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Original Research Article.

Evaluation of Prostate Specific Antigen Levels and Its Correlation with Histopathological Findings in a Tertiary Care Hospital in Bihar

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ABSTRACT

Background: Diseases primarily inflicting prostate gland are inflammation, benign prostatic hyperplasia and cancer. Prostate specific antigen is a glycoprotein and is expressed by both normal and neoplastic prostate tissue. It has been widely used in the diagnosis and management of patients with prostatic cancer. Studies from various research workers discuss the proportion of prostatic disorder among Indian states like Delhi, Mumbai, Bangalore, Chennai, Gujrat etc but there is paucity of data from the rural areas. The present study was conducted to find out the patterns of prevalence of prostatic lesions among people of Rohtas district of Bihar and to correlate histology with respect to serum PSA levels in biopsy specimens of men with prostatic disease.

Materials and Methods: The study included 153 prostatic tissue specimens (both transurethral resection of the prostate and prostatic biopsies) received in the Department of Pathology, over the period of 2-year from October 2017 to September 2019. Relevant clinical data and serum PSA value was recorded, and Gleason's microscopic grading was used to grade malignant lesions. Statistical analysis was performed in Microsoft office excel 2007.

Results: Mean age of presentation was 63 ± 10.56 years with maximum incidence in the seventh decade of life. On histopathological examination, 52.9% had benign prostatic hyperplasia, 35.9% had BPH with chronic prostatitis and 8.5% had adenocarcinoma. Other lesions encountered were high-grade prostate intraepithelial neoplasia (3 cases), sarcomatoid carcinoma (1 case). Inflammatory pathology (55/153) was common at all PSA levels. Patients with PSA >20 ng/ml were were more likely to show cancer. There exists a positive correlation between the increasing PSA levels and chances of adenocarcinoma, the findings were statistically significant.

Conclusion: Our study suggests that most frequently encountered prostatic lesion was BHP, commonly seen in the age group of 51-60 year The malignant lesions were common among the males of more than 60 years. Strong correlation of prostate specific antigen levels of > 20.1 ng/ml with carcinoma prostate was seen.

Key Words: Benign Prostate Hyperplasia, Prostatitis, Serum Prostate-Specific Antigen (PSA), Adenocarcinoma.

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INTRODUCTION

Prostate is one of the most commonly affected organs in males with increasing age, accounting for significant morbidity and mortality. The most important categories of prostatic diseases are inflammatory lesions (prostatitis), benign prostatic hyperplasia, and carcinoma.[1]

Transurethral resection of prostate (TURP) specimens form a significant percentage of diagnostically challenging cases in surgical pathology.[2]

Enlargement of prostate gland causes dysurea and retention of urine leading to prostatectomy. Currently, there is an increasing trend of the occurrence of both neoplastic and nonneoplastic lesions of the prostate, particularly in the elderly.[3] Prostate specific antigen (PSA) is a protein produced by the cells of the prostate gland exclusively.[4] Due to the influence of pathological processes, the cell integrity is lost leading to the release of prostate specific antigen (PSA) into circulation, i.e., the processes inside prostate, such as hyperplasia, inflammation, tumors, may lead to the increase of serum PSA value. The increase in PSA values also depends on upon the differentiation of tumor cells. It can also be raised in benign prostatic hyperplasia (BPH) and in conditions that lead to prostatic ischaemia, inflammation and infarction.[5]

PSA is the most useful tumor marker in diagnosis and first line test in screening of prostate cancer. Currently, many men are identified as having early prostate cancer through the use of prostate specific antigen (PSA) screening.[6] 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. The availability of PSA as a marker has encouraged its use to diagnose both cancer and cancer recurrences.[7] Since PSA level can increase in nonmalignant conditions like benign prostatic hyperplasia, inflammation, diagnostic and surgical procedures, these conditions can mimic cancer and cause confusion in diagnosing especially in prostatic carcinoma where PSA is used as a screening test.[8]

Studies from various research workers have shown that the proportion of prostatic disorders has been done for different states of India [9] but it appears that there has been no study carried out at Bihar. In view of above a study has been made to find out the prevalence of prostatic disorders and determine the correlation between serum PSA level and histological findings in biopsy specimens of men with prostatic disease in Rohtas district of Bihar.

MATERIALS AND METHODS

The hospital based retrospective study was carried out at Department of Pathology, Narayan Medical College & Hospital, Sasaram, Bihar from October 2017 to September 2019. The present study was started after obtaining ethical clearance from the institutional ethical committee. A total of 153 prostatic biopsy specimens were received included simple and radical prostatectomy, transurethral resection of prostate (TURP) and Trucut biopsies. Inadequate biopsy material, follow-up cases, posts therapeutic and recurrent tumours were excluded from the present study. Relevant clinical data of each patient about age, presenting symptoms, and provisional clinical diagnosis were collected from indoor case papers and biopsy requisition forms. The PSA levels were estimated in Department of Biochemistry. Serum PSA level (total PSA assay) of all patients were performed by Erba LISASCAN EM automated microplate analyzer using commercially available BIOS enzyme-linked immunosorbent assay (ELISA) test kit for PSA by enzyme immunoassay quantitative method. The assay procedures followed were as per kit inserts of the manufacturer.

