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Original Research Article

Prostate Specific Antigen (PSA) Levels and its histopathological Correlation with Prostatic Adenocarcinomas: An Observational and Retrospective study

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Abstract

Background: The prostate is a retroperitoneal structure that surrounds the urethra and bladder neck. It is an exocrine gland whose secretions make up a sizable portion of seminal fluid and is the largest auxiliary reproductive organ in males. This study aims to establish a correlation between PSA levels and the grade of prostate carcinoma and prostatic lesions.

Methods: Male patients with lower urinary tract problems who are recommended to have their PSA levels and undergo a prostate biopsy guided by transrectal ultrasonography (TRUS) are included in the study. The study design was retrospective and observational. Selection was done using the universal sample approach from January 2025 to June 2025. During the specified period, we got 116 TRUS biopsies. The departmental and hospital records provided the pertinent information for these.

Results: Of the 116 cases, 59 were benign and 57 were malignant. PSA values were higher than 4 ng/ml in 53 (93%) of the malignant patients and 54 (91.5%) of the benign cases. As a result, it was determined that there was no statistically significant correlation between PSA level and lesion type ($p > 0.05$). Grade 1 prostate adenocarcinoma had a mean PSA level of 19.67 ng/ml, Grade 2 prostate adenocarcinoma had a mean of 10.84 ng/ml, Grade 3 prostate adenocarcinoma had a mean of 21.07 ng/ml, Grade 4 had a mean of 39.06 ng/ml, and Grade 5 had a mean of 399.26 ng/ml. As a result, although the mean PSA level rose with grade, the difference was not statistically significant ($p>0.05$).

Conclusion: There are limits to using serum PSA levels as tumor markers. Therefore, in situations that are clinically suspect, histological investigation is more specific for an accurate diagnosis.

Keywords: Prostate Specific Antigen, Prostatitis, Prostatic Adenocarcinoma.

Introduction

Three pathologic conditions that commonly impact the prostate gland include benign prostate hyperplasia, prostate carcinoma, and prostatitis.[1] The fact that both benign and malignant prostate tumors are hormone (androgen) dependent and associated with substantial morbidity and mortality in man is one of the most intriguing aspects of the prostate.[2]Almost one out of ten men in their seventies will experience acute urinary retention during the next five years. The evaluation and treatment of the prostate is a crucial component of geriatric practice and a topic of interest for gerontological research because these conditions are prevalent in older men.[2] A significant and expanding health issue, prostate cancer poses a challenge to radiologists, pathologists, and urologists. Prostate specific antigen (PSA) screening is currently used to detect early prostate cancer in many men.[3] It is well recognized that non-cancerous diseases like as inflammation, benign prostatic hyperplasia (BPH), and diagnostic and surgical procedures can also result in elevated PSA levels. These illnesses can resemble cancer and lead to misdiagnosis.[4] Therefore, the primary technique for diagnosing prostate cancer is transrectal ultrasonography (TRUS) guided prostate biopsy.[5]

Materials and Methods

This observational and retrospective was conducted in Department of Pathology (Histopathological Section), Patna Medical College and Hospital, Patna, Bihar from January 2025 to June 2025. It includes male patients with lower urinary tract

problems who were recommended to undergo a TRUS-guided prostatic biopsy and have their PSA levels measured. The study design was retrospective and observational. The study was chosen using the universal sampling approach because it was an observational study.

During the specified period, we got 116 TRUS biopsies. The pertinent information for these was gathered from departmental and hospital records. The majority of the cases were six core biopsies, three from the right and three from the left lobe of the prostate, each in a separate container. They were sampled from periurethral zone, peripheral zone and central zone of either lobe of prostate and labelled. Right side of lobe was labelled as I and left side of lobe as II. Periurethral zone was labelled as 'A', Peripheral zone as 'B' and central zone as 'C'. Few specimens were sent in a single container. Special stain (ZN stain) and immunohistochemistry (HMW-CK, p63 and AMACR) were used in granulomatous prostatitis and suspicious lesions respectively. Data entry was done in Excel and analysed with the help of statistician. Microsoft word and excel have been used to generate tables. Qualitative data is presented with the help of Frequency and Percentage table.

