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ORIGINAL RESEARCH ARTICLE

PROSTATE BIOPSIES AND ITS ASSOCIATION WITH PROSTATE SPECIFIC ANTIGEN IN PATIENT ATTENDING BIRAT MEDICAL COLLEGE TEACHING HOSPITAL

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ABSTRACT

Background: Prostate cancer is the most common malignant tumor in men over the age of 65 years. Most frequently encountered diseases of the prostate are benign prostatic hyperplasia, prostatitis and carcinoma. Prostate specific antigen is a tumour marker and is expressed by both normal and neoplastic prostate tissue. This study was done to determine the association between histopathological diagnosis in prostatic biopsy and serum prostatic specific antigen level.

Methods: This was a hospital based cross sectional study carried out in the Department of Pathology, Birat Medical College from February 15, 2020 to October15, 2020. All consecutive patients attending the pathology department with prostate biopsy and serum PSA level were included in the study. Histopathological examination was done and its association with serum prostatic specific antigen level was done.

Results: In the biopsy findings, Benign Prostatic Hyperplasia (BPH)was the most common case seen in 41 (48.8%) cases out of 84 cases. Majority of benign cases (BPH and BPH with prostatitis) were seen in the PSA range of 0-7ng/ml. Maximum cases of adenocarcinoma were seen in the range of >20ng/ml. Chi-Square test showed a value of 5.89 while P value was <0.01 indicating that the increasing serum PSA level is associated with higher chance of adenocarcinoma.

Conclusions: PSA is a specific marker for prostatic tissue. It can be raised in benign lesions of the prostate due to membrane disruption. However, an increased PSA level above 20 ng/ml increases the chance of detecting malignant lesions.

INTRODUCTION

The prostate is a gland of male reproductive system. It has concentric inner and outer zones where clinically detectable benign prostatic hyperplasia (BPH) involves the central inner region and carcinoma affects the outer zone.[1] Microscopically, the prostate gland consists of compound tubule alveolar glands lined by a double layer of cells, a basal layer of low cuboidal epithelium covered by columnar secretory cells. The most frequently encountered diseases of the prostate are BPH, prostatitis and carcinoma whose incidence increases with advancing age.[2]

The prostate specific antigen(PSA) is a glycoprotein secreted by the prostatic epithelial cells.[3] It is present in very low concentration (0.1 to 4.0 ng/ml) in physiological condition.[4] Numerous investigations conducted have revealed that every gram of cancer prostate tissue increases the serum PSA value for 2.3 ng/ml in average, while every gram of hyperplastic tissue increases the same parameter 10 times less compared to cancer tissue.[5] Under the influence of pathological processes, serum PSA level increases due to loss of the cells integrity leading to the release of PSA into circulation.[6]

Prostate Acid Phosphatase (PAP) is also a tumor marker specific for prostate cancer. However, due to simplicity and cost effectiveness which are the essential characteristics of a screening test, PSA remains essential for prostate cancer diagnosis and management.[7] Sometimes, diagnostic dilemmas occur which can be minimized after having the PSA level. The main objective of this study was to see the association of the prostatic biopsies' findings with the PSA level.

METHODS

This was a hospital based cross sectional study carried out from 15th February 2020 to 15th October 2020 in the department of Pathology, Birat Medical College. All consecutive patients attending the histopathology unit of Department of Pathology with prostate biopsy and serum PSA level during the study period were taken. The serum PSA levels were estimated using the Snibe Maglumi 800 system. The received transurethral resection of prostate (TURP) biopsies were fixed in 10% formalin, processed and stained with Hematoxylin and Eosin

stain for histopathological examination.

Biopsy sample without PSA level, patient with complaint of Urinary Tract Infection (UTI) or immediate per rectal examination done, patients under chemotherapy for prostate carcinoma or already undergone surgery for prostate carcinoma were excluded from the study. Ethical clearance was obtained from the Institutional Review Committee (IRC) of the institute to carry out the study.

Histopathological diagnosis were categorized into benign (BPH and BPH with prostatitis), premalignant (LGPIN and HGPIN) and malignant (adenocarcinoma prostate).[10] Due to zero or small numbers of observations in some cells in the classification of histopathology diagnosis, it was further grouped into two categories for analysis. Two categories were (i)Benign with BPH and BPH with prostatitis and (ii) Adenocarcinoma and PIN.

Data were entered into Microsoft excel and the transferred to SPSS version 16 for the analysis. Frequencies and percentages were used to present the data. Chi-square test was used to assess the associations of prostate specific antigen level and histopathological findings. A p-value less than 0.05 was considered as statistically significant.

