carefully decides about the "absolutely necessary" investigations so that the patients maintain the financial strength for relevant treatment.

Conclusion

It is concluded in our study that serum PSA level has a strong correlation with diagnosis and aggressiveness of cancer. Higher the PSA level, more are the chances of diagnosing high Gleason score cancers on TRUSS biopsies. In the present study, at a 50ng/ml cut-off value, the sensitivity and specificity of serum PSA levels to diagnose aggressiveness is 65.7% sensitive and 82.8% specific.

Ethical Approval: The IRB/EC approved this study via letter no. 02-TERC/SZH-NHRC/Internal-SC/565 dated October 7, 2024.

Conflict of Interest: None

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Authors' Contribution

SR: Conception.

UN, MA: Design of the work.

SJ, FBN: Data acquisition, analysis, or interpretation.

SJ, FBN, MA: Draft the work.

UN, SR: Review critically for important intellectual content.

All authors approve the version to be published.

All authors agree to be accountable for all aspects of the work.

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