



Original Article

# Evaluation of Prostate specific antigen levels and its correlation with histopathological findings

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## Keywords:

Benign prostatic hyperplasia;  
Carcinoma;  
Prostate;  
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Prostatitis;

## ABSTRACT

**Background:** Prostate specific antigen is a tumor marker which is a glycoprotein and is expressed by both normal and neoplastic prostate tissue. The absolute value of Prostate specific antigen is useful for determining the extent of prostate cancer and its treatment. Prostate specific antigen also increases in cases like Benign Prostatic Hyperplasia and prostatitis. The availability of Prostate specific antigen as a marker has encouraged its use to diagnose both cancer and cancer recurrences.

**Materials and methods:** This is a cross sectional study conducted in a tertiary hospital over a period of two years. Cases of prostatic disease undergoing surgery during the study period were taken. Prostate specific antigen level of all these cases were correlated with clinical and histopathological findings.

**Results:** A total of 51 cases of prostatic disease underwent surgery during the study period with the mean age of  $66.57 \pm 10.68$  years. On histopathological examination, 70.6% had benign prostatic hyperplasia and 17.6% had prostatic adenocarcinoma. Prostate specific antigen level was  $<4$  ng/ml in 45.1% cases and  $>20.1$  ng/ml in 15.7%. In case of carcinoma prostate, 88.9% had prostate specific antigen level  $>20.1$  ng/ml and 11.1% had prostate specific antigen level in a range of 10.1- 20 ng/ml. In case of chronic prostatitis, 66.7% had prostate specific antigen level in a range of 4.1-10 ng/ml. However, in case of high grade prostatic intraepithelial neoplasia, 66.7% had PSA level  $<4$  ng/ml.

**Conclusion:** Strong correlation of prostate specific antigen levels of  $>20.1$  ng/ml with carcinoma prostate was seen.

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## INTRODUCTION

Prostate specific antigen (PSA) is a protein produced by the cells of the prostate gland. Enlargement of prostate gland causes urinary symptoms.<sup>1</sup> Increased PSA levels is found to be closely associated with prostate cancer. Other reasons for increased PSA could be benign prostatic hyperplasia (BPH), prostatitis or prostatic trauma.<sup>2</sup> The incidence of prostatic diseases, BPH and carcinoma increases with age.<sup>3</sup> In physiological condition, PSA is present in very low concentration (0.1 to 4.0 ng/ml). PSA is prostate specific but not specific to prostate cancer.<sup>4,5</sup> The increased value of PSA is found in 20% to 50% of men with BPH.<sup>4</sup> Approximately 10% of the male population has a PSA value higher than 10 ng/ml but do not have cancer.<sup>4</sup>

**Table 1: Age group wise distribution of various clinical diagnosis**

Age group (years)	BPH	BPH + Vesicular calculi	Ca*	GUTB**	Susp Ca <sup>‡</sup>	Total
<40	0 (0%)	0 (0%)	0 (0%)	1(100%)	0 (0%)	1 (100%)
40-49	2 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (100%)
50-59	6 (85.7%)	0 (0%)	0 (0%)	0 (0%)	1 (14.3%)	7 (100%)
60-69	18 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	18 (100%)
70-79	11 (57.9%)	1 (5.3%)	3 (15.8%)	0 (0%)	4 (21.0%)	19 (100%)
>80	3 (75%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)	4 (100%)
<b>Total</b>	<b>40 (78.4%)</b>	<b>2 (3.9%)</b>	<b>3(5.9%)</b>	<b>1 (2.0%)</b>	<b>5 (9.8%)</b>	<b>51(100%)</b>

\*-Carcinoma; \*\* - Genitourinary tuberculosis; ‡ Suspicious of Carcinoma

**Table 2: Age-group wise frequency of histopathological diagnosis (n=51)**

Age group (years)	BPH	Adeno Ca	Chronic Prostatitis	HGPIN	Total
<40	0 (0%)	0 (0%)	1 (100%)	0 (0%)	1 (100%)
40-49	2 (100%)	0 (0%)	0 (0%)	0 (0%)	2 (100%)
50-59	5 (71.4%)	2 (28.6%)	0 (0%)	0 (0%)	7 (100%)
60-69	16 (88.8%)	0 (0%)	1 (5.6%)	1 (5.6%)	18 (100%)
70-79	10 (52.6%)	7 (36.8%)	1 (5.3%)	1 (5.3%)	19 (100%)
>80	3 (75%)	0 (0%)	0 (0%)	1 (25%)	4 (100%)
<b>Total</b>	<b>36 (70.6%)</b>	<b>9 (17.6%)</b>	<b>3 (5.9%)</b>	<b>3 (5.9%)</b>	<b>51 (100%)</b>

