DIAGNOSTIC UTILITY OF PROSTATE SPECIFIC ANTIGEN FOR DETECTION OF PROSTATIC LESIONS

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Abstract

Background: Carcinoma of prostate is one of the common tumors of old age in men. With digital rectal examination (DRE), prostate specific antigen (PSA) is a major screening tool for prostate cancer. The cutoff value for PSA of 4.0 ng/mL gives the highest sensitivity and highest specificity. Several modifications of PSA testing have been developed and may be beneficial for select populations.

Methods: The study includes 180 cases between 48 to 76 years of age group. Serum PSA level and Histopathology of prostatic biopsy was done and correlate.

Results: Widespread use of PSA for early detection prostate cancer in india. In present study 56% cases of BPH with mean age 57.77 ±4.86. and 33.1% Malignant (Adeno ca. + TCC) with mean age 65.70 ±5.64.

Keywords: Prostate specific antigen, Benign prostate hyperplasia, Adenocarcinoma

1. Introduction

Prostate cancer is an important growing health problem, presenting a challenge to urologists, radiologists and pathologist[1,2] Currently, many men are identified as having early prostate cancer through the use of prostate specific antigen (PSA) screening[3,4,5,6].

Carcinoma of the prostate is the most common malignant tumor in men over the age of 65 years[7], with an estimated 41,000 Americans dying from prostate cancer annually[8]. Currently it is the most common male malignancy in the United States of America and the majority of cases are diagnosed at a time when tumor has extended beyond the confines of the gland, making it incurable. In the European Union 13% of malignancies diagnosed in men comprise prostate cancer[9].

Diagnostics techniques used in prostate cancer have been evolved greatly with technological developments but the classical digital rectal examination is still the mainstay for the diagnosis of any prostatic disease. The accuracy rate of digital rectal examination in detecting malignancy is 20–40% in different series[10,11,12]. Prostatic Acid Phosphatase has been used extensively in the last 50 years as marker to diagnose prostate cancer. PSA was identified 1972. DRE and PSA have been recommended test in guidelines of the American cancer society since 1993 for annual check up of men aged 50 years or above[10,11]. The use of prostate specific antigen coupled with digital rectal examination has led to improved detection of prostate cancer and has resulted in earlier diagnosis and treatment[13,14].

Prostate-specific antigen (PSA) is the most useful tumor marker in the diagnostics of prostate carcinoma[15]. PSA is serin protease produced by ductal and acinal epithelial cells of normal, hyperplastic, and malignant tissue of the prostate. By the influence of pathological processes the cell integrity is destroyed leading to release of PSA into circulation, i.e. the processes inside prostate, such as hyperplasia, inflammation, tumors, lead to the increase of serum PSA value the most frequently[16,17,18]. The investigations have revealed that every gram of cancer prostate tissue increases the value of serum PSA for 2.3 ng/ml in average, while every gram of hyperplasic tissue increases the same parameter 10 times less compared to cancer tissue[19,20]. While PSA is primarily produced by prostatic epithelial cells, PSA has also been noted to be detected in trace amounts in the periurethral glands, endometrium, normal breast tissue, breast tumor, breast milk, adrenal neoplasm, and renal cell carcinoma[21,22]. Because PSA usually found in low concentration in serum, measured elevation of PSA in serum have allowed it to become an important marker for prostate cancer[23].

The measurement of the PSA level has been used as a screening tool for prostate cancer since the mid-1980s. Currently, first-line screening for prostate cancer consists of annual DRE and

determination of serum PSA levels. 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, regardless of DRE results, generally undergo biopsy. The cutoff value of 4.0 ng/mL represents the level at which the highest sensitivity (detection of the largest number of prostate cancers) and highest specificity (exclusion of the greatest number of men without prostate cancer) are present. As there is no value of PSA at which the definitive diagnosis of prostate cancer can be made, and a positive finding on DRE is also not 100% specific, biopsy of the prostate is still required for the diagnosis of prostate cancer[24].

