Original Article

A comprehensive study of prostate pathology in correlation with prostate-specific antigen levels: An Indian study

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ABSTRACT

Background: Diseases are primarily affecting the prostate gland ranged from inflammation to hyperplasia to malignant tumors. Carcinoma of the prostate is most common nonskin cancer in the west and the second leading cause of cancer death among men. Gleason's microscopic grading is a paramount feature and with prostate-specific antigen (PSA) are important for diagnosis, management, and prognosis of carcinoma. **Objectives:** The objectives were to evaluate the patterns of prevalence of prostatic lesions among the insured persons of the model hospital and to correlate histology with respect to serum PSA levels. **Materials and Methods:** Clinicopathological study of prostatic biopsies was conducted over a period of 1-year with emphasis on Gleason's grading and correlation of the same with PSA levels. **Results:** Individuals with PSA >10 had 18 times more chance of being biopsy positive in comparison to PSA <10. **Conclusion:** Confirmation for malignancy/screening in high-risk people is needed when PSA value is more than 4 since sensitivity is 100%, rather than PSA more than 10.

Key words: Gleason's grade, prostate, prostate-specific antigen

INTRODUCTION

Diseases primarily inflicting prostate gland are inflammation, benign nodular enlargement, and tumors.[1] Worldwide benign prostatic hyperplasia (BPH) affects 210 million males and is common over the age of 50 years.[1,2] Carcinoma of the prostate is most common nonskin cancer in the west and the second leading cause of cancer death among men.[2,3] Carcinoma is a disease of elderly men occurring at age 65 years and above; with increasing trend in Asian countries in last 25 years. In India, carcinoma of prostate occupies 2nd to 10th rank among cancers in men, in various metro cities as per national cancer registry.[4,5]

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Among the carcinomas, the majority are adenocarcinomas that develop from the acini of the ducts. Other rare histological subtypes include small cell carcinomas, signet ring carcinoma, adenoid cystic carcinoma, neuroendocrine tumor, transitional cell carcinoma, which account for about 5%. A possible precursor lesion of prostatic malignancy is prostatic intraepithelial neoplasia, which is dysplasia of the epithelium lining the prostatic glands. Studies have shown that the appearance of prostatic intraepithelial neoplasia may precede carcinoma by 10 or more years.[6]

Digital rectal examination (DRE) and transrectal ultrasonography are a preliminary practical diagnostic method but has low specificity and sensitivity.[1,7] A transrectal biopsy is essential to confirm the diagnosis. Most popular is Gleason's microscopic grading system

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development of Donald F Gleason in 1966.[8] Gleason's grading system is superior and the best predictor of disease progression and outcome. Serum prostate-specific antigen (PSA), a marker for prostatic carcinoma has high sensitivity, specificity, and compliments histopathological diagnosis. Gleason's microscopic grading is a paramount feature and with PSA are important for diagnosis, management, and prognosis of carcinoma.[7,8]

MATERIALS AND METHODS

Clinicopathological study of prostatic biopsies was conducted in the Department of Pathology over a period of 1-year from January 1, 2012 to December 31, 2012. Relevant clinical, radiological details, and preoperative PSA levels were collected. Indications for biopsy were clinical history, elevated PSA, and or abnormal DRE. Patients already diagnosed and treatment for carcinoma of the prostate were excluded from the study. All submitted bits were taken for processing. Hematoxylin and eosin stained sections were studied for prostatic pathology and categorized as neoplastic and nonneoplastic. For carcinoma of the prostate, considering the glandular differentiation, the growth pattern of tumor in relation to stroma, Gleason numeric microscopic grading system was applied. Gleason's score (SG) was obtained by the sum of predominant tumor pattern with next common pattern. Most common and highest numeric grade was scored, when the three patterns were present.[1]

The present study was conducted to evaluate the patterns of prevalence of prostatic lesions among the insured persons of the model hospital and to correlate histology with respect to serum PSA levels.

Statistical analysis

Data were analyzed. Fischer exact test, odds ratio, proportion, mean were employed. Sensitivity, specificity, positive predictive value, negative predictive value of PSA were calculated in relation to histopathological grade.

RESULTS

Total surgical specimens received by the Histopathology Department, during the study period was 3683, of which 89 (2.4%) were prostatic biopsies. Table 1 depicts the age distribution of prostatic lesions. The maximum number of prostatic lesions was in the age group of 60–69 years with mean age of 63.9 years.

A total of 63 cases (70.8%) was histologically adenoleiomyomatous hyperplasia; while adenocarcinoma low-grade PIN and high-grade PIN constituted 17 (19.1%), 4 (4.5%), and 5 cases (5.6%), respectively.

Of the 70 clinically suspected BPH cases, 59 cases (84.3%) were nodular hyperplasia on histology, while in 4 case (5.7%) incidental detection of adenocarcinoma was noted. Of 19 cases suspected to be clinically malignant (by DRE), 13 (68. 4%) proved malignant on histopathological evaluation [Table 2].

