UTILITY OF PROSTATE SPECIFIC ANTIGEN IN THE DIAGNOSIS OF VARIOUS PROSTATIC LESIONS

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ABSTRACT

BACKGROUND

Carcinoma of the prostate is the most common internal malignancy among men in the United States and 10th common malignancy in India. It accounts for 33% of all malignant tumours in men and responsible for 9% of all deaths due to cancer. Prostate specific antigen (PSA), a glycoprotein serine protease, was first identified by Wang et al in 1979. Prostate specific antigen (PSA) is a substance produced exclusively by certain cells within the male prostate gland. PSA is the most useful tumour marker in diagnosis and first line test in screening.

The aims of this study were-

1. To evaluate the utility of PSA assay as a method of investigation in diagnosis of prostatic lesions.
2. To correlate morphological types with serum PSA levels.

MATERIALS AND METHODS

The present study was undertaken in a tertiary care hospital of Yenepoya Medical College, Mangaluru and 184 cases were studied over a period of 2 years from 2015 to 2016. In all investigated individuals, the pre-treatment serum PSA levels were measured by chemiluminescence immunoassay technique using Vitros 5600. Serum PSA level <4 ng/mL was considered normal. Histopathological analysis of obtained material was done on standard Haematoxylin-Eosin (H&E) preparations.

RESULTS

Out of 181 cases, 164 cases showed benign prostatic hyperplasia. Among benign prostatic hyperplasia of 164 cases, 100 cases had serum PSA of 0-4 ng/mL, 39 cases with 4-10 ng/mL and 25 cases had >10 ng/mL. We reported 17 cases of adenocarcinoma of 181 cases, in with majority (15 cases) of the patients had serum PSA of >10 ng/mL, and two cases showed serum PSA of 4-10 ng/mL. In our study, positive predictive value (PPV) was found to be 37.5% and negative predictive value (NPV) was 98.58% for cut-off PSA level of 10 ng/mL. Similarly, sensitivity and specificity of our test for PSA level 10 ng/mL was 88.23% and 84.75% respectively.

CONCLUSION

Study confirms the high prevalence of adenocarcinoma of prostate in high serum PSA level of the patient but not all prostate cancers are associated with an elevated serum PSA level. Hence, there is a need of estimation and interpretation of different PSA forms like free PSA levels, prostatic density, PSA velocity, etc. to improve the sensitivity and specificity of PSA.

KEYWORDS

PSA, Benign, Adenocarcinoma, Histopathology, Prostate.

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BACKGROUND

The prostate is a pear-shaped glandular organ that weighs up to 20 g in the normal adult male and that depends for its differentiation and subsequent growth on androgenic hormones synthesised in the testis, acting through a poorly understood mesenchymal–epithelial interaction.[1] The prostate is a retroperitoneal organ encircling the neck of the bladder and urethra, and is devoid of a distinct capsule. In the adult, prostatic parenchyma can be divided into four biologically and anatomically distinct zones or regions: The peripheral, central, and transitional zones, and the region of the anterior fibromuscular stroma.[2] The inner zone is the primary site for nodular hyperplasia (and the rare carcinomas arising from large ducts), whereas the outer zone is the site of predilection for the ordinary adenocarcinoma arising from peripheral ducts and acini.[3,4]

Carcinoma of the prostate is the most common internal malignancy among men in the United States and 10th common malignancy in India.[5] India ranks 5th in incidence and 4th in mortality for men in Mumbai. It accounts for 33% of all malignant tumours in men and responsible for 9% of all deaths due to cancer.[6] The diagnosis requires careful history, physical examination including digital rectal examination (DRE), serum prostate specific antigen (PSA) estimation and transrectal ultrasound (TRUS) and TRUS-guided needle biopsies of the prostate.

