e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2023; 13(7); 79-84

Original Research Article

A Study of Histopathological Spectrum of Prostatic Biopsy and Correlation of Carcinoma Prostate with PSA Levels at A Tertiary Care Center

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Received: 18-03-2023 / Revised: 21-04-2023 / Accepted: 26-05-2023
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Conflict of interest: Nil

Abstract:

Introduction: Prostate Specific Antigen (PSA) is the most important and clinically useful biochemical marker of the prostate diseases. PSA is a good predictor of adenocarcinoma of prostate because adenocarcinoma disrupts the normal architecture of the cells which leads to leakage of PSA into the microvasculature. Gleason scoring and grading is one of the most powerful histopathological predictors of biological behaviour and act as a influential factors in determining the treatment of prostatic adenocarcinoma.

Method: This is a two years prospective study. All the prostate biopsies received during the study period were included as per inclusion and exclusion criteria. PSA levels of all the patients were recorded. After studying the histopathological features, the diagnosis of various types of prostatic lesions was made and Gleason's scoring was done in cases of prostatic carcinoma. Subsequently, a correlation was made between the histopathological diagnosis and serum PSA level.

Results: We received a total 146 prostate needle biopsies in our department. The age ranged from 46 years to 84 years with the mean age of the patients was 65.7±8.9 years. Maximum number of patients (32.69%) were in age group 61-70 years. On histopathological examination, the most common type of lesion was benign with 72 (46.1%) cases followed by 46 (29.5%) cases of malignant lesions and 6.41% cases were pure inflammatory lesion. PSA levels was done in all the patients. On comparing PSA levels with types of lesions of prostate, we observed that most of the inflammatory and benign lesions, majority of patients had PSA of <10 ng/ml whereas the PSA was >20 ng/ml in most of the patients with malignant lesion. The distribution was statistically significant (p-value <0.0001). We found that 100% of the cases with PSA levels of more than 100ng/ml has shown various grades of adenocarcinoma. On calculating the sensitivity and specificity of PSA to detect malignancy at different cut off points, we found that serum PSA has a good sensitivity and specificity at a cut off value of 19.5ng/ml, with a sensitivity of 92.3 and specificity of 84.2. It was found that cases with a PSA level above 19.5ng/ml were more of malignant lesions compared to benign.

Conclusion: Prostatic adenocarcinoma is one of the leading causes of morbidity and mortality in males, especially in elderly males. PSA is proved to a good marker for the screening of prostatic cancer as it is specific for prostate.

Keywords: Prostate carcinoma, Prostate specific antigen, Gleason's scoring.

Introduction

Prostate adenocarcinoma is a leading cause of morbidity and mortality among men worldwide. It is estimated that prostate cancer is the second most commonly diagnosed cancer in men worldwide and the fifth most common cancer overall. [1] It is reported as 6th most common cause of death among men. [2] The incidence of prostate cancer show highest rates in Australia/New Zealand (104.2/100,000), Western and Northern Europe, and other developed countries mainly due to prostate-specific antigen (PSA) screening used widely in these regions.[3] However, the mortality rates are reported highest in low to middle-income group countries like the Caribbean, and sub-Saharan Africa.[4] Prevalence of prostate cancer is lower in India as compared to the western countries, but time has shown increasing trend of this disease in India which is mainly due to increased migration of rural population to the urban areas, life style change, increased and easy access to medical facility, and better diagnostic facilities, more cases of prostate cancer are being picked up.

There are various factors, like age, race, family history, hormone levels, and environmental influences which play a role in pathogenesis of prostatic adenocarcinoma. Urinary obstruction symptoms are the most common clinical presentation in cases with enlargement of prostate because of the location of prostate gland at bladder neck. The incidence of prostatic diseases, benign prostatic hyperplasia, and carcinoma increases with age.[5] Benign prostate hyperplasia, prostate carcinoma and prostatitis are three pathologic processes which frequently affect the prostate gland.

Prostate Specific Antigen (PSA) is the most important and clinically useful biochemical marker of the prostate diseases because it is produced only by prostatic epithelial cells and thus is specific for prostatic tissue. [6] Normal levels of PSA are within 4 ng/ml, but the levels vary according to the age of the patient, and increase with increase in age. This increase with age is thought to be an evolutionary adaptation that confers genetic fitness and promotes fertility over other competing males.[7]

PSA is a good predictor of adenocarcinoma of prostate because adenocarcinoma disrupts the normal architecture of the cells which leads to leakage of PSA into the microvasculature. PSA may also increases in benign conditions of the prostate like Infection, trauma, inflammation, and benign prostatic hyperplasia (BPH). Previous studies have demonstrated that up to 86% of individuals with BPH may have an elevated serum PSA. [8]

Gleason scoring and grading is one of the most powerful histopathological predictors of biological behaviour and act as an influential factors in determining the treatment of prostatic adenocarcinoma.

