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# Original Article

## Prostein in the diagnosis of prostate carcinoma- An immunohistochemistry study

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***ABSTRACT:***
**Background:** Prostate cancer is the second most frequently diagnosed cancer as well as the sixth leading cause of death in males with increasing incidence worldwide. The present study was conducted to assess role of P501S (prostein) in the diagnosis of prostate carcinoma. **Materials & Methods:** 58 prostate samples were fixed in buffered formalin, followed by paraffin embedding and stained with hematoxylin and eosin (H and E). Immunohistochemistry (IHC) was performed on Ventana automated stainer. The intensity of positivity was scored from 0 to 3 as follows: score 0 = nonstained; score 1 = weak; score 2 = moderate; and score 3 = strong. **Results:** Diagnosis found to be normal epithelium in 8, benign prostate hyperplasia (BPH) in 15, primary adenocarcinoma in 22, metastatic adenocarcinoma in 7 and HGPIN in 6. The difference was significant (P< 0.05). Protein expression and intensity score for normal epithelium was 100% and 1-8-2, in BPH was 100%and 2-2-7, in primary adenocarcinoma was 100% and 2-2-4, in metastatic adenocarcinoma was 100% and 1-2-2 and in HGPIN was 100% and 2-2-2 respectively. **Conclusion:** Prostein showed a specificity of 100% in differentiating various prostatic carcinoma hence, can be used in prostate lesions.
**Key words:** Adenocarcinoma, Prostein, Prostate.

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### INTRODUCTION

Prostate cancer is the second most frequently diagnosed cancer as well as the sixth leading cause of death in males with increasing incidence worldwide. Several Indian registries have revealed an increasing trend in the incidence of prostate cancer and the mean annual percentage change has ranged from 0.14 to 8.6%.[1]

Although prostate cancer is often a slow-growing malignancy, it remains the third leading cause of cancer deaths in men. Most patients are asymptomatic at diagnosis; prior to the availability of prostate-specific antigen (PSA) testing, the most common presenting symptoms were urinary retention, back pain, bone pain, and hematuria. Risk factors for prostate cancer include sub-Saharan African ancestry, family history, certain genetic mutations (BRCA 1 or 2), and older age. Due to the indolent course of the disease and the morbidity associated with overtreatment, prostate cancer screening remains a controversial topic.[3] In the past decade, a number of advances have been made in characterizing disease risk and expanding therapeutic options.[2]

The diagnosis of prostatic adenocarcinoma on histopathology depends on architectural and cytomorphological features supported by immunohistochemistry (IHC). The utility of IHC in prostate cancer is primarily for confirming the diagnosis of carcinoma in biopsy material containing atypical glands.[3] In addition, IHC helps confirm the prostatic origin of the tumor. Though all the prostate markers show excellent specificity, the sensitivity and percentage positivity vary. P501S (prostein) is a prostate-specific marker that is expressed in the

cytoplasm of benign and malignant prostatic glandular cells. It has not been detected in any other normal or malignant tissues. The new IHC markers include prostein (P501S) and NKX3.1.[4] The present study was conducted to assess role of P501S (prostein) in the diagnosis of prostate carcinoma.

## MATERIALS & METHODS

The present study comprised of 58 prostate samples obtained from general surgery department suspected of prostate carcinoma.

Information such as name, age etc. was obtained from laboratory information system. Information of cases such as ultrasound (US) or magnetic resonance imaging (MRI) findings and serum PSA values were obtained. Samples were fixed in buffered formalin, followed by paraffin embedding and stained with hematoxylin and eosin (H and E). Diagnosis of samples were performed. Immunohistochemistry (IHC) was performed on Ventana automated stainer. The intensity of positivity was scored from 0 to 3 as follows: score 0 = nonstained; score 1 = weak; score 2 = moderate; and score 3 = strong. Results thus obtained were subjected to statistical analysis. P value less than 005 was considered significant.