Among these, the biopsies are considered as gold standard for the tissue diagnosis of the prostatic cancer.[7] Prostate specific antigen (PSA), a glycoprotein serine protease, was first identified by Wang et al in 1979. Prostate specific antigen (PSA) is a substance produced exclusively by certain cells within the male prostate gland. Biochemically, it belongs to the protease family of kallikrein and is also known as human kallikrein 3 (hK3).[8]

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PSA is the most useful tumour marker in diagnosis and first line test in screening. The increase in serum PSA depends on differentiation of tumour cells.[1]

The first line of screening for prostatic cancer consists of annual digital rectal examination (DRE) and estimation of serum PSA level. The upper limit of normal for PSA values is generally considered to be 4.0 ng/mL; between 4 and 10 ng/mL is considered borderline and more than 10 ng/mL is considered high. Patients with a PSA value greater than 4 ng/mL, irrespective of DRE results, generally undergo biopsy.[9]

Aims and Objectives

(i) To study prevalence of distribution of various prostatic lesions, in the region of Dakshina Kannada (Karnataka).
(ii) To evaluate the utility of PSA assay as a method of investigation in diagnosis of prostatic lesions.
(iii) To correlate morphological types with Serum PSA levels.

MATERIALS AND METHODS

Yenepoya Medical College, Mangaluru is one of the largest and well-known urology, nephrology, transplant and diagnostic centre in Dakshina Kannada (Karnataka)

The present study was undertaken in a tertiary care hospital of Yenepoya Medical College, Mangaluru and 184 cases were studied over a period of 2 years from 2015 to 2016.

A thorough clinical 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 also abnormality on DRE were recorded.

All patients underwent thorough general physical examination, abdominal examination including genitourinary examination.

In all investigated individuals, the pre-treatment serum PSA levels were measured by chemiluminescence immunoassay technique using Vitros 5600. Serum PSA level <4 ng/mL was considered normal.

Histopathological analysis of obtained material was done on standard Haematoxylin-Eosin (H&E) preparations, statistical analyses were done wherever necessary.

RESULTS

In present study, out of 181 cases, 164 cases showed benign lesions with mean age 65 years and 15 malignant lesions with mean age 70.66 years, and 2 cases of PIN (Prostatic Intraepithelial Neoplasia) with mean age of 64 years (Table 1).

Sl. No.	Mean Age in Years	No. of Cases (%)
Benign Lesions	65	90.60
Malignant Lesions	70.66	8.28
PIN	64	1.10

Table 1. Distribution of Patients age in Various Prostatic Lesions

In our study, the mean serum PSA was 19.2. Out of 181 cases, 164 cases showed benign prostatic hyperplasia. Among benign prostatic hyperplasia of 164 cases, 100 cases had serum PSA of 0-4 ng/mL, 39 cases with 4-10 ng/mL and 25 cases had >10 ng /mL.

We reported 17 cases of adenocarcinoma of 181 cases, in with majority (15 cases) of the patients noted with serum PSA of >10 ng/mL, and two cases showed serum PSA of 4-10 ng/mL.

PSA ng/mL	BPH (No. of Cases)	Carcinoma (No. of Cases)
0-4	100	0
4-10	39	2
>10	25	15
TOTAL	164	17

Table 2. Histopathology Diagnosis with Corresponding PSA level

Mean Serum PSA was 19.52

In our study, positive predictive value (PPV) was found to be 37.5% and negative predictive value (NPV) was 98.58% for cut-off PSA level of 10 ng/mL

Similarly, sensitivity and specificity of our test for PSA level 10 ng/mL was 88.23% and 84.75% respectively.

Out of 181 cases, 164 cases (90.60%) showed benign prostatic hyperplasia with benign tumour cells arranged in nodules consisting hyperplastic fibromuscular stroma and benign hyperplastic prostatic glands showing branching and double layer epithelium. Many of the glands showed corpora amylacea (Figure A).

17 cases (8.28%) were reported as adenocarcinoma of prostate showing tumour cells arranged in glandular, acini, crowded, cords and scattered singly. These glands are lined by single layer of cells with no outer basal layer. The tumour cells may be clear, dark and eosinophilic cells. Clear cells have foamy cytoplasm, dark cells have homogeneous basophilic cytoplasm, and eosinophilic cells have granular cytoplasm. The cells may show varying degree of anaplasia and mild-to-moderate nuclear atypia (Figure B).

