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*Full Length Research Paper*

# Histopathological study of prostatic lesions on needle biopsies with serum prostate-specific antigen (PSA)

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**Prostate develops from a series of endodermal buds from the lining of primitive urethra and the adjacent portion of urogenital sinus during the first 3 months of intra-uterine life. A prostate needle biopsy is a surgical procedure in which a small sample of tissue is removed from the prostate gland and examined under the microscope by a pathologist. In all investigated individuals, the level of prostate-specific antigen (PSA) was determined in identical way. PSA was estimated in venous blood by electro-chemiluminescence method. Histopathological analysis of obtained material was done on standard hematoxylin-eosin (H&E) preparations. Out of 60 patients studied, most of the patients 30 (50%) were diagnosed with benign prostatic hyperplasia (BHP). Higher levels of PSA (>20) was found in 57.1% of patients of BHP with chronic prostatitis table 11. Out of the total number of adenocarcinoma patients, 77.8% of the patients were having preoperative PSA levels greater than 20. In our study, the positive predictive value for increasing PSA levels was 8.3% for PSA <4 ng/ml, 16.6% for PSA >4 ng/ml, 24.2% for PSA >10 ng/ml and 83.3% for PSA >100 ng/ml.**

**Key words:** Prostate, lesions, histopathology, needle biopsies, serum prostate-specific antigen (PSA).

## INTRODUCTION

Prostate develops from a series of endodermal buds from the lining of primitive urethra and the adjacent portion of urogenital sinus during first 3 months of intra-uterine life. The surrounding mesenchyme condenses to form the stroma of the gland. Prostate utricle develops in the region of mullerian tubercle similar to uterus or vagina in females. The prostate is an accessory gland of the male reproductive system. It is a firm conical fibromuscular gland and lies in the lesser pelvis below the neck of the urinary bladder behind the lower part of the pubic symphysis and the upper part of the pubic arch anterior to the rectum. The prostate consists of stromal and glandular components. Smooth muscle cells, fibroblasts and endothelial cells are in the stroma. The glandular component is composed of acini and ducts. Both acini and ducts contain secretory cells, basal cells and neuroendocrine cells. The columnar secretory cells, stain positively with prostate specific antigen and prostatic acid phosphatase (Bostwick et al., 1997). Basal cells are less differentiated than secretory cells and so are devoid of secretory products such as prostate-specific antigen (PSA) (Warhol and Longtine, 1985). The prostate has the greatest number of neuroendocrine cells of any of the genitourinary organs (Di Sant'Agnese, 1992). Glands are structured with open and closed cell types with the open type facing the inside of the duct having a monitoring role

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**Table 1.** Histopathological diagnosis of patients (N=60).

| Diagnosis | N | % |
|---|---|---|
| BHP | 30 | 50 |
| Adenocarcinoma | 09 | 15 |
| BHP with chronic prostatitis | 07 | 11.6 |
| BHP with basal cell hyperplasia | 02 | 3.3 |
| PIN | 04 | 6.6 |
| Chronic granulomatous prostatitis | 01 | 1.6 |
| Atypical suspicious of malignancy | 01 | 1.6 |
| Inadequate | 06 | 10 |

**Table 2.** PSA in patients with BHP (N=30).

| PSA (ng/ml) | N | % |
|---|---|---|
| <4 | 11 | 36.6 |
| 4 to 10 | 09 | 30 |
| 10.1 to 20 | 07 | 23.3 |
| >20 | 03 | 10 |

95% CI of difference, P = 0.00677.

over its contents. Most cells contain serotonin, but other peptides present include somatostatin, calcitonin, gene-related peptides and katacalcin (Epstein, 1997). The cells co-express PSA and prostatic acid phosphatase. Their function is unclear but it is speculated that these cells are involved with local regulation by paracrine release of peptides (Epstein, 1997). Prostatic ducts and acini are distinguished by architectural pattern at low power magnification. The prostate becomes more complex with ducts and branching glands arranged in lobules and surrounded by stroma with advancing age.