## RESULTS

**Table I Age distribution**

| Age group (Years) | Number | P value |
|---|---|---|
| 30-50 | 9 | 0.05 |
| 50-70 | 35 | |
| >70 | 14 | |

Table I shows that age group 30-50 years had 9, 50-70 years had 35 and >70 years had 14 patients. The difference was significant (P< 0.05).

**Table II Diagnosis of specimens**

| Diagnosis | Number | P value |
|---|---|---|
| Normal epithelium | 8 | 0.02 |
| BPH | 15 | |
| Primary adenocarcinoma | 22 | |
| Metastatic adenocarcinoma | 7 | |
| HGPIN | 6 | |

Table II, graph I shows that diagnosis found to be normal epithelium in 8, benign prostate hyperplasia (BPH) in 15, primary adenocarcinoma in 22, metastatic adenocarcinoma in 7 and HGPIN in 6. The difference was significant (P< 0.05).

**Graph I Diagnosis of specimens**

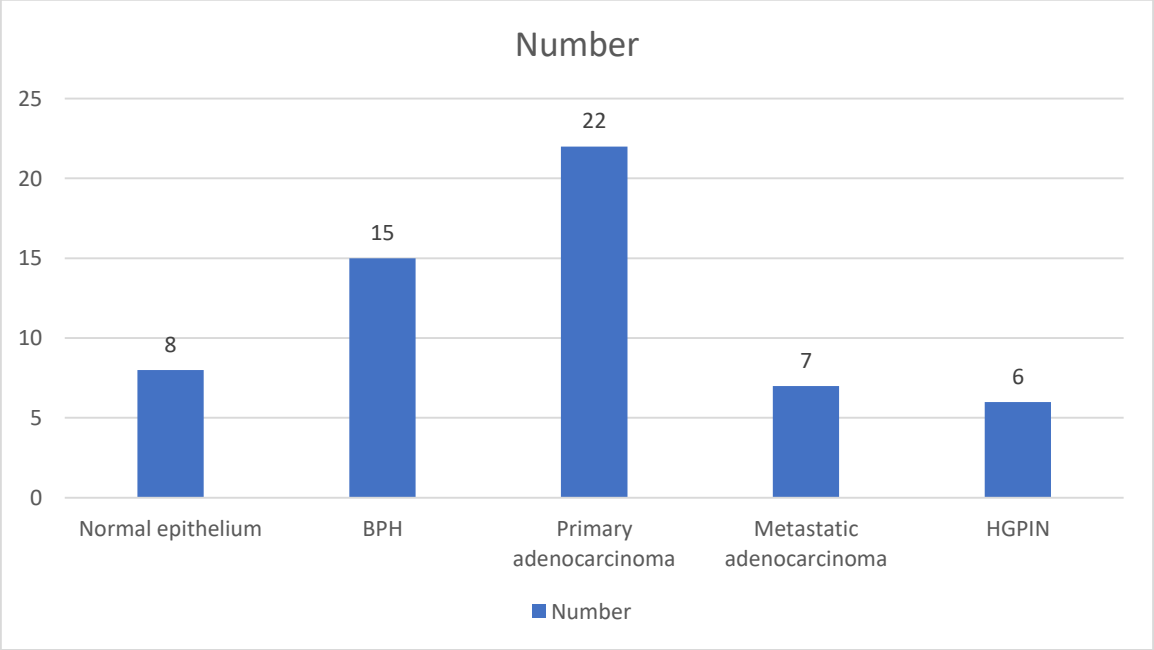

**Table III Protein expression and intensity score**

| Diagnosis | Protein expression | Intensity score |
|---|---|---|
| Normal epithelium | 100% | 1-8-2 |
| BPH | 100% | 2-2-7 |
| Primary adenocarcinoma | 100% | 2-2-4 |
| Metastatic adenocarcinoma | 100% | 1-2-2 |
| HGPIN | 100% | 2-2-2 |

Table III shows that protein expression and intensity score for normal epithelium was 100% and 1-8-2, in BPH was 100% and 2-2-7, in primary adenocarcinoma was 100% and 2-2-4, in metastatic adenocarcinoma was 100% and 1-2-2 and in HGPIN was 100% and 2-2-2 respectively.

