



### Original Research Article

## Histomorphological Spectrum of Prostatic Lesions and Its Correlation with Prostate Specific Antigen Level

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### Abstract

**Background:** Prostatic lesions are important health problem among Indian men. Currently Prostate specific antigen (PSA) test is used widely in the diagnosis of prostatic lesions

**Aim:** To evaluate the prevalence and distribution of prostatic lesions in kanchipuram and the diagnostic use of PSA levels in screening malignant lesions of prostate.

**Material & Methods:** Prospective study of 60 cases including both benign and malignant lesions of prostate are taken as study sample, received in the department of pathology at Meenakshi medical college, Kanchipuram from January to December 2017. Sections are H&E stained and studied under microscope. PSA values are collected for all the 60 cases.

**Results:** Out of 60 cases, 20 are benign prostatic Hyperplasia (BPH), 25 are BPH with prostatitis, 7 are prostatic intra-epithelial neoplasia and 8 are prostatic adenocarcinoma. PSA values are classified as : 0-4 ng/dl as normal , 4.1-10 ng/dl mild, 10.1- 20 ng/dl moderate and >20 ng/dl severe .There is mild PSA value elevation in 40% cases, moderate elevation in 8.9% cases and severe elevation in 2.2% cases of non-neoplastic prostatic lesions. Similarly there is mild elevation of PSA value in 6.7% cases, moderate elevation in 6.7% cases and severe elevation in 60% cases in neoplastic lesions of prostate. Elevated PSA value is significantly associated with the malignant lesions with p value < 0.0001.

**Conclusion:** Prostatic lesions are more common seen in the elderly. BPH are more common than prostatic carcinoma. Prostate specific antigen level is raised in both the neoplastic and non-neoplastic lesions of prostate. But the values are significantly raised in the neoplastic lesions prostatic carcinoma. Hence the estimation of PSA level in serum can be used as a diagnostic tool for screening malignant lesions of prostate.

**Keywords:** Prostatic lesions, PSA, screening tool.

### Introduction

Prostatic carcinoma is an important growing health problem in India and is at present the second leading site cancer among males in the urban Indian population<sup>(1)</sup>. It is also the most common malignant

tumour in men over the age of 65 years. The prevalence of prostate cancer rises with age, and can reach up to 60% in men at the of age of 80.<sup>(2)</sup>. Currently prostate specific antigen (PSA) levels are being used widely for the screening and the

diagnosis of carcinoma prostrate. Its level may be elevated in patients with prostate cancer due to the leakage of PSA into the blood which are widely produced by the prostatic cancer cells and they precede clinical disease by 10 years or longer<sup>(3)</sup>. PSA has been

Used extensively over the past five decades as a marker in the diagnosis of prostate cancer along with Digital rectal examination (DRE). DRE and PSA has been recommended test in guidelines of the American cancer society since 1993 for annual check-up of men aged 50 years or above and has resulted in early diagnosis and treatment<sup>(4)</sup>.

PSA is normally formed as a proenzyme, secreted primarily by the secretory acinar cells that line the prostate and are secreted into the lumen<sup>(5)</sup>. Elevated PSA is also found in pathological conditions of the prostate such as hyperplasia, inflammation and tumours where the destruction of cell membrane leads to the release of PSA into the circulation<sup>(6)</sup>. PSA has also been noted to be detected in trace amounts in the peri-urethral glands, adrenal neoplasm, renal cell carcinoma, endometrium, normal breast tissue, breast tumour, breast milk<sup>(6)</sup>. Since PSA is normally found in low concentration in serum, elevated PSA in serum makes it an important marker of cancer<sup>(7)</sup>. Investigations reveal that every gram of cancer prostate tissue increases the value of serum PSA for 2.3 ng/ml in average, while every gram of hyperplastic tissue increases the same parameter 10 times less compared to cancer tissue<sup>(8)</sup>. The upper limit of normal for PSA values is generally considered to be 4.0ng/mL, between 4 and 20ng/mL is considered borderline and more than 20ng/mL is considered high. Patients with a PSA value greater than 4 ng/mL, regardless of DRE results, generally undergo biopsy. The cut-off value of 4.0ng/mL represents the level at which the highest sensitivity and highest specificity are present. At present there is no value of PSA for the definitive diagnosis of prostatic malignancy and a positive finding on DRE is also not always 100% specific, hence biopsy of the prostate is still required for the diagnosis of prostate malignancy<sup>(9)</sup>.