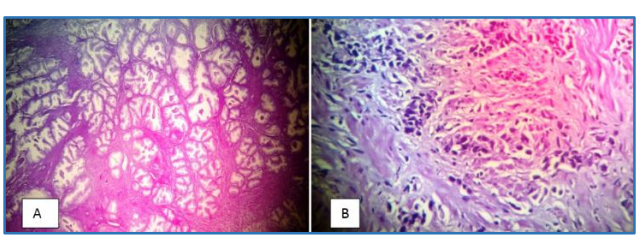

Figure 1. H & E Sections showing Benign Prostatic Hyperplasia (A) and Adenocarcinoma of Prostate (B)

DISCUSSION

PSA is one of the most important biomarkers for diagnosing prostate cancer and helps the clinicians to decide for the biopsies. The gold standard triad for diagnosing prostate cancer comprised DRE, PSA level and transrectal ultrasonography aiding to improve the detection rate of the prostate cancer.

Patients were aged predominantly between 45-78 Yrs. The mean age at diagnosis in this study was 58 yrs.

In patients with benign prostatic hyperplasia, 100 (61%) had serum PSA of less than 4 ng/mL, 39 (23.8) had serum PSA in the range of 4 to 10 ng/mL and 25 (15.2%) patients had serum PSA more than 10 ng/mL.

Almost all patients (89%) with adenocarcinoma had raised serum PSA of more than 10 ng/mL, only two patients (11.76%) were having a serum PSA of than 4-10 ng/mL. This study revealed a statistically significant correlation between serum PSA and adenocarcinoma. These findings were consistent with the study conducted by Janardan et al.

Lesion	Present Study	Alpesh et al[7]	Jevan et al[10]	Arun Chitale[11]	Janardan et al[7]
BPH	90.60%	81.53%	83%	89%	93.90%
CAP	8.28%	6.87%	17%	11%	6.06%

Table 3. Comparison of Benign and Malignant Proliferative Lesions with Other Studies

In this study, the positive predictive value for increasing PSA levels was 37.5% for PSA >10 ng/mL compared to Akther et al[12] which was 24.2%.

PSA Range ng/mL	Benign Prostatic Hyperplasia				Carcinoma Prostate				
	Present Study	Kshitij et al[13]	Eshtiaq Ali[14]	Prabhat[15]	Kshitij et al [13]	Mwaaykoma[16]	Sladana [17]	Prabhat [15]	Present study
0-4	60.9%	71.6	-	-	10.5	-	2.5	-	-
4-10	23.7 %	22.6	85	87.6	23.6	5.3	27.50	14.9	11.6
>10	15.2 %	3.0	15	12.4	63.7	94.7	70.0	74.2	88.3

Table 4. Benign and Malignant Prostatic Lesion. Comparison with Other Studies

In our study, 39 (23.8%) had serum PSA in the range of 4 to 10 ng/mL and 25 (15.2%) patients had serum PSA more than 10 ng/mL diagnosed as benign prostatic hyperplasia. The above findings i.e. a rise in serum PSA level ≥4 ng/mL does not always indicate the presence of prostatic cancer because benign conditions such as hyperplasia and prostatitis can also increase the serum PSA levels.[18,19,15]

Similarly, only two patients (11.76%) were diagnosed as adenocarcinoma in spite of having a serum PSA of 4-10 ng/mL. This is explained by few cancers that are so poorly differentiated that the epithelial cells lose expression of a PSA encoding gene.[20] Therefore, a proliferating tumour does not reveal increased serum PSA levels and this can practically lead to diagnosis of tumour at later stages and poor prognosis than tumours producing more PSA.[15]

CONCLUSION

Study confirms the high prevalence of adenocarcinoma of prostate in patients with high serum PSA levels, but not all prostate cancers are associated with an elevated serum PSA level. Hence, there is a need of estimation and interpretation of different PSA forms like free PSA levels, prostatic density, PSA velocity, etc. to improve the sensitivity and specificity of PSA. To conclude histopathological evaluation is confirmatory for diagnosis of prostatic lesions.

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