Prostatic biopsies were sent to department of Pathology for evaluation. Biopsies were fixed in 10% formalin. Routine paraffin processing of tissue and hematoxylin and eosin staining was done. In cases of Trucut biopsies, all the tissue received was fixed and processed. In cases of TURP chips 3-4 cassettes were prepared in each case. In case of prostatectomy specimens, multiple sections were made at the distance of 3-5 mm; the slice in which tumor appears closest to the resection margin was submitted entirely after dividing into an adequate number of sections. Special stains like ZN were performed whenever necessary. Sections were examined under light microscopy. Diagnostic criteria followed for diagnosing benign prostatic hyperplasia (BPH), prostatitis, prostatic intraepithelial neoplasia (PIN), and adenocarcinoma were adapted from guidelines laid down by World Health Organization (WHO) 2004.[9] Gleason's score as laid down by WHO was followed for grading adenocarcinoma.[9] The data were then entered and descriptive analysis was performed in Microsoft office excel 2007.

The histopathological diagnosis was compared with PSA levels to determine the sensitivity and specificity of PSA assay.

Table 1: Frequency of Cases in Different Age Groups

Age Interval (in years)	Frequency	Percentage (%)
40-49	11	7.2
50-59	37	24.1
60-69	54	35.3
70-79	39	25.5
80-89	11	7.2
90-99	01	0.7
TOTAL	153	100

Table 2: Distribution Of Different Types Of Lesions

LESION	No of Patients	Percentage (%)
BPH	81	52.9
BPH with prostatitis	55	35.9
Adenocarcinoma	13	08.5
HGPIN	03	02.0
Sarcomatoid carcinoma	01	0.7
Total	153	100

Table 3: Age Distribution Of Various Prostatic Lesions.

Age group	BPH	BPH with prostatitis	Adenocarcinoma	HGPIN	Sarcomatoid carcinoma	Total n (%)
40-49	6	5	0	0	0	11 (7.2)
50-59	27	7	3	0	0	37 (24.1)
60-69	23	24	6	1	0	54 (35.3)
70-79	20	15	2	2	0	39 (25.5)
80-89	5	3	2	0	1	11 (7.2)
90-99	0	1	0	0	0	01 (0.7)
TOTAL	81	55	13	3	1	153(100)

Table 4: Histopathology Diagnoses Related With Mean PSA Level

HP diagnosis	PSA level (mean±SD)
BPH	7.32 ± 5.74
Adenocarcinoma	79.40 ± 52.78.
Prostatitis	15.19 ± 14.38
HGPIN	28.63 ± 5.07

PSA: Prostate specific antigen, HGPIN: High grade proastatic intraepithelial neoplasm,
BPH: Benign prostatic hyperplasia

Table 5: Correlation of PSA Level And Various Prostatic Lesions

PSA level (ng/ ml)	BPH	BPH with prostatitis	Adenocarcinoma	HGPIN	Sarcomatoid carcinoma	Total n (%)
0-4	19	02	0	0	0	21(13.7)
4.1-10	50	20	1	0	0	71(46.4)
10.1-20	09	24	1	1	0	35(22.9)
>20	03	09	11	2	1	26(17)
TOTAL	81	55	13	3	1	153(100)

RESULTS

The present study constituted a total of 153 cases, age ranged from 41 to 90 years (mean 63± 10.5 years) diagnosed with benign (BPH and BPH with prostatitis), premalignant (LGPIN and HGPIN) and malignant (adenocarcinoma prostate) lesions of prostate. Maximum number of cases (n=54; 35.3%) were in the age group of 60-69 years followed by 70-79 years age group (n=39; 25.5%) and 50-59 years age group (n=37; 24.1%). 11 cases (7.2%) were observed younger than 50 years of age while 12 cases were older than 80 years. The spectrums of lesions in prostatic biopsy seen in our institution were as follows-of 153cases, 81 (52.9%) were of BPH, which formed the majority of lesions, followed by BPH with prostatitis, 55 (35.9%). 13 (8.5%) cases were of adenocarcinoma. There were 3 (2%) cases of HGPIN and 1 (0.7%) of sarcomatoid carcinoma. [table 2]

Benign prostatic hyperplasia (BPH) was the most common histological lesion encountered (n=81; 52.9%) with maximum incidence seen in 50-59 age group (27 cases). Prostatic adenocarcinoma was seen a decade older than those with benign lesions. BPH with prostatitis was seen in all age groups with maximum incidence in 60-69 age groups (Table 3)

BPH cases had mean PSA level of 7.32±5.74 ng/ml with normal level (<4 ng/ml) found in 19 (23.46%) cases; mild elevation (4-10 ng/ml) was seen in 50 (61.73%) cases; modest elevation (10.1-20 ng/ml) was seen in 9 (11.11%) cases; marked elevation of PSA (>20 ng/ml) was seen in 3 (3.70%) BPH cases. Adenocarcinoma cases had mean PSA level of 79.40±52.78 ng/ml and marked elevation of PSA (>20 ng/ml was seen in 11 (84.6%) cases out of which 6 cases had PSA level of >90 ng/ml. Prostatitis cases showed mean PSA level of 15.19±14.38 ng/ml and HGPIN cases had mean PSA level of 28.63±5.07 (Table 4-5)