The present study is carried out to determine the incidence of various lesions of prostate, classification, and grading of prostate tumors, serum PSA levels of patients and the association of PSA levels with the grade of tumor.

Methods:

This is a two years prospective study between Jan 2021 to Dec 2022 at the Department of Pathology, RUHS Medical College and Associated Group of Hospitals, Jaipur. All the prostate biopsies received during the study period were included as per inclusion and exclusion criteria.

Inclusion criteria:

1. All prostate biopsy samples received at department of Pathology.

Exclusion Criteria

1. Degenerated samples.
2. Samples received with formalin.
3. Incomplete clinical records.
4. PSA levels not available.

Clinical details of the patients were recorded, including age, habits, clinical examination. PSA levels of all the patients were recorded. Biopsies were grossed as per institutional protocols and processed with wax block method. Three-to-five-micron thin sections were prepared and stained with H&E stain. The slides were observed under light microscope.

A total 146 prostatic needle biopsies were included. The section was examined for histomorphological characters of prostate like stromal and glandular proliferation, presence of myoepithelial cell layer in nodular hyperplasia of prostate and irregularity of glandular contour, nuclear enlargement, hyperchromasia, and most important prominent nucleoli in carcinoma prostate.

After studying the histopathological features, the diagnosis of various types of prostatic lesions was made and Gleason's scoring was done in cases of prostatic carcinoma. Subsequently, a correlation was made between the histopathological diagnosis and serum PSA level.

Results

In the present study, we received a total 146 prostate needle biopsies in our Department of Pathology during the study period. The age ranged from 46 years to 84 years with the mean age of the patients was 65.7±8.9 years. Maximum number of patients (32.69%) were in age group 61-70 years followed by 28.21% in age group 71-80 years. [Image no. 1]

On histopathological examination, the most common type of lesion was benign with 72 (46.1%) cases followed by 46 (29.5%) cases of malignant lesions and 6.41% cases were pure inflammatory lesion. The spectrum of various lesions is shown in table no. 1.

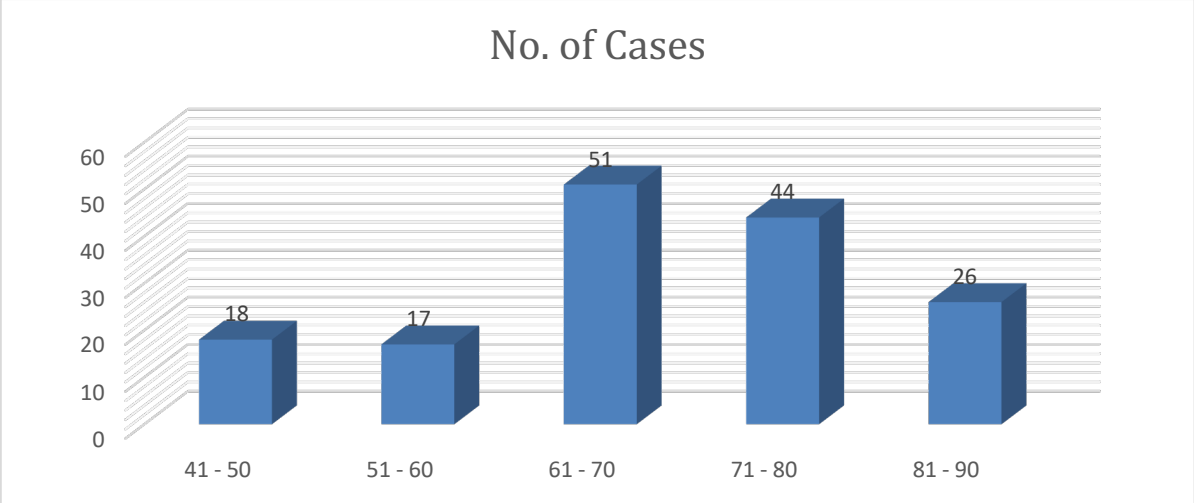

Figure 1: Age group wise distribution of cases

Table No. 1: Distribution of Cases According to Histopathological Diagnosis

Group of Lesion	Lesion	No. of Cases	Percent
Inflammatory	Acute	1	0.64%
	chronic	5	3.21%
	Granulomatous	4	2.56%
	Total	10	6.41%
Benign	BPH With Prostatitis	17	10.90%
	BPH Without Prostatitis	55	35.26%
	Total	72	46.15%
PIN	LGPIN	11	7.05%
	HGPIN	17	10.90%
	Total	28	17.95%
Malignant	Adenocarcinoma	45	28.85%
	Metastatic TCC	1	0.64%
	Total	46	29.49%
	Overall Total	156	