Variations of PSA level could be due to genetic factors or many other factors that influence PSA level. Age specific reference range of PSA has the possibility to make it a good tumor marker for prostate cancer in older men. This can also be used for early detection of cancer in young men.<sup>6-8</sup> PSA is the most useful tumor marker in diagnosis and first line test in screening.<sup>3</sup> PSA levels are influenced by the patient's age and prostatic size. In healthy elderly male with no evidence of prostatic cancer, PSA increases by 3.2% per year. PSA value varies not only with advancing age but also with different geographical areas.<sup>9</sup> The availability of PSA as a marker has encouraged its use to diagnose both cancer and cancer recurrences. This study was conducted with the aim of finding out the level of PSA in prostate disease and to compare the PSA levels in different age group and to find out their correlation with histopathological diagnosis.

## MATERIAL AND METHODS

This is a cross sectional study conducted in a tertiary hospital, Nepal Medical College Teaching Hospital over a period of two years (January 2017 to December 2018). Ethical clearance to carry out the study was obtained from Institutional Review Committee (IRC) of the institute. All the cases of prostate disease presenting to Urology department and undergoing surgery during the study period were taken. PSA levels were estimated in VITROS ECiQ Immunodiagnostic System - Ortho Clinical Diagnostics. Related clinical findings were obtained from the patient's medical record file. Prostatic biopsies were sent to department of Pathology for evaluation. These biopsies were fixed overnight in 10% formalin, processed in automatic

tissue processor (Yorco) and paraffin blocks were prepared. Paraffin embedded sections were stained with Hematoxylin and Eosin (H and E) for histopathological examination and diagnosis. The data were then entered and descriptive analysis was performed in Microsoft office excel 2003.

## RESULTS

There were total of 51 cases of prostatic diseases, of which both PSA and histopathology was done. The mean age  $\pm$  SD of the patient with prostatic disease was  $66.57 \pm 10.68$  years. The youngest patient was 35 years old and eldest patient was 89 years old. The most affected group with prostatic disease was 70- 79 years (n=19; 37.3%) followed by 60- 69 years (n=18; 35.3%). BPH was the most common clinical (n=40; 78.4%) as well as histopathological diagnosis (n=36; 70.6%). (Table 1 and 2) There were 9.8% clinically suspicious carcinoma cases and 5.9% clinically diagnosed carcinoma cases. High Grade Prostatic Intraepithelial Neoplasia (HGPIN) was diagnosed in 5.9% cases on histopathology. (fig. 1)

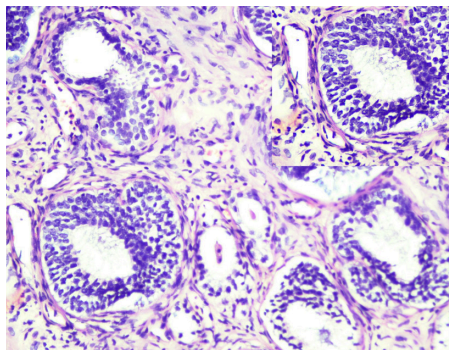
Table 3 shows clinical and histopathological diagnosis of all the cases. Different PSA value was seen in different age groups (Table 4). All the cases of clinically diagnosed carcinoma and clinically suspicious carcinoma had PSA level  $>20.1$  ng/ml. (Table 5) There were 9 cases (17.6%) of carcinoma prostate diagnosed on histopathology and out of that 8 cases (88.9%) had PSA of  $>20.1$ ng/ml. Higher range of PSA level was seen in chronic prostatitis, with 66.7% cases having PSA of 4.1-10 ng/ml and 33.3% cases having PSA of 10.1- 20 ng/ml. Out of 36 cases of BPH, 58.3% had

**Table 3: Clinical and Histopathological diagnosis of prostatic lesions (n=51)**

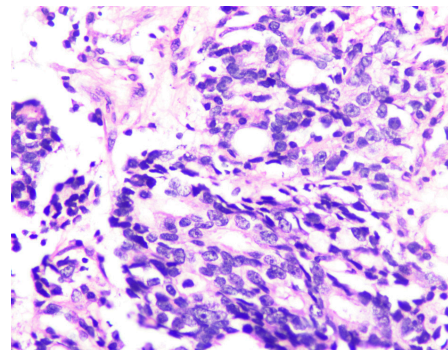
Clinical diagnosis	Number	Percentage	Biopsy Diagnosis	Number	Percentage
BPH	40	78.4%	BPH	36	70.6%
BPH with vesicular calculi	02	3.9%	Chronic Prostatitis	03	5.9%
GUTB	01	2.0%	HGPIN	03	5.9%
Ca prostate	03	5.9%	Ca Prostate	09	17.6%
Suspicious for Ca	05	9.8%			
<b>Total</b>	<b>51</b>	<b>100%</b>	<b>Total</b>	<b>51</b>	<b>100%</b>