Results

Out of 116 cases, 57 cases were malignant and 59 cases were benign. Age wise, upto 49 years, 2 benign cases (3.4%) and 2 malignant cases (3.5%) were noted. In 50-70 years age range, 30 benign cases (50.8%) and 22 malignant cases (38.6%) were noted. The maximum number of cases belonged to the age group 70 years and above (60 cases ie 51.7%). Of these, 33 were malignant (57.9%) and 27 were benign (45.8%) group.

The spectrum of lesions in prostatic biopsy seen in our institution were as follows- Prostatic adenocarcinoma- 57 cases (49.14%), Chronic prostatitis- 32 cases (27.59%), Benign prostatic tissue- 15 cases (12.93%), Acute prostatitis and Granulomatous prostatitis- 4 cases each (3.45% each), Chronic prostatitis with microabscess- 2 cases (1.72%), Chronic prostatitis with eosinophilia and chronic prostatitis with sheets of foamy histiocytes-1 case each (0.86% each).

ZN stain was carried out on cases of granulomatous prostatitis. All turned out to be negative for tubercle bacilli. Broadly, the lesions can be distributed as- Benign prostatic tissue 15 cases (12.93%), Prostatitis 44 cases (37.93%) and Prostatic adenocarcinoma 57 cases (49.14%).

Tables 1 and 2, show the association of PSA levels as per type of lesion. 53 (93%) of the malignant cases and 54 (91.5%) of the benign cases had PSA levels above 4 ng/ ml. 7% malignant cases had PSA levels upto 4ng/ml. Thus, association of PSA levels and type of lesion is found to be statistically insignificant (p >0.05).

Table 1: PSA level in malignant and benign lesions

PSA level (nanogram/millilitre)	Type of Lesion		Total
	Malignant	Benign	
Above 4 ng/ml	53(93.0%)	54(91.5%)	107 (92.2%)
Upto 4 ng/ml	4 (7.0%)	5 (8.5%)	9 (7.8%)
Total	57(100.0%)	59(100.0%)	116(100.0%)

Table 2: Association of PSA level with benign and malignant lesions

Chi-Square test	Value	df	P Value	Remarks
Pearson Chi-Square	0.086	1	0.769	Not Significant
Fisher's Exact Test			1.000	Not Significant

Table 3 shows the distribution PSA level as per grade of Prostatic adenocarcinoma. Pearson Chi Square test was carried out to associate PSA level with Grade of Prostatic adenocarcinoma. Test value was 20.463(a), degree of freedom was 12, P value was 0.059. Thus, association of PSA level with Grade of adenocarcinoma was found to be insignificant (p >0.05).

Table 3: Distribution of PSA levels in different Grades of Prostatic adenocarcinoma

PSA level (nanogram/millilitre)	Grade					Total
	1	2	3	4	5	
Upto4ng/dl	2 (22.2%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	1 (3.8%)	4 (7.0%)
4to10 ng/ml	3 (33.3%)	2 (50.0%)	2 (28.6%)	3 (27.3%)	1 (3.8%)	11(19.3%)
10to20ng/ml	1 (11.1%)	2 (50.0%)	2 (28.6%)	1 (9.1%)	5 (19.2%)	11(19.3%)
Above20 ng/ml	3 (33.3%)	0 (0.0%)	2 (28.6%)	7 (63.6%)	19(73.1%)	31(54.4%)
Total	9 (100.0%)	4 (100.0%)	7 (100.0%)	11(100.0%)	26(100.0%)	57(100.0%)

- For Grade 1, the minimum PSA level was 0.18ng/ml, the maximum PSA level was 54.42ng/ml and the mean PSA level was 19.67ng/ml.
- For Grade 2, the minimum PSA level was 6.06ng/ml, the maximum PSA level was 18.58ng/ml and mean PSA level was 10.84ng/ml.
- For Grade 3, the minimum PSA level was 2.98ng/ml, the maximum PSA level was 70.77ng/ml and mean PSA level was 21.07ng/ml.
- For Grade 4, the minimum PSA level was 4.50ng/ml, the maximum PSA level was 102.10ng/ml and mean PSA level was 39.06ng/ml.
- For Grade 5, the minimum PSA level was 0.38ng/ml, the maximum PSA level was 2,521.58ng/ml and mean PSA level was 399.26ng/ml.