## Materials and Methods

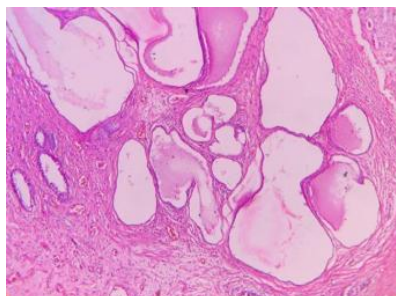
This is a prospective study done in 60 prostatic specimens including Trans-Urethral resection of prostate (TURP) and prostatic biopsies received in Meenakshi medical college hospital and research institute, Enathur, Kanchipuram from December 2016 to 2017 done on patients who had the clinical symptoms of prostatism on digital rectal examination (DRE). Specimens were fixed in 10% neutral buffered formalin, sections taken at 4 micron thickness, stained in Haematoxylin & Eosin and studied under microscope. Blood samples were collected and serum prostate specific antigen levels were evaluated. The standard protocol diagnostic methods applied for prostatic lesions were digital rectal examination (DRE), Trans abdominal ultrasonography of prostate, determination of serum PSA and biopsy of prostate. The test used for statistical analysis is the calculation of Mean, standard deviation and chi square test by using graph iPad software.

## Observations and Results

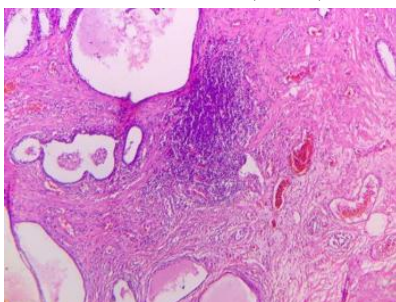
As shown in table1 the study group of 60 cases were in the age group between 45-90 years. In that, 16 cases (26.7%) were distributed in the age group of 45-60, 31 cases (51.7%) in 61-75 years and 13 cases (21.6%) in age group > 75 years. Out of the total 60 cases, 20 cases were diagnosed as Benign prostatic hyperplasia (BPH)(Fig.1), 25 cases as BPH with prostatitis (Fig.2), 7 cases as prostatic intra-epithelial neoplasia (PIN) (Fig.3) and 8 cases as prostatic adenocarcinoma (Fig.4). BPH is the most common lesion encountered among all prostatic lesions and most of the cases are associated with prostatitis with maximum incidence in age group between 61-75. Prostatic intraepithelial lesion is found from 45 years of age. Prostatic adenocarcinoma is seen more in elderly age group of more than 60 years. The mean age of the patients with BPH is 67+/-8.69, in BPH with prostatitis 68.84+/-11.56, in PIN is 68.28+/-10.98 and prostatic adenocarcinoma is 75.25+/-10.60.

**Table 1** showing age-wise distribution of prostatic lesions

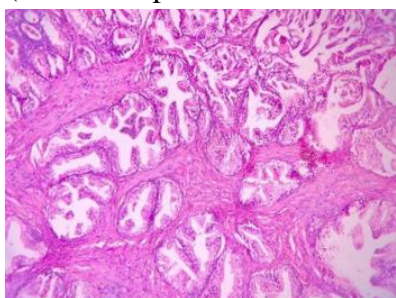
Age	BPH	BPH with prostatitis	PIN	Adenocarcinoma
45-60	6	5	4	1
61-75	12	15	0	4
>76	2	5	3	3
Total	20	25	7	8



