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CLINICAL SIGNIFICANCE OF TOTAL AND FREE PROSTATE SPECIFIC ANTIGEN (PSA) AND THEIR RATIO IN DIAGNOSIS OF VARIOUS PROSTATIC LESIONS-A PROSPECTIVE STUDY AT A TERTIARY CARE CENTRE

Pathology

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ABSTRACT

Background: Prostate specific antigen (PSA) is a protein produced by normal as well as malignant cells of prostate gland. Normally it is present in small quantity in men with healthy prostate (<4 ng/ml), but is often elevated in pathological conditions like prostatitis, benign prostatic hypertrophy or prostate cancer. **Material and methods:** 80 patients who presented with urine retention, dribbling of urine, residual urine and enlarged prostate gland on digital rectal examination were selected. Tests were performed on random blood serum by 3rd generation ELISA (immunoassay principle). **Results:** Most patients (51) had total PSA moderately elevated (4.0-10.0ng/ml) suggesting high risk category. 18 Patients with PSA<4ng/ml were considered low risk. 34 Patients had low % Free PSA and were referred for biopsy to confirm prostatic malignancy. **Conclusion:** PSA in the range of 4 to 10 ng/ml identified men as high risk. Most patients with PSA in this range were observed to have early stage disease, while more than half of the men with PSA levels above 10ng/ml had advanced disease. Thus, the detection of prostate cancer in its potentially curable stages requires the use of % FPSA to group individual men into low risk (high %FPSA & low Total PSA) to high risk (low% FPSA & high total PSA) to help in biopsy decisions.

KEYWORDS

Benign Prostatic hyperplasia, Prostatic adenocarcinoma, Prostatic biopsy

INTRODUCTION

Tumor markers are substances that can be detected in higher than normal amount in the blood, urine or body tissue of some patient with certain type of cancer. A tumor marker may be produced by a tumor itself or by the body in response to the presence of cancer.[1]

PSA is synthesized in the ductal epithelium and prostatic acini. The lumen of the prostatic gland contains the highest concentration of PSA in the body, a number of barriers exist between the glandular lumen and the capillaries. Disease such as infections, inflammations and cancer may produce a breakdown in this barrier allowing more PSA to enter the circulation.[2,3]

PSA is a protein produced by both normal and abnormal prostate cells. The prostate specific antigen level in the blood may be elevated in men who have prostatitis, prostatic hyperplasia or malignant growth in the prostate. While PSA does not allow to distinguish between benign prostatic condition and cancer, an elevated serum PSA level may indicate that other tests are necessary to determine whether cancer is present.[1] Total PSA, free PSA & Percentage free PSA level which is the ratio of free PSA & total PSA is studied here to correlate the significance in the early diagnosis of prostatic cancer.

AIMS AND OBJECTIVES:

1. To introduce Prostate Specific Antigen in routine diagnosis as well a screening procedure.
2. To assess the diagnostic accuracy of Prostate Specific Antigen in prostatic enlargement.
3. To correlate the serum Prostate Specific Antigen findings with histopathological findings.
4. To promote Serum Prostate Specific Antigen as an important frontline investigation in diagnosis and differentiating various prostatic enlargement.

MATERIAL AND METHOD:

Type of study: Prospective study

Duration of study: The present study consists of 80 cases of prostatic enlargement for a period of 1 year and 10 months between Feb 2020 to Nov 2021.

Type of sample: Whole blood was collected in plain vacuette and serum was separated for test.

Inclusion criteria:

1) All male patient with urinary symptoms of;
   a) Urinary retention
   b) Dribbling of urine
   c) Urinary hesitancy
2) Residual urine
3) All male patient with enlarge prostate gland on DRE (Digital Rectal Examination)

Exclusion criteria:

1) Men with late stage prostate cancer.
2) Men with refractory, hormone refractory or recurrent prostate cancer.

Method & Principle of the test[4]:

This test is based on two-site sandwich enzyme immunoassay principle. Tested sample were placed into the microwells coated by specific murine monoclonal to human total/free PSA-antibodies. Antigen from specimen was captured by the antibodies coated onto the microwell surface. Unbound material was removed by washing procedure. Second antibodies-murine monoclonal to human total/free PSA, labelled with peroxidase enzyme was then added into microwells. After washing procedure, the remaining enzymatic activity bound to the microwell surface was detected and quantified by addition of chromogen-substrate mixture, stop solution and photometry at 450 nm.

Optical density in microwell was directly related to quantity of the measured analyte in the specimen.

RESULTS

In present study, the presenting complaints of cases with prostatic disease included difficulty in initiation of urination, dribbling of urine after completing of urination and incomplete emptying sensation.

In all the cases a detailed history was taken and physical examination was done which include digital rectal examination. All the cases had suspicious DRE.

All the 80 cases were evaluated by serum PSA level. In all cases (80) histopathological examination of prostate biopsy was done in histopathology section of our college.