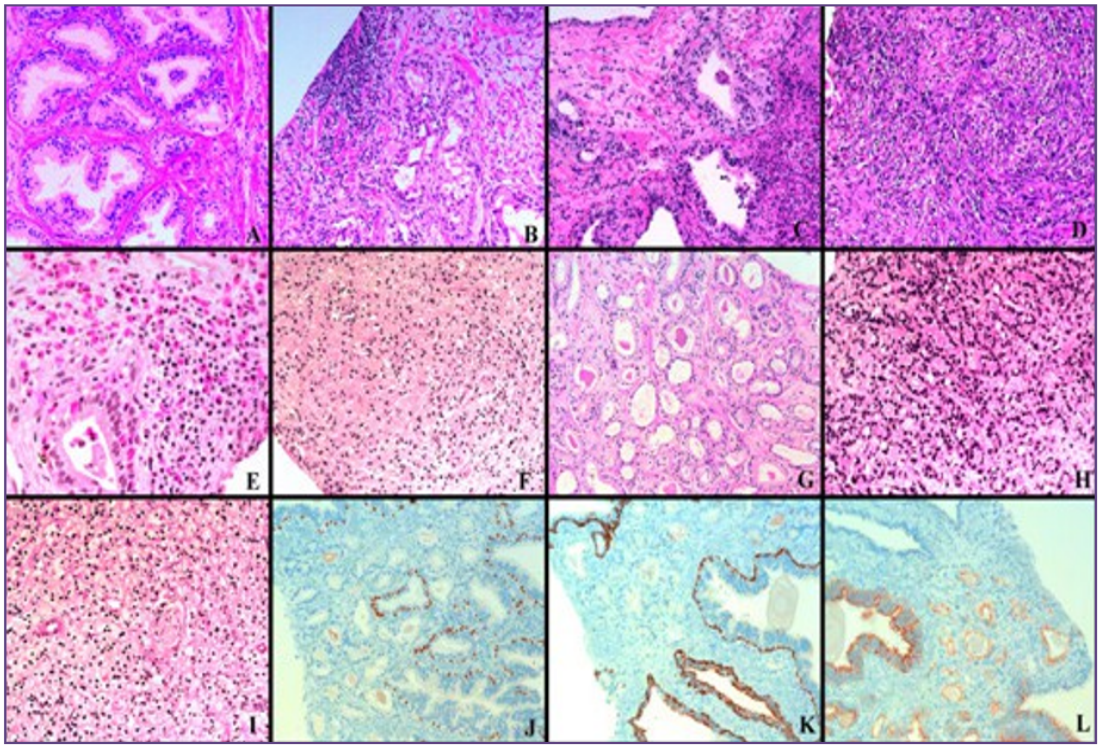

Figure 1: A- Benign Prostatic tissue (H&E, 20X), B- Chronic prostatitis(H&E, 20X),C-Acute prostatitis (H&E, 20X), D-Granulomatous prostatitis(H&E, 20X), E- Chronic prostatitis with eosinophilia (H&E, 40X), F- Chronic prostatitis with foamy histiocytes (H&E, 20X), G- Prostatic adenocarcinoma Gleasons score 3 (H&E, 20X), H- Prostatic adenocarcinoma Gleasons score 4 (H&E, 20X), I- Prostatic adenocarcinoma Gleasons score 5 (H&E, 20X).On Immunohistochemistry(20X), J- suspicious focus of glands with negative nuclear staining of p63, K- suspicious focus of glands with negative cytoplasmic staining of HMW CK (marker of basal cell), L- AMACR positivity in suspicious malignant glands.