Approximately 95-98% of prostate cancer are adenocarcinomas developning in acini of prostate ducts[25].Other histologic types of carcinoma prostate occur in approximately 5% of patients; these include small cell carcinoma, signet ring carcinoma, adenoid cystic carcinoma, neuroendocrine tumor, transisnational cell carcinoma (TCC). Prostatic intraepithelial neoplasia (PIN), which is a dysplasia of the epithelium lining prostate glands, is a proble precursor of prostate carcinoma. The appearance of PIN may precede carcinoma by 10 or more years[26,27]. Other common prostate lesion are benign prostatic hyperplasia (BPH), Acute and chronic prostatitis.

Aims And Objective:

- To determine the age distribution of patients with prostatic lesion.
- To determine histological types related with prostate specific antigen.
- To study prevalence of distribution of various prostatic lesions, admitted in Dhiraj hospital, Piparia, Vadodara.
- To evaluate the utility of PSA as a method of investigation in diagnosis of prostatic lesion.

2. Material and Methods

This Retrospective Study was done from January 2010 to January 2012 in S.B.K.S. Medical institute and research center & Dhiraj Hospital, Piparia, Baroda [Gujarat] under Sumandeep Vidyapeeth.

Study was done in department of Pathology, 180 patients aged between 48 to 76 years, sample was examined (serum and biopsy), the level of serum PSA and histology of prostate was reported.

Who had the clinical symptoms of prostatism at digitorectal examination (DRE), established enlargement of prostate suspected to malignant process or benign prostate enlargement Using this protocol the standard diagnostic methods have been applied: DRE, trans abdominal ultrasonography of prostate, determination of serum PSA, biopsy of prostate.

Serum PSA was done on IMMUNOASSAY on AIA 360 [TOSHO] by immunofluorescent method. The range of PSA determination using this equipment is 0.1-100ng/ml.

The biopsy was performed with "Tru-cut" needle using transrectal or transperineal approach with previous preparing of patient (purgation and antibiotic protection). Also, the material obtained by transurethral resection (TUR) of prostate, used in diagnostic and therapeutic purposes, was analyzed. Fixation of tissue samples has been done in 10% formaldehyde solution for 24 hours. The tissue was prepared routinely, put in paraffin, cut on microtome to the thickness of 4 microns, and then the sections were stained by H& E stain, and reported.

Statistical Analysis: Data from the study was analysed separately using statistical Package for Social Sciences. Results are presented as Mean ± SD (Standard deviation).

3. Result and observations

Table: 01 No. of cases according to histopathology diagnosis.

Sr. No.	HP Diagnosis	No. of Cases	Age (Mean ± SD)
1	BPH	102 (56%)	57.77 ±4.86
2	ADENO CA.	58 (32%)	65.82±5.61
3	PIN	13 (7.22 %)	58.84±5.84
4	TCC	2 (1.11 %)	63±2
5	PROSTATITIS	5 (2.7 %)	53.2.09
6	TOTAL	180 (100%)	60.44±6.41

Table No: 01 show that most common prostate lesion is BPH (56%) with mean age 57.7 ± 4.86 and second most common lesion is Adenocarcinoma of Prostate (32%) with mean age 65.82 ±5.61.

Table: 02 Age wise distribution of cases.

Age	Adeno Ca.	BPH	PIN	TCC	Prostatitis	Total
<50	0	4	0	0	1	5
51-60	9	71	7	0	4	91
61-70	36	27	5	2	0	70
>70	13		1			14
Total	58	102	13	2	5	180

Table No.02 shows adenocarcinoma is more common between 61-70 years of age and BPH is more common in 51-60 years of age.

Table: 03 Histopathology diagnoses related with Mean PSA level

Sr.No	HP Diagnosis	PSA LEVEL [MEAN ± SD]
1	BPH	4.86 ± 3.03
2	ADENO CA.	21.87± 14.7
3	PIN	9.26 ± 4.34
4	TCC	27.4± 4.1
5	PROSTATITIS	4.36±3.59

Table No.03 shows for diagnosis of BPH mean level of PSA is 4.86 ±3.03 and for Adenocarcinoma mean level of PSA is 21.87 ± 14.7.