DISCUSSION

The present study was conducted over the period of 2-year from October 2017 to September 2019.The study included 153 prostatic tissue specimens (both transurethral resection of the prostate and prostatic biopsies) received in the Department of Pathology, Narayan Medical College, Sasaram, Bihar. Out of which 81 cases of BPH, 55 cases of BPH with prostatitis, 13 cases of adenocarcinoma, 3 cases of prostatic intraepithelial neoplasia and 1 case of sarcomatoid carcinoma were identified. The result of our study showed that prostatic diseases were more common after 40 years. In the present study age ranged from 41 to 90 years and mean age was 63± 10.5 years. This is in agreement with the mean age reported by multiple studies including Khant et al.[10] (66.9 ± 9.4 years), and Lakhey et al.[8] (67.6 years). Maximum (35.3%) patients were in the sixth decade. BPH was more common in age group of 50-59 years and malignant lesion in age group of 60-69 years. In a similar study, Anunobi et al.[11] described prostate carcinoma to be prevalent in a mean age of 66 years and peak prevalence in the age group of 60–69 years. No case was found below the age of 40 and there were only 7.2% cases in age group 40- 49 years. This showed that prostatic diseases increase with increasing age.

This study shows 88.8% of the cases as benign (BPH and BPH with prostatitis) while 11.2% of cases malignant (HGPIN and adenocarcinoma). Similar studies done by Puttaswamy et al.[12] and Benerjee B et al.[13] also encountered benign lesions constituting 80.6%, 75% and malignant lesions constituting 19.4%, 25% respectively. In our study, we found 2.0% cases of HGPIN lesions. This is almost correlating with the findings of the study by Shakya et al.[13] they found two cases of PIN among 106 cases (1.88%). The incidence of prostatic adenocarcinoma was 8.5% in our study, which correlates with studies done by Kshitij et al.[14] and Shashidhar MR et al.[15] where they reported 8.35% and 8.1 % malignant cases in their studies.

PSA is the preferred serum marker for Prostatic carcinoma. Unfortunately, PSA is specific for prostate tissue but not for prostate cancer. It is also found in abnormal concentrations in normal and benign changes of the prostate such as BPH and other non-neoplastic prostatic lesions.[16] The usefulness of PSA as an early detector of prostate cancer by itself is questionable, owing to the overlap in PSA values seen in patients with BPH and in those with organ-confined Prostate cancer. Apart from prostatic volume, other factors contributing to increase in PSA in men is age, episodes of subclinical or clinical prostatitis, intermittent bouts of prostatic ischemia, infarction and the presence of prostate cancer.[17]

In the present study, Majority (61.73%) of the BPH cases had mild elevation (4-10 ng/ml) of PSA level. Only 3.7% of the BPH cases had PSA level >20.1 ng/ml. Our finding is very similar to the finding in a study done by Hirachand S et al.[18] 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.

BPH with prostatitis was seen in 35.9% cases with 43.6% having PSA range of 10.1-20ng/ ml and 36.4% having PSA range of 4.1-10ng/ml. Umbehr MH et al.[19] and Kiehl R et al.[20] in their studies concluded that BPH and prostatitis is associated with high serum PSA, when glandular epithelium is disrupted which support this finding in the present study.

There were 13 (8.5%) cases of carcinoma prostate in our study. Mean PSA level in Adenocarcinoma was 79.40 ± 52.78ng/ml. 11(84.6%) cases of carcinoma patients had PSA level >20 ng/ml. Out of these 11 cases, 6 cases were having prostate specific antigen level of even more than 90 ng per ml. Similar finding was seen in several other studies.[21,22] In a study by Dr. Nirav Hingrajia 26.5% patients had PSA levels of ≥ 20ng/ml, of which 70% patients had adenocarcinoma and 30% patients had hyperplasia. It showed that patients with markedly elevated serum PSA levels are more likely to harbor adenocarcinoma in their biopsies than benign changes. One case of sarcomatoid carcinoma of prostate was found in a labourer class patient having PSA value 168ng/ml.

A higher incidence of HGPIN was found in a study by Maru et al.[17] in Gujrat with a majority showing a modest to severe elevation of PSA compared to our case which showed a severe elevation of (PSA>20 ng/ml). This difference could be due to very small size of our study.

CONCLUSION

Our study concluded that BPH was the commonest pathology followed by adenocarcinoma encountered in prostate specimens. Most of the diseases of prostate occur in the age group of 60–69 years. Adenocarcinoma patients have higher age group affected as compared to BPH patients. Serum PSA is a sensitive marker for prostatic disease and value of Serum PSA > 4 ng/ml is usually associated with prostatic disease. PSA is raised in both neoplastic and non-neoplastic conditions but the chances of finding malignancy increases with rising values of PSA. So PSA alone should not be used as a marker of malignancy but should be measured periodically in elderly men as a screening tool.

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