Discussion

Out of the 116 cases that were studied, 59 cases were benign and 57 were malignant. In present study, 50.86% cases were benign and 49.14% cases were malignant, comparable to 60.91% benign cases and 37.27% malignant cases in the study done by Varsha Khant et al).[6] Another study by Dr. Atchyuta .M et al [7] had 79.7% benign cases and 20.3% malignant cases.

Geographical location and environment may account for this uneven distribution of benign and malignant lesions. The above studies by Varsha Khant et al [6] and Atchyuta .M et al [7] included prostatic biopsies as well as prostate chips(Transrectal Urethral Resection of Prostate chips), whereas we included only TRUS biopsies. This can also account for more benign cases in these studies. The lesions were classified into three main categories- Benign prostatic tissue, Prostatitis and Prostatic adenocarcinoma. Benign prostatic tissue was seen in 12.93% cases in present study, 85.8% in a study by Kshitij et al,[8] 64.48% in a study by Azmi A. Haroun et al,[9] 56% in a study by Jasani et al [3] and 38% in a study by Bedarshi Banerjee et al.[10] Prostatic adenocarcinoma was seen in 49.14% cases in present study, 8.35% in a study by Kshitij et al,[8] 27.1% in a study by Azmi A. Haroun et al,[9] 32% in a study by Jasani et al [3] and 15% in a study by Bedarshi Banerjee et al.[10] Prostatitis was seen in 37.93% cases in present study, 0.64% in a study by Kshitij et al,[8] 2.7% in a study by Jasani et al [3] and 37% in a study by Bedarshi Banerjee et al.[10] The above

mentioned studies included prostate chips (TURP) as well. TURP is the gold standard of surgical treatment for benign prostatic hyperplasia.[11] Thus, more percentage of benign lesions were found in these studies and greater percentage of malignant lesions were found in present study as compared to the above mentioned studies.

Prostatic Intraepithelial Neoplasm (PIN) was reported in few studies like by Bedarshi Banerjee et al,[10] Jasani et al [3] and Kshitij et al.[8] These studies predominantly included prostate chips (TURP). In TURP specimens, the entire part of gland is sampled and examined under microscope, thus allowing more chances of diagnosing PIN as it may occur in small foci within a gland, which might go unnoticed in a biopsy, hence limiting the usefulness of prostatic biopsy.[10]

The cases of prostatic adenocarcinoma were graded according to the new ISUP/WHO classification 2019 in present study. Nine cases of Grade 1(15.79%), 4 cases of Grade 2(7.02%), 7 cases of Grade 3(12.28%), 11 cases of Grade 4(19.30%) and 26 cases of Grade 5(45.61%) were reported. In the study done by Manjit Singh Bal et al,[12] Gleason score 5-7 were seen in 62.71% cases. The next Gleason score was 2-4, seen in 23.72% cases (Total 86.43%) and in 13.55% cases the Gleason score was 8-10. In the study done by Atchyuta .M et al,[7] Gleason grade 3 was the most common primary pattern in their study. The most common secondary pattern was Gleason grade 4. Thus, the most common Gleason's score was 7 in 43% cases, 5 in 17% of cases, 8 and 9 in 12% of cases each (Total 24%), 6 and 4 in 8 % of cases. However, in present study, Grade 4 and 5 (Gleasons score 8 and 9) were most common, accounting for 64.91% of the malignant cases. Grade 1-3 were seen in 35.09% cases.

Only the cases with PSA levels were included. PSA levels in benign and malignant lesions were compared to other studies. In present study, PSA levels upto 4ng/ml was found in 8.5% of benign cases. Rest 91.5% had PSA level above 4ng/ml. In comparison, study done by Jasani et al,[3] 62.6% of benign cases had PSA upto 4ng/ml while 37.02% benign cases had PSA level above 4ng/ml.