The preoperative PSA was available in 59 cases (66.3%) [Table 3]. The range of PSA in nodular hyperplasia was 0.24–27 with an average PSA of 6.8 ng/ml. The range of PSA in carcinoma was 5–221, with an average of 107.0 ng/ml. Individuals with PSA >10 had 18 times more chance of being biopsy positive in comparison to PSA <10 [Tables 4-6].

Table 1: Age distribution of prostatic lesions (*n*=89)

Age group	Histopathology (HPE)				Total *n* (%)
	Nodular hyperplasia	Adenocarcinoma	PIN (L)	PIN (H)	
40-49	2	0	1	0	3 (3)
50-59	19	6	1	0	26 (29)
60-69	29	3	0	1	33 (38)
70-79	10	5	1	3	19 (21)
80-89	2	3	1	1	7 (8)
90-99	1	0	0	0	1 (1)

HPE: Histopathological examination, PIN: Prostatic intraepithelial neoplasia, L: Low-grade, H: High-grade

Table 2: Comparison of clinical diagnosis with HPE (*n*=89)

Clinical diagnosis	Histopathology			
	Nodular hyperplasia	Adenocarcinoma	PIN (L)	PIN (H)
BPH (*n*=70)	59	4	3	4
Carcinoma (*n*=19)	4	13	1	1
Total	63	17	4	5

*PIN(L): Prostatic intraepithelial neoplasia (Low-grade), PIN(H): Prostatic intraepithelial neoplasia (High-grade), HPE: Histopathological examination, BPH: Benign prostatic hyperplasia

Table 3: Stratification of PSA and comparison with histopathology (*n*=59)

PSA	Histopathology		*P*
	Nodular hyperplasia	Adenocarcinoma	
<4	16	0	
≥4–10	14	2	Reference
11–20	9	2	
>21	3	13	0.001*

*<0.05 is significant. PSA: Prostate-specific antigen

Table 4: Comparison between GS and PSA (*n*=17 cases)

PSA	Histopathology GS			Total *n* (%)
	Up to 6	Up to 7	>8	
<4	0	0	0	0
4–10	2	0	0	2 (12)
11–20	2	0	0	2 (12)
≥21	3	5	5	13 (76)

No statistical difference in distribution of Gleason grade based on PSA group. PSA: Prostate-specific antigen, GS: Gleason's score

Table 5: Comparison of PSA with HPE (with PSA cut-off 4) (*n*=59)

PSA	Histopathology		
	Biopsy positive	Biopsy negative	*P**
≥4	17	26	0.001
<4	0	16	
	17	42	

*Fishers exact test; <0.05 is significant. PSA: Prostate-specific antigen, HPE: Histopathological examination

Table 6: Comparison of PSA with HPE (with PSA cut-off 10) (*n*=59)

PSA	Histopathology		
	Biopsy positive	Biopsy negative	OR (95% CI)
>10	15	12	18.75 (3.27-140.80)
<10	2	30	
	17	42	

OR: Odds ratio, CI: Confidence interval, PSA: Prostate-specific antigen, HPE: Histopathological examination

Adenocarcinoma was the only type of malignancy noted in our study. The range of GS was 5–9, with 12 cases showing a score of moderately differentiated adenocarcinoma and 5 cases showing score compatible with poorly differentiated adenocarcinoma, as per the older classification of differentiation.[2]

DISCUSSION

Cancer of prostate commonly affects men over age 50 years, however, in men with increased risk; screening for prostatic cancer is recommended to begin at the age of 40.[1] In our study, age group afflicted with prostatic pathology was 42–95 years with mean age of 63.9 years similar to Indian study by Sinha *et al*.[9] Most common pathology was nodular hyperplasia 70.8% occurring commonly in the age group of 60–69 years, with a mean of 62.6 years. A recent study by Albasri *et al*. showed similar mean age; however, the youngest case reported in their study was 20-year-old. A constant feature seen in all the nodular hyperplasia was lymphocytic infiltrate. Hence, we also appreciate the fact that in nodular hyperplasia, chronic inflammation has a pathogenic role as reported in various studies.[2,9,10]

Carcinoma of the prostate occurs in 50–79 years, seen in 19.1.%, and this is in concordance with Indian and western studies who reported a prevalence of 24% and 17.7%, respectively.[2,11] The prevalence of prostatic pathology was 2.4% of all histopathology specimens received, and carcinoma constituted 5.1% of all malignancies. The mean age of patients with carcinoma of the prostate was 63.8 years, and this is comparable to Anderson-Jackson, *et al*. hence substantiates the fact of being disease around 65 years.[3,4]

All were histologically adenocarcinoma during the study period, however, a study by Albasri *et al*. reported adenocarcinoma in 95.9%. Rare incidence of squamous cell carcinoma and transitional cell carcinoma (<3%) is reported.[2] Moderately differentiated adenocarcinoma comprised large group, next being poorly differentiated carcinoma similar to other studies.[2,3] Perineural invasion suggesting an extension to periprostatic tissues was seen in 11.8%, similar to various other studies who observed 7–47% incidence.[3,12] In our study, the prevalence of BPH was 70.8%, carcinoma 19.1%, and precursor lesion 10.1%. Benign to malignant ratio 63:17, that is, 3.7:1.