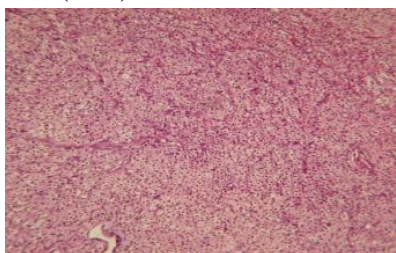
**Fig. 1** H&E (10x) showing hyperplasia of the glandular and stromal tissues (BPH)



**Fig. 2** H&E (10x) showing features of BPH along with infiltration by lymphocytes and plasma cells in the stroma (BPH with prostatitis)



**Fig.3** H&E (10x) showing prostatic glands with features of crowding, nuclear stratification and pleomorphism (PIN)



**Fig.4** H&E (40x) - showing fused glands without any intervening stroma, gleason scoring of 8 (4+4) (prostatic adenocarcinoma)

Table 2 shows the most common clinical symptom encountered in prostatic lesions is increased frequency of micturition. Second most common symptom being acute retention of urine, and the other symptoms observed are painful micturition and Hematuria.

**Table 2-** showing various clinical symptoms seen in prostatic lesions

Symptoms	No. of cases	BPH	BPH with prostatitis	PIN	Adenocarcinoma
Increased frequency of urination	34	17	10	3	4
AUR	20	1	14	2	3
Painful micturition	3	0	1	2	0
Haematuria	3	2	0	0	1
Total	60	20	25	7	8

PSA values were normal in 10 cases of BPH, 12 cases of BPH with prostatitis, 3 cases of PIN (2 low grade & 1 High grade) and 1 case of prostatic adenocarcinoma also were noted to have normal PSA levels. Mild elevation of PSA was noted in 7 cases of BPH, 11 cases of BPH with prostatitis and in 1 case of PIN( High grade). Marked elevation in of PSA was noted in 1 case of BPH, 3 cases of PIN (High grade)and 6 cases of prostatic adenocarcinoma. Mean PSA value in BPH was 4.47+/- 4.21, in BPH with prostatitis is 4.79 +/- 4.22, in PIN 19.95 +/- 28.83, and in prostatic adenocarcinoma 109.35+/-142.05was noted as shown in Table 3

**Table 3-** showing PSA levels with various prostatic lesions

PSA Level(ng /dl)	BPH	BPH with prostatitis	PIN	Adenocarcinoma
0-4	10	12	3	1
4.1-10	7	11	1	0
10.1-20	2	2	0	1
>20	1	0	3	6
Mean PSA Value	4.47 +/- 4.21	4.79+/- 4.22	19.95 +/- 28.83	109.35 +/- 142.05

**Discussion**

Carcinoma of prostate is the most common cancer in India among males due to increasing life expectancy and relatively better diagnostic methods. The gold standard triad for diagnosing prostate cancer comprised of Digital rectal examination (DRE), Prostate specific antigen (PSA) level and Transrectal ultrasonography<sup>(10)</sup>. The Digital rectal examination (DRE) has always been the primary method for evaluating the prostate.. Digital rectal examination (DRE) is neither specific nor sensitive enough to detect prostate cancer<sup>(11)</sup>. To improve the detection rate of the prostate cancer, the Digital rectal examination (DRE) should be followed by a diagnostic test with high sensitivity. Prostate specific antigen (PSA) testing provides such a method, being very sensitive. The frequency of the diagnosis of prostatic carcinoma has been substantially increased after the introduction of Prostate specific antigen (PSA) screening test.

In our study the incidence of BPH is 80% which is close with studies done by Wadgaonkar et al<sup>(12)</sup> (83.7%). The incidence of prostatic adenocarcinoma is 13.3% which is also close with studies by Wadgaonkar et al<sup>(12)</sup> (13.75%) and PIN is 11.7% which is close with Jasani et al<sup>(13)</sup> study (7.2%). The common presenting symptom is increased frequency of micturition followed by acute retention of urine. Prostatic lesions are more common in the elderly age group . Mean age is 67+/-8.69 in BPH, 68.84+/-11.56 in BPH with prostatitis, 68.28+/-10.98 in PIN and 75.25+/-10.60 in prostatic adenocarcinoma Table 4 .