Normal levels of serum PSA vary according to the age of the patient, in several disease processes like prostate cancer, prostatic intraepithelial neoplasia and prostatitis.[10] Serum PSA levels are slightly elevated in cases of Benign Prostatic Hyperplasia (BPH) because of prostate tissue specific protease property of PSA.[13] Kiehl and associates[14] in their study also concluded that BPH and prostatitis is associated with PSA elevation when glandular epithelium is disrupted.[14] Thus, such high percentage of benign cases with PSA level above 4ng/ml in our study can be attributed to more number of (acute, chronic and granulomatous) prostatitis cases. As high PSA levels can be found in benign conditions also, histopathology is necessary to confirm the diagnosis. In the malignant lesions, in present study 93% cases had PSA level above 4ng/ml comparable to other studies, Sladana et al [13] and Jasani et al [3] had 97.5% cases and 98.2% cases with PSA level above 4ng/ml. In a study by Dr. Nirav Hingrajia,[15] 26.5% patients had PSA levels of ≥ 20ng/ml, of which 70% patients had adenocarcinoma, 30% patients had hyperplasia; one of the later had active prostatitis. It showed that patients with markedly elevated serum PSA levels are more likely to harbor adenocarcinoma in their biopsies than benign changes.

Likewise, majority of the malignant cases in present study had PSA level above 4ng/ml. However, a small percent, 7% (4 out of total 57 malignant cases) of the malignant cases had PSA level below 4ng/ml. The lowest PSA level of 0.18ng/ml was seen in Grade 1 prostatic adenocarcinoma.

As a significant number of malignant cases (7%) had low PSA levels (upto 4ng/ml), it is imperative to carry out a TRUS biopsy whenever a clinician palpates a suspicious nodule on per rectal examination. This will enable an accurate diagnosis and early carcinomas will be detected. Thus, serum PSA determination alone, has certain limitations for the diagnosis of prostate cancer.

The study done by Atchyuta .M et al [7] showed that there is strong positive correlation between Gleason score given in prostatic adenocarcinomas and serum PSA values. The results were similar to the studies done by Karazanashvili G et al [16] and Wei -Jen Shih et al.[17] In a study by Dr. Nirav Hingrajia,[15] it was observed that the levels of serum PSA increased with increasing Gleason grade and score of the tumor. In their study, majority of cancers (76%) belonged to intermediate to high grade category. Similarly, scores were also moderate to high in majority of cases. Most of the patients having grade 3 or above showed markedly high levels of PSA. In present study, 73.1% of Grade 5 Prostatic adenocarcinoma,63.6% of Grade 4 Prostatic adenocarcinoma, 28.6% of Grade 3 Prostatic adenocarcinoma, 0% of Grade 2 Prostatic adenocarcinoma and 33.3% of Grade 1 Prostatic adenocarcinoma had PSA level > 20ng/ml.

The minimum PSA level of 0.18ng/ml and maximum PSA level of 2,521.58ng/ml was seen in Grade 1 and Grade 5 Prostatic adenocarcinoma respectively. The mean PSA level was 19.67ng/ml in Grade 1 Prostatic adenocarcinoma, 10.84ng/ml in Grade 2 Prostatic adenocarcinoma, 21.07ng/ ml in Grade 3 Prostatic adenocarcinoma, 39.06ng/ml in Grade 4 Prostatic adenocarcinoma and

399.26ng/ml in Grade 5 Prostatic adenocarcinoma. Thus, the mean PSA levels increased as the grade increased but it was statistically not significant ($p>0.05$).

Conclusion

The study demonstrates that prostatic adenocarcinoma detection requires histology. PSA levels and the results of a digital rectal examination are insufficient. Therefore, whenever a clinician palpates a hard lump during a rectal examination, a TRUS biopsy and histological study are imperative. Early diagnosis and treatment will be made possible by this. Consequently, the patient's 5-year survival rate increased.

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