RESULTS

The total number of TURP samples received was 84, of which both prostatic biopsy and PSA was done. Thirty-seven (44.0%) cases were seen in the age group of 70-79 years. Histopathological diagnosis was categorized into benign (BPH and BPH with prostatitis), premalignant (LGPIN and HGPIN) and malignant (adenocarcinoma prostate). In the biopsy findings, BPH was the most common case seen in 41 (48.8%) with maximum incidence seen in the 60-69 years age group (13 cases). A total of 25 (29.8%) biopsies were of BPH with prostatitis. Low grade intraepithelial neoplasia (LGPIN) and high-grade intraepithelial neoplasia (HGPIN) cases were 5(5.9%) and 3 (3.6%) cases respectively. A total of 10 (11.9%) cases were those of prostatic adenocarcinoma and were seen predominantly in the 70-79 years age group (Table 1).

The PSA values were classified into intervals of 7ng/ml. 10The different PSA value was seen in different age groups. The PSA value, when correlated with age group, showed that maximum number of cases (n=49;58.3%) had PSA within range of 0-7 ng/ml and lowest number of cases (n=2;2.4%) had PSA within range of 28.1-35 ng/ml (Table 2).

Table 1: Histopathological diagnosis in different age group

Age group (years)	BPH	BPH with prostatitis	LGPIN	HGPIN	Adenocarcinoma	Total
40-49	2 (4.9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (2.4%)
50-59	3 (7.3%)	4 (16.0%)	0 (0%)	0 (0%)	1 (10.0%)	8 (9.5%)
60-69	13 (31.7%)	4 (16.0%)	3 (60.0%)	0 (0%)	2(20.0%)	22 (26.2%)
70-79	12 (29.3%)	13 (52.0%)	2 (40.0%)	3 (100%)	7 (70.0%)	37 (44.0%)
>80	11 (26.8%)	4 (16.0%)	0 (0%)	0 (0%)	0 (0%)	15(17.9%)
Total (%)	41 (48.8%)	25 (29.8%)	5 (5.9%)	3 (3.6%)	10 (11.9%)	84 (100%)

Table 2: Serum PSA value (ng/ml) in different age group

Age group (years)	PSA (ng/ml)						
	0-7	7.1-14	14.1-21	21.1-28	28.1-35	>35	Total
40-49	2 (4.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (2.4%)
50-59	5 (10.2%)	1 (7.7%)	1 (20.0%)	0 (0%)	0 (0%)	1 (14.3%)	8 (9.5%)
60-69	11 (22.4%)	8 (44.4%)	1 (20.0%)	2 (66.7%)	0 (0%)	0 (0%)	22 (26.2%)
70-79	21 (42.9%)	5 (27.8%)	2 (40.0%)	1 (33.3%)	2(100.0%)	6 (85.7%)	37 (44.0%)
>80	10 (20.4%)	4 (22.2%)	1 (20.0%)	0 (0%)	0(0%)	0 (0%)	15 (17.9%)
Total (%)	49 (58.3%)	18 (21.4%)	5(6.0%)	3 (3.6%)	2 (2.4%)	7 (8.4%)	84 (100%)

Table 3 shows distribution of lesions depending upon the histopathological diagnosis and PSA values. Majority of benign cases (n=43; 51%) had PSA within range of 0-7ng/ml. Maximum cases of PIN (n=5;6.0%and n=3;3.6%) had PSA within range of 0-7 or 7.1-14 ng/ml respectively. Majority of adenocarcinoma (n=8; 9.5%) had PSA within range of >21ng/ml.

Table 3: PSA range and Histopathological diagnosis

PSA (ng/ml)	Histopathological Diagnosis					
	BPH	BPH with prostatitis	LGPIN	HGPIN	Adenocarcinoma	Total
0-7	27(65.9%)	16(64.0%)	3(60.0%)	2(66.7%)	1(10.0%)	49(58.3%)
7.1-14	12(29.3%)	3(12.0%)	2(40.0%)	1(33.3%)	0(0%)	18 (21.4%)
14.1-21	2(4.9%)	2(8.0%)	0(0%)	0(0%)	1(10.0%)	5 (6.0%)l
21.1-28	0(0%)	0(0%)	0(0%)	0(0%)	3(30.0%)	3 (3.6%)
28.1-35	0(0%)	0(0%)	0(0%)	0(0%)	2(20.0%)	2 (2.4%)
>35	0(0%)	4(16.0%)	0(0%)	0(0%)	3(30.0%)	7(8.3%)
Total	41	25	5	3	10	84 (100%)

Table 4: Association between prostate specific antigen (PSA) level and histopathological findings among study subjects (n=84)

PSA level (ng/ml)	Benign (BPH and BPH with prostatitis)	Adenocarcinoma and PIN	χ2	p-value
≤7	43 (65.2%)	6 (33.3%)	5.89	<0.01.
>7	23 (34.8%)	12 (66.7%)		

The study found serum PSA levels is associated with Histopathology. Increased PSA levels was found in Adenocarcinoma and PIN (66.7%) compared to Benign (BPH and BPH with prostatitis) (34.8%) and the association was found to be significant (p<0.01) shown in Table 4.