A prostate needle biopsy is a surgical procedure in which a small sample of tissue is removed from the prostate gland and examined under the microscope by a pathologist. Prostate needle biopsy may be performed either transrectal ultrasound (TRUS) guided or by transrectal or transurethral routes. Needle biopsy of the prostate plays a central role in the evaluation of prostate cancer. The main aims and objectives of the study to be undertaken were to study the histopathology of prostatic needle biopsies for diagnosing various prostatic lesions, to correlate the histopathological findings with preoperative serum PSA levels for confirmation of diagnosis in cases with diagnostic dilemma. The present study was conducted from May 2009 to May 2010 in the Department of Pathology, Government Medical College, Srinagar, in collaboration with the Department of Surgery. This study was conducted on 60 patients present with abnormal digital rectal examination (DRE) or elevated serum PSA of >4 ng/ml or both abnormal DRE and elevated serum PSA.

## MATERIALS AND METHODS

A detailed history of every patient with particular reference to age, presenting complaints of obstructive voiding such as hesitancy, poor flow, intermittent stream, dribbling, sensation of poor bladder emptying, episodes of retention and irritative symptoms like frequency, nocturia, urgency, urge incontinence and abnormality on DRE were recorded. All patients underwent thorough general physical examination, abdominal examination including genito-urinary examination.

### PSA determination

In all investigated individuals, the level of PSA was determined in identical way. PSA was estimated in venous blood by sandwich electro-chemiluminescence method that employs a biotinylated monoclonal PSA specific antibody and a monoclonal PSA specific antibody labeled with ruthenium complex. PSA in the specimen reacts with both the antibodies forming the sandwich complex. Streptaviden coated micro particles are added and the mixture is aspirated into the measuring cell where the microparticles are captured onto the surface of electrode. Unbound substances are then removed with procell. Application of voltage to the electrode induces the chemiluminescent emission which is then measured against a calibration curve to determine the amount of PSA in the patient's specimen.

There was no immediate manipulation on prostate (DRE, prostate massage, endoscopic examination) before taking a blood sample for PSA.

### Indications for biopsy

The biopsy was performed with "Tru-cut" needle using transrectal or transperineal approach with previous preparing of patient (purgation and antibiotic protection). The indications for biopsy were an abnormal DRE suspicious of malignancy and/or high serum PSA values.

### Histopathological analysis

Histopathological analysis of obtained material was done on standard hematoxylin-eosin (H&E) preparations. Fixation of tissue samples has been done in 10% formaldehyde solution for 24 h. The tissue was processed routinely in an automatic tissue processor. Blocks were prepared and the sections cut on microtom to the thickness of 4 microns. The sections were then stained routinely by H&E method and examined under microscope. Histopathologic diagnosis was made as benign prostatic hyperplasia (BHP), chronic prostatitis, basal cell hyperplasia, prostatic intraepithelial neoplasia (PIN), adenocarcinoma and atypical suspicious of malignancy. Gleason's grading was done in the adenocarcinoma patients. The histopathological results were correlated with preoperative serum PSA levels and clinical features.

All the data was subjected to statistical analysis by simple interactive statistical analysis (SISA).

### Observation

Out of 60 patients studied, most of the patients 30 (50%) were diagnosed with BHP. Out of 60 patients studied, lesser number of patients were diagnosed with chronic granulomatous prostatitis (1.6%) and atypical suspicious of malignancy (1.6%). Out of the 4 patients diagnosed as PIN, 3 were having high grade PIN and 1 was diagnosed as low grade PIN (Table 1). The higher level of PSA (>4) was recorded in nineteen (19) patients out of 30 patients which were diagnosed with BHP (Table 2). Out of the total number of

**Table 3.** PSA in patients with adenocarcinoma (N=09).

| PSA (ng/ml) | N | % |
|---|---|---|
| <4 | 01 | 11.1 |
| 4 to 10 | 0 | 0 |
| 10.1 to 20 | 01 | 11.1 |
| >20 | 07 | 77.8 |

Median 200 (Range 3.15 to 4240), 95% CI, P = 0.0001.