Of 70 clinically suspected BPH by DRE, 5.7% of cases showed malignancy on HPE. This incidence of malignancy in clinically unsuspected can appear to be large enough to emphasize the absolute importance of histopathological evaluation. The range of PSA in carcinoma varied from 5.0 to 221 with an average of 107.0. A consistent increase in PSA value was observed as SG increased similar to Albasri *et al*.[2] However, a contrasting observation was put forth by Anderson-Jackson, *et al*., that is, the inverse relation of PSA in poorly differentiated carcinomas due to decreasing production of antigen by high-grade lesions as tumor volume increases.[3]

Table 3 depicts the prostatic pathology occurring in stratified PSA values and PSA more than 21 was statistically significant, implying as PSA increases, the probability of getting carcinoma among patients is increased. In this context, an increasing PSA level implies underlying malignancy and more so of a high-grade as evidenced with a significant relationship between PSA level and histopathology, especially when PSA was more than 21.

Sensitivity and specificity with cut-off PSA value of 4 were 100% and 38.1%, respectively. Sensitivity and specificity with cut-off PSA value of 10 were 21.4% and 71.4%, respectively. Positive predictive value and negative predictive value with a cut-off of PSA 4 were 39.5% and 100%, and with cut-off 10 were 55.5% and 93.7%, respectively. Albasri *et al*. made an interesting observation in patients with negative biopsy and increased PSA; wherein subsequent treatment with antibiotics and reduced PSA upon successful completion of antibiotic treatment does not warrant further evaluation.[2] In the light of no PSA levels being normal and recent recommendation to lower PSA cut-off value to 1.0 ng/ml to rule out carcinoma.[13]

CONCLUSION

Biopsy confirmation of malignancy/screening in high-risk people is needed when PSA value is more than 4, since sensitivity is 100% rather than PSA more than 10. In the light

of no PSA levels being normal and recent recommendation to lower PSA cut-off value to 1.0 ng/ml to rule out carcinoma; study is required for a longer duration on a larger population.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Epstein JI. The lower urinary tract and male genital system. In: Kumar V, Abbas AK, Fausto N, Aster JC, editors. Abbas, Robbins and Cotran Pathologic Basis of Disease. 8th ed. Philadelphia, Pennsylvania: Saunders; 2010.
2. Albasri A, El-Siddig A, Hussainy A, Mahrous M, Alhosaini AA, Alhujaily A. Histopathologic characterization of prostate diseases in Madinah, Saudi Arabia. Asian Pac J Cancer Prev 2014;15:4175-9.
3. Anderson-Jackson L, McGrowder DA, Alexander-Lindo R. Prostate specific antigen and Gleason score in men with prostate cancer at a private diagnostic radiology centre in Western Jamaica. Asian Pac J Cancer Prev 2012;13:1453-6.
4. Lalitha K, Suman G, Pruthvish S, Mathew A, Murthy NS. Estimation of time trends of incidence of prostate cancer – An Indian scenario. Asian Pac J Cancer Prev 2012;13:6245-50.
5. Yeole BB. Trends in the prostate cancer incidence in India. Asian Pac J Cancer Prev 2008;9:141-4.
6. Jasani JH, Patel HB, Gheewala B, Vaishnani HV, Bhuva K, Sancheti S, *et al*. Diagnostic utility of prostate specific antigen for detection of prostate lesions. Int J Biomed Adv Res 2012;3:268-72.
7. Rosai J. Rosai and Ackerman's Surgical Pathology. 10th ed. New Delhi: Reed Elsevier India Private Limited; 2011.
8. De Lima NG, Soares Dde F, Rhoden EL. Importance of prostate-specific antigen (PSA) as a predictive factor for concordance between the Gleason scores of prostate biopsies and RADICAL prostatectomy specimens. Clinics 2013;68:820-4.
9. Bostanci Y, Kazzazi A, Momtahen S, Laze J, Djavan B. Correlation between benign prostatic hyperplasia and inflammation. Curr Opin Urol 2013;23:5-10.
10. Vral A, Magri V, Montanari E, Gazzano G, Gourvas V, Marras E, *et al.* Topographic and quantitative relationship between prostate inflammation, proliferative inflammatory atrophy and low-grade prostate intraepithelial neoplasia: A biopsy study in chronic prostatitis patients. Int J Oncol 2012;41:1950-8.
11. Sinha S, Siriguri SR, Kanakmedala SK, Bikkasani K. Prostate biopsy findings in Indian men: A hospital-based study. Indian J Cancer 2011;48:175-80.
12. Ahmad Z, Arshad H. Needle biopsy findings in prostatic adenocarcinoma: Experience at a tertiary care center in a developing country. Ann Diagn Pathol 2013;17:235-8.
13. Holmström B, Johansson M, Bergh A, Stenman UH, Hallmans G, Stattin P. Prostate specific antigen for early detection of prostate cancer: Longitudinal study. BMJ 2009;339:b3537.