**Table 4: PSA range in different age group (n=51)**

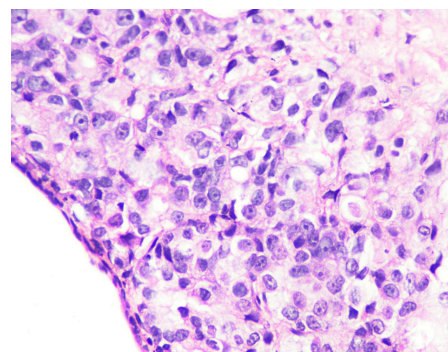
Age (years)	PSA (ng/ml)				Total
	<4	4.1-10	10.1-20	>20.1	
<40	0 (0%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)
40-49	2 (100%)	0 (0%)	0 (0%)	0 (0%)	2 (100%)
50-59	3 (42.8%)	1 (14.3%)	1 (14.3%)	2 (28.6%)	7 (100%)
60-69	10 (55.5%)	3 (16.7%)	5 (27.8%)	0 (0%)	18 (100%)
70-79	8 (42.1%)	3 (15.8%)	2 (10.5%)	6 (31.6%)	19 (100%)
>80	0 (0%)	2 (50%)	2 (50%)	0 (0%)	4 (100%)
<b>Total</b>	<b>23 (45.1%)</b>	<b>10 (19.6%)</b>	<b>10 (19.6%)</b>	<b>8 (15.7%)</b>	<b>51(100%)</b>



**Figure 1:** High Grade Prostatic Intraepithelial Neoplasia (HGPIN); (HE stain; X200). Inset showing in high power view.



**Figure 2:** Carcinoma prostate with Gleason grade 4. (HE stain; X200)



**Figure 3:** Carcinoma prostate with Gleason grade 5 (HE stain; X400)

PSA < 4 ng/ml, 19.4% had PSA level of 4.1- 10ng/ml and 22.2% had PSA level of 10.1-20 ng/ml. (Table 6)

All the cases of prostatic carcinoma were adenocarcinoma. The new grading system (5 Grade Group system), 2016 World Health Organization (WHO) for prostate cancer was used for grading all these cases. Out of the total cases, 55.6% cases were Grade Group 4 (Gleason score 8; fig. 2) and 44.4% were Grade Group 5 (Gleason score 9-10; fig. 3).

## DISCUSSION

Serum PSA levels can be influenced by any inflammation of the prostate and its mechanical stimulation.<sup>6</sup> Benign prostatic hyperplasia and prostate carcinoma are increasing

in number with advancing age and are usually uncommon before the age of 40 years.<sup>10</sup> Clinically applicable reference value for PSA is 0- 4.0 ng/ml but they don't point out the

**Table 5: Clinical diagnosis and PSA range**

Clinical Diagnosis	PSA (ng/ml)				Total
	<4	4.1-10	10.1-20	>20.1	
BPH	22 (55%)	8 (20%)	9 (22.5%)	1 (2.5%)	40 (100%)
BPH with vesicular calculi	1 (50%)	1 (50%)	0 (0%)	0 (0%)	2 (100%)
GUTB	0 (0%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)
Ca prostate	0 (0%)	0 (0%)	0 (0%)	3 (100%)	3 (100%)
Suspicious for Ca	0 (0%)	0 (0%)	1 (20%)	4 (80%)	5 (100%)
<b>Total</b>	<b>23 (45.1%)</b>	<b>10 (19.6%)</b>	<b>10 (19.6%)</b>	<b>8 (15.7%)</b>	<b>51(100%)</b>

**Table 6: Histopathological diagnosis and PSA range**

Histopathological Diagnosis	PSA (ng/ml)				Total
	<4	4.1-10	10.1-20	>20.1	
BPH	21 (58.3%)	7 (19.4%)	8 (22.2%)	0 (0%)	36 (100%)
Ca Prostate	0 (0%)	0 (0%)	1 (11.1%)	8 (88.9%)	9 (100%)
Chronic Prostatitis	0 (0%)	2 (66.7%)	1 (33.3%)	0 (0%)	3 (100%)
HGPIN	2 (66.7%)	1 (33.3%)	0 (0%)	0 (0%)	3 (100%)
<b>Total</b>	<b>23 (45.1%)</b>	<b>10 (19.6%)</b>	<b>10 (19.6%)</b>	<b>8 (15.7%)</b>	<b>51(100%)</b>

absence of carcinoma always. PSA value of 4.0- 10.0 ng/ml could be present in patients with BPH, prostatitis, intraepithelial neoplasia and prostate carcinoma.<sup>11</sup>