Table No.1: Age wise distribution of 80 patients with prostatic lesions at different cut off level of serum PSA level (n=80)

Age	Serum PSA level (ng/ml)			No. of patients
	<4.0	4 to 10	>10	
40-49	1	2	0	3
50-59	6	8	1	15
60-69	10	22	5	37
70-79	1	15	3	19
>80	0	4	2	6
Total	18	51	11	80

In Table No.1, maximum no. of patients were from 6th decade, 72.97% (27 out of 37) had serum PSA value higher than 4 ng/ml.

In patients above 7th decade, 96% (24 out of 25) had serum PSA value higher than 4 ng/ml.

In patients below 5th decade, 61.11% (11 out of 18) had serum PSA value higher than 4 ng/ml.

Table No.2 Age wise distribution of free PSA value in patients with total serum PSA >4ng/ml (n=62)

Age (Years)	Mean free PSA value (ng/ml)
<50	0.539 (n=2)
50 to 59	0.765 (n=9)
60 to 69	1.44 (n=27)
70 to 79	1.46 (n=18)
>80	1.63 (n=6)

Table No.2 shows age wise distribution of mean free PSA value, 0.539 ng/ml in <50 years,0.765 ng/ml in 50 to 59 years,1.44 ng/ml in 60 to 69 years,1.46 ng/ml in 70 to 79 years and 1.63 ng/ml in >80years.

Table No.: 3 Comparison of malignant and non malignant prostatic lesion according to % free PSA value (Serum PSA value >4ng/ml) (n=62)

% Free PSA	Probability of cancer (%)	No. of Patients	Malignant	Non-Malignant
0-10	56	16	06	10
10-15	28	10	01	09
15-20	20	08	02	06
20-25	16	16	00	16
>25	08	12	00	12

Table No.3 shows out of 16 patients with 0-10% free PSA, 06 patients had a malignant lesion and 10 patients had non malignant lesion.

Out of 10 Patients with 10-15% free PSA, 01 patient had a malignant lesion and 09 patients had non malignant lesion.

Out of 08 Patients with 15-20% free PSA, 02 patients had a malignant lesion and 06 patients had non malignant lesion.

Out of 16 Patients with 20-25% free PSA, all were non malignant on histopathology.

Out of 12 Patients with >25% free PSA, all were non malignant on histopathology.

DISCUSSION

Prostate cancer is very uncommon before the age of 50 years, but its frequency climbs steeply with age to peak in the 9th decade for both incidence and mortality rate.[5] Two of the reasons for the high mortality are that many patients have incurable disease at the time of diagnosis and patients with potentially curable tumors are rarely symptomatic. To reduce mortality from this disease, screening has frequently been recommended for asymptomatic men in the high risk age group.[6]

Prostate specific antigen is the initial screening test and most useful marker for early detection of prostate cancer. Although PSA is invaluable marker for screening, it is prostate specific but not cancer specific, since PSA may also be elevated in prostatic hyperplasia. The discrimination between prostate carcinoma and prostatic hyperplasia is potentially more problematic in patients with serum PSA values between 4 to 10 ng/ml. Several other methods have been proposed to identify cancer patients with intermediate serum PSA level.[7]

The finding of present study are consistent with other studies when using serum PSA cut off level 10 ng/ml. But the detection rate of other studies is higher when using serum PSA cut off level 4 ng/ml especially in those selected cases suspicious for malignancy on digital rectal examination or ultrasonography or both. This is because in the present study all cases were selected whether suspicious for malignancy by other parameter or not.

Table No.:4 Shows comparison of sensitivity, specificity and positive predictive value of serum PSA test at different cut off level to detect prostatic malignancy.

Study	Serum PSA cut off level	Sensitivity %	Specificity %	Positive predictive value%
Roger et al10 (1997)	4 ng/ml 10 ng/ml	86.7 63.9	27.7 73.1	43.4 60.2
Muhittin et al11 (2002)	4 ng/ml 10 ng/ml	93.88 44.90	21.05 68.42	60.53 64.71
Amayo et al12 (2004)	4 ng/ml 10 ng/ml	89.8 -	37 -	49 -

In table no.4, the present study using cut off value 10ng/ml, the findings of sensitivity, specificity and positive predictive value were 77.77%, 94.36 % and 63.63 % respectively which are quite comparable with other authors.

LIMITATION OF STUDY

Serum PSA estimation is invaluable test for detection of prostatic malignancy but as it is affected by many factors and also increases in prostatic non malignant lesions, limiting its diagnostic accuracy especially when the values obtained are between 4.0 to 10.0 ng/ml. In such cases it requires help of other parameters also to confirm or rule out the diagnosis.

CONCLUSION

- The serum PSA levels are a good indicator for the glandular proliferation of the prostate and they can be used as a marker to check for the diagnosis and progression of prostate carcinoma.
- Serum PSA can be used as marker of choice in primary diagnosis of a prostatic enlargement when an early diagnosis is required or when an invasive methods like FNAC/Biopsy is not possible due to patient`s condition.
- Percentage of free PSA is more significant than total PSA & free PSA alone.
- Percentage free PSA also helps in selecting the patients who will require prostate biopsy and unnecessary biopsies can thus be prevented.

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