**Table 4.** PSA in patients of BHP with chronic prostatitis (N=07).

| PSA (ng/ml) | N | % |
|---|---|---|
| <4 | 01 | 14.3 |
| 4 to 10 | 01 | 14.3 |
| 10.1 to 20 | 01 | 14.3 |
| >20 | 04 | 57.1 |

Mean 28.3.

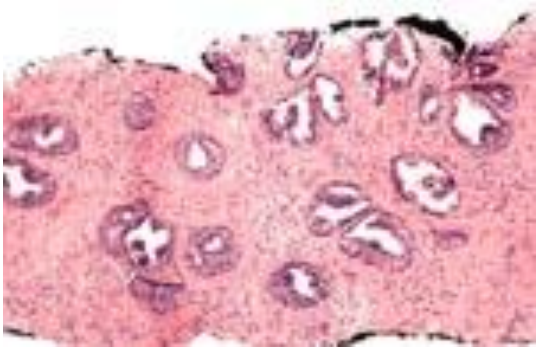

**Figure 1.** Benign prostatic hyperplasia with basal cell hyperplasia (10×).

adenocarcinoma patients, 77.8% of the patients were having preoperative PSA levels greater than 20 (Table 3). Higher levels of PSA (>20) was found in 57.1% of patients of BHP with chronic prostatitis (Table 4).

## DISCUSSION

Prostatic cancer among adult males is the most common neoplasm in most developed countries. It has been estimated that over 200,000 men in United States are diagnosed annually with prostate cancer and 300,000 men still die from this disease each year. The age-standardized incidence of prostate cancer in the European Union (EU) is 65/100,000 and the EU mortality rate is 26/100,000 per year (Brauer M). Prostate cancer incidence is increasing in India. Currently, it ranks 5th in incidence and 4th in mortality for men in Mumbai (Farnswork 1973). Prostatic carcinomas can be divided into two major categories: (1) adenocarcinoma of peripheral (secondary) ducts and acini and (2) carcinoma of large (primary) duct. There are three different growth patterns of prostatic carcinoma: glandular, cribriform and solid-undifferentiated. The prognosis of prostate carcinoma depends largely on the degree of differentiation. Therefore, the pathologist plays an important part in diagnosis and therapeutic decisions (Foster and Deshmukh, 1992).