**Table 4** Histopathological diagnosis in various studies

Histopathological Diagnosis	Wadgaonkar et al <sup>(12)</sup> .	Jasani et al <sup>(13)</sup>	Present stud-y
BPH +/- prostatitis	83.75%	56%	80%
Prostatic Adenocarcinoma	13.75%	32%	13.3%
PIN	1.25%	7.22%	11.7%
Transitional cell carcinoma	1.25%	11%	

In our study, Benign prostate hyperplasia is seen in maximum number 45 (75%) of cases and in that

,more than half of the cases 26 (56%) are associated with chronic prostatitis, which is comparable with the study done by Wadgaonkar et al<sup>(12)</sup>. Metaplastic changes are seen in 2 (4.4%) of the cases -one with clear cell change and the other with transitional cell metaplasia. Out of 7 cases of Prostatic intra-epithelial neoplasia (PIN), 2 are low grade and 5 are high grade lesions. Incidence of low grade lesions are less because of the difficulty in distinguishing the lesion from reactive atypia. Of total 8 cases of prostatic adenocarcinoma, 4 cases showed gleason scoring of 8, 2 cases showed 7 and 2 cases showed scoring of 2 . 8 is the commonest gleason scoring in our study with 4 as predominant architectural pattern and among 8 cases, 1 case showed peri-neural invasion. The Prostate specific antigen (PSA) values are classified as follows: 0-4 ng/dl as normal, 4.1-10 ng/dl as mild, 10.1- 20 ng/dl as moderate and >20 ng/dl as severe. Out of 60 cases, 26 (43.3%) showed normal PSA value, 19 (31.7%) showed mild elevation, 5 (8.3%) showed moderate elevation and 10 cases (16.7%) had severe elevation. In our study Mean PSA value in BPH is 4.47+/- 4.21, in BPH with prostatitis is 4.79 +/- 4.22, in Prostatic intra-epithelial neoplasia (PIN) 19.95 +/- 28.83, and in prostatic adenocarcinoma 109.35+/-142.05. There is mild PSA value elevation in 40% cases, moderate elevation in 8.9% cases and severe elevation in 2.2% cases of non-neoplastic prostatic lesions. PSA value is elevated in non-neoplastic lesions because of the disrupted glandular epithelium and digital rectal examination<sup>(12)</sup>. Similarly there is mild elevation of PSA value in 6.7% cases, moderate elevation in 6.7% cases and severe elevation in 60% cases in neoplastic lesions of prostate which is close to the study of Sanjay Kumar C. Chauhan et al<sup>(15)</sup>. Out of 5 high grade PIN lesions, one case showed normal PSA value may be because of technical error. While rest of the 4 cases showed elevated PSA levels. All the four cases with Gleason scoring 8 showed severe elevation in PSA value (>20ng/dl). Increase in PSA value is significantly associated with malignant lesions with p value <0.0001 Table 5&6.



**Table 5-** PSA value in non-neoplastic prostatic lesions

PSA value	Jasani et al(13)	Alpesh puri p.et all(14)	Sanjaykumar c. Chauhan et al(15).	Present study
Mild	63.7%	23.9%	21.6%	40%
Moderate	27.4%	69%	11.3%	8.9%
Severe	8.8%	7%	7.2%	2.2%
Normal			59.8%	48.9%

**Table 6-** PSA value in neoplastic prostatic lesions

PSA value	Jasani et al(13)	Sanjaykumar C. Chauhan et al(15).	Alpesh puri P. et al(14)	Present study
Mild	12.3%	11.7%	0%	6.7%
Moderate	82.2%	9.3%	22.2%	6.7%
Severe		74.4%	77.8%	60%
Normal	5.5%	4.6%		26.7%

**Conclusion**

Prostatic lesions are more common in the elderly age group, BPH more common than carcinoma of prostate. Prostate specific antigen level is raised in both the neoplastic and non-neoplastic lesions of prostate. But the values are significantly raised in neoplastic lesions (prostatic carcinoma). Hence the estimation of PSA level in serum can be used as a diagnostic tool for screening malignant lesions of prostate.

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**Conflict of Interest:** Nil

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