The result of our study showed that prostatic diseases were more common after 40 years. The mean age of the patient with prostatic disease was  $66.57 \pm 10.685$  years. This correlates with several studies.<sup>1,2,4,6</sup> Maximum number of patients were in age group 70 -79 years followed by 60- 69 years. This finding was similar to studies done in different parts of India.<sup>1,2,6</sup> A study done in Kathmandu valley showed that the maximum number of patients with prostatic disease was seen in 61-70 years age group.<sup>10</sup>

There were 36 cases (70.6%) of BPH with maximum number of cases in age group 60- 69 years. There was no case of BPH in patient less than 40 years and only 5.6% cases in age group 40- 49 years. This showed that BPH cases increases with increasing age. Majority (58.3%) of the BPH cases in our study had PSA level < 4 ng/ml. None of the BPH cases had PSA level >20.1 ng/ml. Chronic prostatitis was seen in 5.9% cases with 66.7% having PSA range of 4.1-10ng/ml and 33.3% having PSA range of 10.1-20ng/ml. Our finding was very similar to the finding in a study done by Hirachand S et al where BPH (74.2%) was the most common histological lesion seen in age group 61-70 years and among these 73.4% had PSA range of 0-7ng/ml. Prostatitis was seen in 5.5% cases and 71% of prostatitis had PSA range of 0-7 ng/ml.<sup>10</sup> Benerjee B et al also showed that BPH, BPH with prostatitis and only prostatitis were seen in 38.8%, 28.75% and 7.5% cases respectively and all these benign cases had PSA range of 0-7 ng/ml.<sup>1</sup> Similarly other studies also showed that PSA level is usually < 20 ng/ml in

case of benign conditions like BPH.<sup>12,13</sup>

Prostatic intraepithelial neoplasia was seen in 5.9 % cases in our study and all the cases were HGPIN with PSA level <10ng/ml. The studies done in two different parts of India showed similar finding (1.8% cases of PIN in each study) and the PSA level was <10 ng/ml.<sup>2,13</sup> Other studies showed 10% and 10.2% cases of PIN where PSA level was <14ng/ml.<sup>1,10</sup> Study had suggested that HGPIN is associated with carcinoma and usually if it is so the incidence of HGPIN is high as 78.9 -88%.<sup>14,15</sup> However, in our study there was no HGPIN associated carcinoma.

There were 17.6% cases of carcinoma prostate in our study. Majority of the malignant cases (77.8%) were seen in age group 70- 79 years. 88.9% had PSA level >20 ng/ml. Similar finding was seen in several other studies.<sup>10,12,15</sup> In a study done by Sridevi N et al, all the cases of carcinoma prostate showed significant elevation of PSA > 20 ng/ml.<sup>16</sup>

All the cases of carcinoma prostate were adeno carcinoma. According to new grading system (5 Grade Group system), 2016 World Health Organization (WHO) for prostate cancer, 55.6% cases were Grade Group 4 with Gleason score of 8 and 44.4% were Grade Group 5 with Gleason score of 9-10. In contrast to our study, Yelda D et al showed 5.6% cases in Grade Group 5 with maximum cases of adeno carcinoma in Grade Group 2.<sup>15</sup> Khant VS et al. showed 26.8% cases in Grade group 5.<sup>13</sup>

Studies which do not use the 5 Grade Group system had

graded tumor according to Gleason score. Bikkasani K et al found 20.7% cases with Gleason score of 8-10 in their study.<sup>12</sup> Similarly, Gleason score of 7 was seen in 51.6% and 15% cases respectively in studies done by Jaypradeep DP et al and Carter HB et al.<sup>2,17</sup>

The reason for high Gleason score in our study could be due to the late presentation of the disease. The rate of change in PSA appears to be greater in men with prostate carcinoma compared with men without disease. The change may occur at a time when the disease is not clinically evident. Hence, serial measurement of PSA may be a useful clinical marker of prostate carcinoma.<sup>18</sup>

## CONCLUSION

Serum PSA is a sensitive marker for prostatic disease and value of > 4 ng/ml is usually associated with prostatic disease. PSA is raised in both neoplastic and non neoplastic conditions. With increasing PSA, chance of carcinoma prostate is also high.

## Acknowledgement

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**Conflict of Interest:** None

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