## DISCUSSION

Although PSA is specific to prostate tissue, it is not specific to cancer. Other factors that may increase PSA levels include prostate manipulations (DRE, biopsy), prostatitis, benign prostatic hyperplasia (BPH), and ejaculation. Use of 5 alpha-reductase inhibitors leads to about a 50% decrease in PSA levels after 1 year of therapy. Some experts suggest doubling the PSA results for patients on chronic 5 alpha-reductase inhibitors to correctly interpret them. Traditionally, a PSA >4 ng/mL is considered abnormal. However, PSA values between 4 and 10 ng/mL have poor discriminating ability between BPH and prostate cancer.[5]

Prostein is a prostate-specific 553 amino acid protein identified by cDNA subtraction. Its expression is restricted to prostatic tissue and not detected in normal heart, kidney, liver, lung, or colon. Moreover, prostein expression is not related to Gleason grading; hence, it is a useful IHC marker to discriminate a prostatic origin of cancer from tumors of the bladder and the colon. Prostate carcinoma metastatic to lymph node, bone, and liver also express high levels of prostein; therefore they were regarded among the best validated immunohistochemical markers of prostatic origin.[6]

Several methods can be used to increase the specificity of PSA results and decrease unnecessary biopsies. For men with PSA values between 4 and 10 ng/mL, measurement of the percentage of free PSA should be considered. Free PSA values >25% most likely indicate BPH; these patients do not require a biopsy.[7] The rate of change in PSA over time, PSA velocity, is another tool that can be used with a PSA level between 2 ng/mL and 10 ng/mL to improve specificity. Most experts agree that for men with PSA velocity value of more than 0.35 ng/mL per year, a further workup, including biopsy, should be strongly considered.[8] The present study was conducted to assess role of P501S (prostein) in the diagnosis of prostate carcinoma.

In present study, age group 30-50 years had 9, 50-70 years had 35 and >70 years had 14 patients. Carder et al[9] studied the expression of PSA and prostein in 54 metastatic prostatic carcinomas (30 lymph nodes and 24 distant metastasis), where PSA was expressed in 87% and prostein in 86.7% of samples. The mechanisms responsible for the diminished expression of P501S in metastatic prostatic carcinomas are unknown but could be similar to those for PSA. Queisser[10] showed sensitivity of PSA, PSMA, and androgen receptor to be 97%, 94%, and 91%, respectively and concluded that sensitivity can be increased up to 98% to 100% with the combined use of PSMA and P501S.

We found that diagnosis found to be normal epithelium in 8, benign prostate hyperplasia (BPH) in 15, primary adenocarcinoma in 22, metastatic adenocarcinoma in 7 and HGPIN in 6. Protein expression and intensity score for normal epithelium was 100% and 1-8-2, in BPH was 100% and 2-2-7, in primary adenocarcinoma was 100% and 2-2-4, in metastatic adenocarcinoma was 100% and 1-2-2 and in HGPIN was 100% and 2-2-2 respectively.[11]Though all the prostate markers show excellent specificity, the sensitivity and percentage positivity vary. P501S (prostein) is a prostate-specific marker that is expressed in the cytoplasm of benign and malignant prostatic glandular cells. It has not been detected in any other normal or malignant tissues.[12] The new IHC markers include prostein (P501S) and NKX3.1. Prostein (P501S) is a prostate-specific 553 amino acid protein identified by complementary DNA (cDNA) subtraction. It is an organ-specific marker for benign and malignant prostatic epithelial cells. Its expression is restricted to prostatic tissues and unrelated to Gleason grade.

## CONCLUSION

Authors found that Prostein showed a specificity of 100% in differentiating various prostatic carcinoma hence, can be used in prostate lesions.

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