DISCUSSION

Prostate gland enlarges slowly from birth to puberty after which it increases rapidly in size until the age of 21 to 30 years, at which point the prostate weighs 20 gram on average. BPH and carcinoma cases are extremely low in men younger than 40 years, after which it"s frequency increases with advancing age and becomes the most common urologic disorder in men.

In the context of histopathological findings in this study, there were 41 cases (48.8%) of BPH, 25 cases (29.8%) of BPH with prostatitis, 8 cases (9.6%) of PIN and 10 cases (11.9%) of adenocarcinoma. Our finding was very similar to the finding in a study done by Shetty P et al where 36.6% cases were of BPH, 30 % cases were of prostatitis, 15.3% cases were of PIN and18% cases were of adenocarcinoma.[8] Murthy et al also had the similar findings, with majority of cases being of BPH and few of which were with prostatitis.[9]This study reveals BPH as the most common prostatic pathology which can be due to excessive androgen dependent growth of stromal and glandular elements.

In this study, the peak age group of BPH was 60-69 years which was similar to the study done by Pudasaini S et al (44.4%) and Hirachand S et al (36.8%) where the peak age group of BPH was 61-70 years. [4,10]This study reveals that BPH cases increases with increasing age which can be due to the role of androgen dihydrotestosterone (DHT). In the prostate gland, type II 5-alpha-reductase metabolizes circulating testosterone into DHT, which binds to androgen receptors in the cell nuclei, resulting in BPH.

Prostatic intraepithelial neoplasm (PIN) includes both low grade and high grade.In this study, LGPIN and HGPIN were seen in 8 cases (9.52%) which was similar to the study done by Banerjee B et al (10%), Hirachand S et al (10.16%) and Maru AM et al (10.99%).[6,10,11] Very few cases (1.88%) of PIN lesions were found in a study done by Shakya et al. [12]In our study, higher incidence of PIN lesions may be due to the fact that samples received were TURP specimens where the entire tissue is sampled and examined. This allows more chance of diagnosing PIN as it may occur in a small focus within a gland which might go unnoticed in a biopsy.

In this study, prostatic adenocarcinoma was seen in 10 cases (11.9%) which is similar with the findings of the study done by Banerjee B et al (15%), Hirachand S et al (10.16%), and Wadgaonkar AR et al (15%). [6,10,13] This lower incidence of adenocarcinoma may be due to early detection of the disease through screening.

The maximum number of adenocarcinoma cases were seen in the age group of 70-79 years which is similar to the findings seen in Pudasaini S et al (n=7;36.8%).[4] The prevalence of adenocarcinoma with advancing age may be due to the role of androgen which provide the soil for development of cancer.

Serum PSA level may vary according to the age of the patient. In various prostatic pathologies such as BPH, prostatitis, PIN and carcinoma- serum PSA level is increased due to the breakdown of protective layers between prostatic lumen and capillary. In a study done by Kiehl et al and Umbehr et al, they concluded that BPH and prostatitis are associated with high Serum PSA, when glandular epithelium is disrupted. [14,15] Whereas, Papsidero LD et al concluded that elevation of PSA is due to release of unknown substances by epithelial cells during inflammatory processes. [16]In this study, most benign cases had PSA within range of 0-7ng/ml (65.2%), with another 34.8% cases having PSA level above 7ng/ml owing to the fact as mentioned above.

The PSA level in 5 cases of PIN (62.5%) were in the range of 0-7ng/ml, with another 3 cases (37.5%) having PSA level above 7ng/ml. In this study, we found 80% of adenocarcinoma had PSA values over 21 ng/ml while 20% of cases had PSA values less than 21ng/ml. Our findings was very similar to the finding in a study done by Pudasaini S et al, Hirachand S et al and Sridevi N et al.[4,10,17]In our study, serum PSA level more than 21ng/ml was present predominantly (8 out of 10 cases) in case of prostatic carcinoma. This study shows that an increasing PSA level of more than 21 ng/ml reveals an underlying malignancy showing a significant relationship between prostatic carcinoma and PSA level.

In this study, p value was<0.01 indicating that there is a positive association between the increasing serum PSA level and chances of malignant lesions which is similar to the study done by Banerjee B et al (P value <0.01).[6]

The study has very few adenocarcinoma cases, stage of disease is unknown, PSA level could not be studied according to the stage of adenocarcinoma and it also failed to sub-classify adenocarcinoma of prostate into acinar or ductal type, due to lack of immunohistochemical markers. Also special stains were not done.

CONCLUSION

Benign prostatic hyperplasia is the most common prostatic pathology. PSA is a specific marker for prostatic tissue. It can be raised in benign lesions of the prostate due to membrane disruption. However, an increased PSA level above 20 ng/ml increases the chance of detecting malignant lesions. In cases with increased PSA level above 20 ng/ml, prostatic core biopsy

needs to be considered to rule out the possibility of malignancy.

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CONFLICT OF INTEREST: None

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