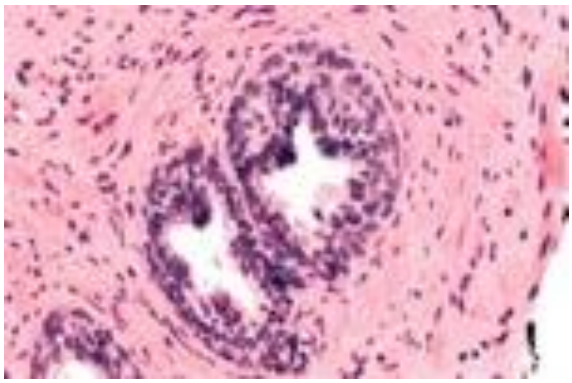

**Figure 2.** Basal cell hyperplasia (40×).

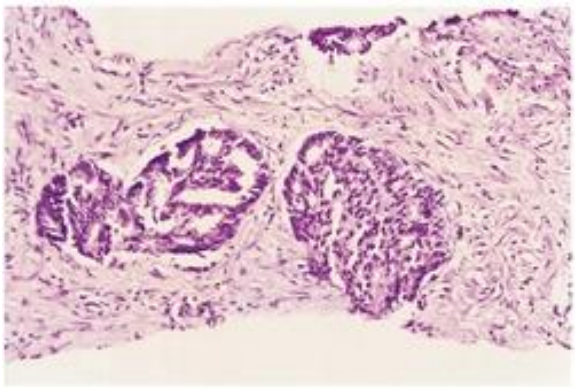

**Figure 3.** High grade prostatic intraepithelial neoplasia (PIN; 40×).

Out of 60 patients, 30 (50%) patients were diagnosed as benign prostatic hyperplasia (BPH) (Figures 4 and 5), 7 (11.6%) patients were diagnosed as BHP with chronic prostatitis, 2 (3.3%) were diagnosed as BHP with basal cell hyperplasia (Figures 1 and 2), 9 (15%) were diagnosed as adenocarcinoma (Figures 6, 7 and 8), 4 (6.6%) were diagnosed as prostatic intraepithelial neoplasia (PIN) (Figure 3) and 1 (1.6%) was diagnosed as chronic granulomatous prostatitis (Figure 5). Out of 60 patients, 6 (10%) patients had an inadequate biopsy material on histopathological examination and 1 (1.6%) patient was having atypical glands suspicious of adenocarcinoma. These results were nearly comparable with the studies conducted by Gupta et al. (2005) and Iczkowski et al. (1998) Mean age of the patients was 64.8 years and mean serum PSA was 120.5 n/ml.