Table: 04 Histopathology diagnosis related with range of PSA level

PSA	ADENO CA.	BPH	PIN	TCC	PROSTATITIS
0 -4.0 ng/ml	1(1.7%)	65(63.72%)	3(23.0%)	0	2(40%)
4 - 10.0 ng/ml	7(12.0%)	28(27.4%)	2(15.3%)	0	3(60%)
>10 ng/ml	50(86.2%)	9(8.8%)	8(61.53%)	2(100%)	
Total	58 (100%)	102(100%)	13(100%)	2(100%)	5(100%)

Table no 04 shows there are 86.2 % cases of adenocarcinoma shows PSA level >10ng/ml. and 65%cases of BPH shows PSA level 0 to 4.0 ng/ml.

4. Discussion

Carcinoma of prostate is common cancer in India due to increasing life expectancy and relatively better diagnostic method. The gold standard triad for diagnosing prostate cancer comprised DRE, PSA level and transrectal ultrasonography[28]. The DRE has always been the primary method for evaluating the prostate. It is easy to conduct and cause little discomfort to the patient but Smith and Catalona showed that the DRE depends on the investigator and has great inter-examiner variablility[29].DRE is neither specific nor sensitive enough to detect prostate cancer and is unlikely to be improved[30].

To improve the detection rate of the prostate cancer, the DRE should be followed by a test with high sensitivity. PSA testing provides such a method, being very sensitive.The frequency of the diagnosis of prostate cancer has increased substantially since the introduction of PSA screening[31,32].

In the Present study most common lesion is BPH with mean age 57.77 ±4.86. and BPH is more common between 51 to 60 years of age. Adenocarcinoma is second most common lesion in our study. And adenocarcinoma is most common type of malignancy in prostate. Mean age is 65.82±5.61, and more common between 61 to 70 years of age in this study. This figures are comparable with finding from other studies which report mean age of 69 years by Thompson IM *et al*[33],other shows mean age 65 years by Lyn *et al*[34] been reported and mean 68 years by H A Mwakyoma *et al* [35]for carcinoma of prostate.

For diagnosis of BPH mean PSA level is 4.86 ± 3.03 and for Adenocarcinoma mean PSA level is 21.87± 14.7 and for PIN mean PSA level is 9.26 ± 4.34.

Table No 05:- Comparison between different types of lesion with other study

S. N.	HP Diagnosis	Kshitij *et al*[36]	Azmi A. Haroun *et al*[37]	Jevan *et al*[38]	Arun chitale *et al*[39]	Janardan *et al*[39]	Present study
1	BPH	85.8 %	64.48%	83%	89%	93.9%	102 (56%)
2	ADENO CA.	8.35%	27.1%	17%	11%	6.06%	58 (32%)
3	PIN	4.48%					13 (7.22 %)
4	TCC	0.32%					2 (1.11 %)
5	PROSTATITIS	0.64%	8.4%				5 (2.7 %)

Table no.05 shows in present study cases of BPH is 56% which is less then other study and cases of Adenocarcinoma is 32% which is more than other study. It shows Adenocarcinoma is more prevalent in our resion.

Table No 06:- **Benign and malignant Prostatic lesion: Comparison between PSA level with other study.**

PSA range	Benign Prostatic hyperplasia			Malignant prostatic lesion			
(ng/ml)	Kshitij *et al*[36]	Ishtiaq Ali Khan *et al*[40]	Present study	Kshitij *et al*[36]	H.A Mwalyoma *et al*[35]	Sladana Zivkovic *et al*[41]	Present study
0 -4.0	71.6%		63.7%	10.5%		2.50%	1.7%
4 - 10.0	22.6%	85%	27.4%	26.3%	5.3%	27.50%	12%
>10	3%	15%	8.8%	63.15%	94.7%	70.0%	86.2%

Table no 06 shows cases of BPH most commonly present between PSA level 0 -4.0 ng/ml (63.7%), which is compared with study of Khitij *et al*. and cases of Adenocarcinoma is more commonly present at PSA level >10.0 ng/ml (86.2%) and it is compared with other study.

Conclusion

Prostate specific antigen (PSA) is specific for the prostate. PSA is raise >10 ng/ml in adenocarcinoma and in TCC. In Benign prostatic lesion PSA level is in between 0 to 4.0 ng/ml. In present study shows that DRE and PSA are the most useful front line methods for assessing and individual's risk of prostate cancer. In addition elevated level more than 4.0 ng/ml and abnormal DRE with TURP biopsy is most useful and accurate diagnostic method for prostate.

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