Table no. 2: Correlation of PSA levels and histopathological category of Prostate lesions

PSA Level (ng/ml)	Pure Inflammatory Lesion	Benign	PIN	Malignant
<4	7	41	6	0
4.1-10.0	3	19	9	4
10.1-19.9	0	11	6	10
20.0 - 100.0	0	1	7	27
>100.0	0	0	0	5
Total	10	72	28	46

Chi-square = 95.27; DF=12; P < 0.0001(HS)

PSA levels was done in all the patients. On comparing PSA levels with types of lesions of prostate, we observed that most of the inflammatory and benign lesions, majority of patients had PSA of <10 ng/ml whereas the PSA was >20 ng/ml in most of the patients with malignant lesion. The distribution was statistically significant (p-value <0.0001). We found that 100% of the cases with PSA levels of more than 100ng/ml has shown various grades of adenocarcinoma. On histopathological examination of adenocarcinoma, we did Gleason's scoring of all cases. Tumours with a Gleason's score of 5 to 7 were considered as moderately differentiated which constitute the majority of adenocarcinoma cases in our study with 39 (84.78%) cases among adenocarcinomas. With a score of 8 to 10 were considered as poorly differentiated with 5 (10.87%) cases. There were only 2 (4.35%) cases with a score of 2 to 4 which are well differentiated tumors. Moderately differentiated tumors had PSA levels above 10ng/ml but less than 100ng/ml except for 1 case where the value was 104 ng/ml. In case of poorly differentiated tumors 4 of total 5 cases had PSA levels above 100ng/ml. Hence the values were higher in poorly differentiated tumors.

On calculating the sensitivity and specificity of PSA to detect malignancy at different cut off points, we found that serum PSA has a good sensitivity and specificity at a cut off value of 19.9ng/ml, with a sensitivity of 92.3 and specificity of 84.2. It was found that cases with a PSA level above 19.9ng/ml were more of malignant lesions compared to benign [Table no. 2].

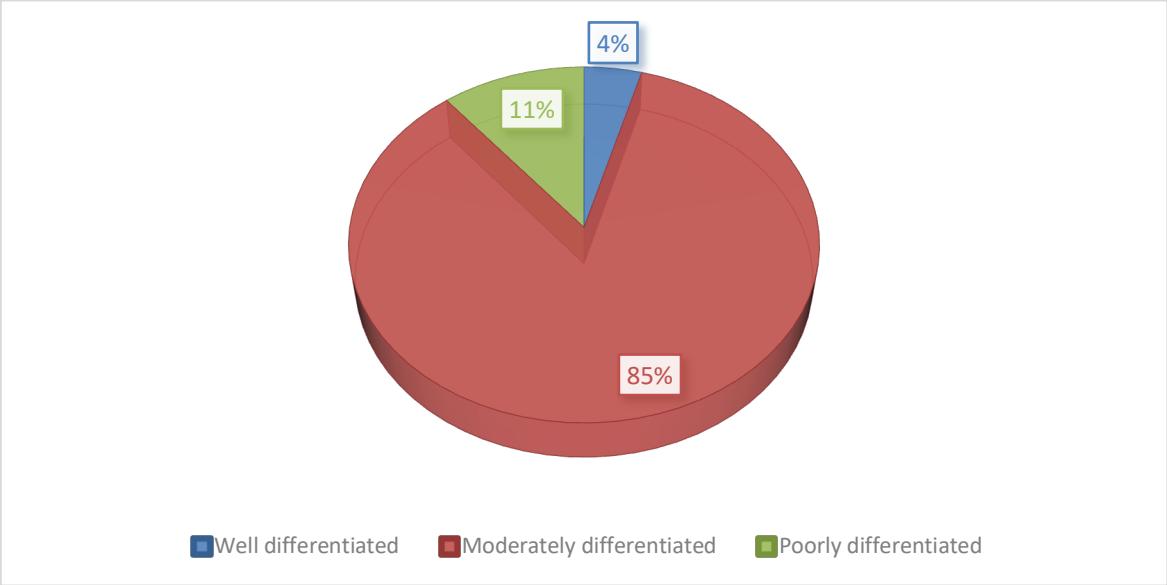

Figure 2: Distribution of cases according to the grade of prostatic adenocarcinoma

Discussion:

Prostate related diseases are common in elderly males. It is estimated that almost 8-10 males out of 100 suffer from some sort of prostatic problem in their lifetime. [9] In the present study, the mean age of presentation of patients was 65.7±8.9 years which is in agreement with the findings of studies done by Khant et al. [10] who reported mean age of 66.9 ± 9.4 years. The majority of patients (32.69%) in our study were in age group 61-70 years followed by 28.21% in age group 71-80 years. Jayapradeep et al. [11] found that maximum number of patients were in the age group of 60-70 yrs. with mean age of the patients as 65.58 years, the findings are consistent with the present study. Lakhey M et al, [12] and Goswami et al [13] also reported 7th decade as most common age of involvement.