**Figure 4.** Benign prostatic hyperplasia showing corpora amylacea (40×).

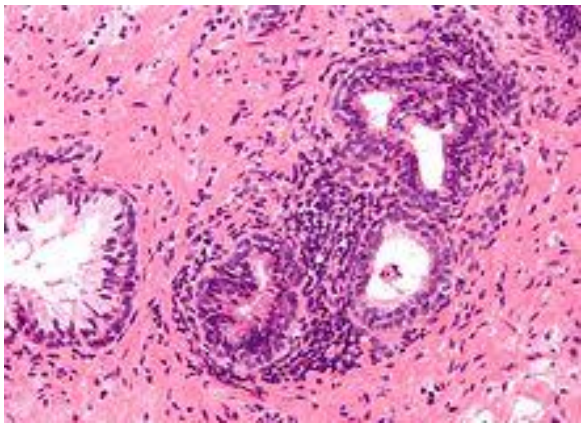

**Figure 5.** Benign prostatic hyperplasia with chronic prostatitis (40×).

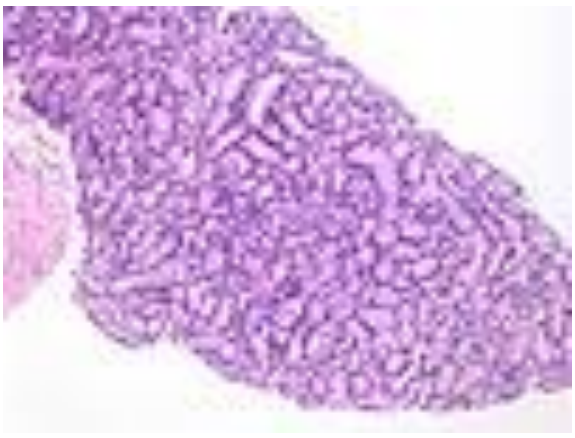

**Figure 6.** Prostatic adenocarcinoma (Gleason's pattern 4; 10×).

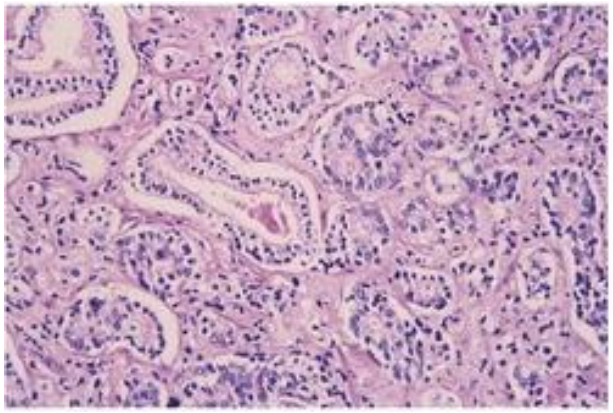

**Figure 7.** Prostatic adenocarcinoma (Gleasons pattern 3 & 4; 40×).

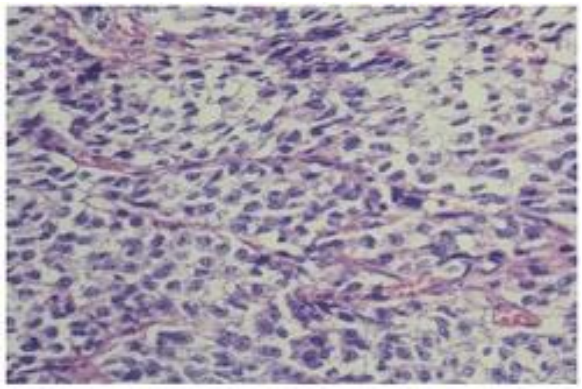

**Figure 8.** Prostatic adenocarcinoma (Gleasons pattern 5; 40×).

In patients with BHP, 11 (36.6%) had serum PSA of less than 4 ng/ml, 9 (30%) had serum PSA in the range of 4 to 10 ng/m and 10 (33.3%) patients had serum PSA more than 10 ng/ml. Mean serum PSA was 8.9 ng/ml. Our results were comparable with the studies conducted by Ferro et al. (1987) and Amayo and Obara (2004).

Almost all patients (89%) with adenocarcinoma had raised serum PSA of more than 10 ng/ml, only one patient (11%) was having a serum PSA of less than 4 ng/ml. Mean serum PSA was 703.95 ng/ml. Median PSA was 200 ng/ml (range 3.15 to 4240 ng/ml). This study revealed a statistically significant correlation between serum PSA and adenocarcinoma. These findings were consistent with the study conducted by Berman et al. (1994)

In this study, the positive predictive value for increasing PSA levels was 8.3% for PSA <4 ng/ml, 16.6% for PSA >4 ng/ml, 24.2% for PSA >10 ng/ml and 83.3% for PSA >100 ng/ml. In this study, the detection rate of prostate cancer in patients with serum PSA between 3 and 4 ng/ml was 14%. These findings were consistent with the study conducted by Aus (1998).

Our study revealed a PSA value of >4 ng/ml in men of 50 years age or older was associated with 20% chance of

detecting prostate cancer on the initial diagnostic biopsy. These interpretations were not comparable with the study conducted by Catalona et al. (1998) and this may be due to smaller number of patients in the study.

In the study, 22 patients present with acute urinary retention and had raised PSA values. Out of these, only 6 (22%) were positive for adenocarcinoma, which raised the false positive rate of PSA as a method for detecting carcinoma. It was concluded that acute urinary retention is associated with raised PSA levels. These findings were comparable with the studies conducted by McNeal (1978) and Chawla et al. (2003)

In the study, there was a statistically significant correlation between serum PSA and prostatomegaly. With increase in prostate size, serum PSA was also increasing, and there was also statistically significant correlation between serum PSA and histological inflammation in the prostate. These interpretations were comparable with the studies conducted by Okada et al. (2000).

In patients with BHP, 11 (36.6%) had serum PSA of less than 4 ng/ml, 9 (30%) had serum PSA in the range of 4 to 10 ng/m and 10 (33.3%) patients had serum PSA more than 10 ng/ml. Mean serum PSA was 8.9 ng/ml and almost all patients (89%) with adenocarcinoma had raised serum PSA of more than 10 ng/ml, only one patient (11%) was having a serum PSA of less than 4 ng/ml. Mean serum PSA was 703.95 ng/ml. Median PSA was 200 ng/ml (range 3.15 to 4240 ng/ml).

This study revealed that no level of PSA was associated with a 100% positive predictive value and negative biopsy can occur virtually at any PSA level.

## Conflict of Interests

The author(s) have not declared any conflict of interests.

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