In our study the most common type of lesion was benign with 72 (46.1%) cases including benign prostatic hyperplasia with and without prostatitis, followed by malignant lesions with 46 (29.5%) cases and 6.41% cases were pure inflammatory lesion. Khant et al. [10] in their study found that 69 (62.72%) cases were benign and 41 (37.2%) were malignant which is agreement with our study. Jayapradeep et al. [11] found 125 (73.5%) cases of benign lesions, and 31 (18.2%) cases of prostatic adenocarcinoma. Maru et al. [14] found 81.5% Benign and 6.87% adenocarcinoma.

Prostate specific antigen (PSA) is produced by the epithelial cells lining the prostatic acini and ducts of prostatic tissue. PSA is exclusively produced by prostate. This is the reason PSA is a preferred serum marker for carcinoma prostate. PSA can be increased in various conditions of prostate like prostatitis and prostatic adenocarcinoma. The clinically applicable reference values of PSA is 0 - 4.0ng/mL. Intermediate values that are from 4.0ng/ml to 10.0ng/mL could be seen in patients with BPH, prostatitis, PIN and Prostatic cancer.

In the present study we observed that maximum number of patients with 102 (92.73%) cases out of 110 cases with BPH, PIN and inflammation had PSA levels below 20 ng/ml. Only one case of BPH with prostatitis had PSA levels of 23.1 ng/ml. Seven cases of PIN had PSA levels between 20 – 100 ng/ml however the maximum value was 27.0 ng/ml. In cases of adenocarcinoma prostate 32 (69.57%) cases had PSA levels of >20 ng/ml in which 5 cases had levels above 100 ng/ml. In the Study by Khant et al [10], in benign lesion 63 cases had serum PSA level <4- 10 ng/ml, 12 cases had serum PSA level >10.1-20 ng/ml and 4 cases had serum PSA level >20.1 ng/ml, and in cases of malignant lesion 10 cases had serum PSA level <4-10 ng/ml, 14 cases had serum PSA level >10.1-20 ng/ml and 17 cases had serum PSA level >20.1 ng/ml. The results are in agreement with our present study. Koteswari M [15] found that 75% of malignant cases had PSA level >10 ng/ml. Nadam et al. [16] found 82.3% malignant cases having PSA level >10 ng/ml and 11.76% malignant cases having PSA level 4.1-10 ng/ml. Majority of previous studies found that the PSA levels rise

significantly in cases of adenocarcinoma of prostate.

On doing Gleason's scoring of adenocarcinoma cases in the present study, there were 39 (84.78%) cases of adenocarcinoma with a Gleason's score of 5 to 7, 5 (10.87%) cases with a score of 8 to 10. There were only 2 (4.35%) cases with a score of 2 to 4 which are well differentiated tumors. In the study done by Nwafor et al [17] found Moderately, differentiated PCa (GSs 5-7) accounted for 58.1% of cases, while poorly differentiated cases (GSs 8-10) accounted for 33.8% of cases, and well-differentiated cases (GSs 2-4) accounted for the least number of cases (8.1%).

Prostate-specific antigen is a serine protease enzyme produced by the columnar epithelium of prostatic tissue. [18] A small portion of this active PSA undergoes proteolysis, becoming inactive or "free" PSA and it enters the bloodstream and remains unbound.

We found sensitivity and specificity of PSA levels at the cutoff point of 19.5 ng/ml in detecting malignancy, with a sensitivity of 92.3 and specificity of 84.2. In a study of W. Obara et al [18] the sensitivity of PSA for carcinoma prostate at cut off point of 4ng/ml and 10ng/ml were 89.8% and 83.7% respectively, specificity was 37% at 4ng/ml and 66% at 10ng/ml. The cut-off point of 19.5 ng/ml in our study is much higher compared to other studies.

Conclusion

Prostatic adenocarcinoma is one of the leading causes of morbidity and mortality in males, especially in elderly males. PSA is proved to a good marker for the screening of prostatic cancer as it is specific for prostate.

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