Original Article

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Pathology Section

The Efficiency of the Serum Prostate Specific Antigen Levels in Diagnosing Prostatic Enlargements

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ABSTRACT

Background: The objective of this study was to evaluate the serum PSA levels in patients presenting with enlarged prostate and to evaluate the efficiency of serum PSA to diagnose and differentiate benign and malignant enlargements.

Methods: The authors evaluated the patients coming in surgical OPD with enlarged prostate and were advised to undergo serum PSA testing.

Results: The efficiency of serum PSA to differentiate Benign and malignant lesions was 97.18% and 83.33% respectively.

Key Words: Prostate Specific Antigen

INTRODUCTION

The approach to the diagnosis of prostate cancer has changed radically in the recent years. The emphasis is on an early diagnosis while the process is still localized to the prostate and on radical prostatectomy which is expected to cure the disease. An early diagnosis can be achieved by measuring the PSA levels, by doing an USG examination and by doing FNAC/Biopsy of the Prostate. The incidence of Prostate cancer has been reported to be about 6.8/100000 (Anil Mandhani) [1] and it has been observed that the incidence has been increasing (B Yeole) [2].

Serum Prostate Specific Antigen (Sr PSA) is an affordable, non-invasive tool for screening and diagnosing prostate cancers and it has been used consistently for many years in the west for screening purposes (Placer et al.,) [3].

PSA is a glycoprotein which is secreted exclusively by the prostatic epithelium. It is not a tumour specific antigen as it reacts with the prostatic material in benign and malignant tissues. It can transiently increase after the manipulation and the irritation of the genitourinary tract. Nevertheless, PSA is expressed by the cancer tissues at 3ng/ml in the blood per gram of cancer, as against 0.3ng/ml/gm of tissue in BPH. The normal level values in healthy males are usually <4ng/ml. Serum PSA levels above the reference range have been reported in 50% of the men with stage A prostate cancer, in 80% of the men with stage B disease and in 100% of the men with stage C and D disease.

The serum PSA levels are influenced by the patients' ages and prostatic sizes. In a healthy 60 yrs old man with no evidence of prostatic carcinoma, the serum PSA concentration increases by approximately 3.2% per year (0.04 ng/ml). The utilization of age specific ranges has been found to be useful in predicting the survival outcomes in Asian men (Chen et al.,) [4].

AIMS AND OBJECTIVES

In the present study, 102 cases of prostate enlargements were selected to:

- Observe the serum PSA levels in patients with prostatic enlargements.
- Categorize the prostatic enlargements as benign and malignant based on the serum PSA levels.

MATERIALS AND METHODS

The patients who attended the OPD and those who were admitted in wards, who were clinically and radiologically recognized or suspected to have an enlarged prostate were included in the present study.

The estimation of sr. PSA was done quantitatively by a chemiluminescence method. The serum PSA levels which were used were those which were given by Osterling et al., [5], which were age specific reference ranges in a population of healthy men without a clinically evident prostatic enlargement. The reference which was used was as follows:

40 – 49 yrs	0 – 2.5 ng/ml
50 – 59 yrs	0 – 3.5 ng/ml
60 – 69 yrs	0 – 4.5 ng/ml
70 and above	0 – 6.5 ng/ml

OBSERVATIONS

1. Age Incidence: Most of the cases with prostatic enlargements were in the age group of 60-79 years (89.2%). Few cases were in the 40-49 years age group (9.8%).

2. Of the three cases which were diagnosed as BPH, one was diagnosed as Rhabdomyosarcoma cytohistologically and one was diagnosed as adenocarcinoma, while one was lost to follow up.

Thirty cases which were categorized as malignant on the basis of the serum PSA levels were all confirmed by cytology and six were reconfirmed by histopathology. One case which was classified as BHP by Sr PSA (value 4.92) was diagnosed as well differentiated adenocarcinoma by Cytology. The age of this patient was 50 years [Table/Fig-1].

Category	No. Of cases	Histopathological Diagnosis	%
Benign	72*	68	94.44
Malignant	30	31	96.77

[Table/Fig-1]: Categorization of Prostatic lesions with serum PSA levels

Age Distribution	Benign Hyperplasia of Prostate	Adenocarcinoma of Prostate
40 – 49	0.3 – 0.7	0.23 – 120
50 – 59	0.3 – 3.0	4.92 – 120
60 – 69	0.1 – 3.9	55 – 200
70 – 79	0.8 – 3.9	27.32 - 300

[Table/Fig-2]: Age wise distribution of Sr PSA(ng/ml) levels in BPH and Adenocarcinoma of Prostate

3. No False positive or false negative cases were observed in the present study [Table/Fig-2].

4. Histopathological Categorization of the Prostatic lesions: All the cases were confirmed by a histopathological examination. Of the 31 cases of malignancy, 2 cases underwent prostatectomy, while 4 underwent a biopsy and were confirmed by HPE. 27 cases were labelled as inoperable and they underwent bilateral orchidectomy, followed by radiotherapy.

5. Categorization of the Prostatic lesions on the basis of the Sr P.S.A. levels , which were confirmed by Cyto-HPE: The accuracy of Sr PSA in diagnosing BPH was 97.18%, while for the malignant enlargements, its accuracy was 83.33%.

DISCUSSION

The serum PSA levels can be influenced by any inflammation of the prostate and its mechanical stimulation (digital rectal examination). Haid et al., [6] reported an accuracy rate of 68% with sr PSA and many patients with PSA values which were between 4 -9ng/dl had benign biopsies. In the present study, the accuracy rate was 95.6%, which can be attributed to the method of estimation. Babaian et al., [7] suggested that PSA levels of < 4ng/ml conferred a low cancer risk, that PSA levels of >4 ng/dl but of <10ng/dl suggested an intermediate risk and that PSA levels of >10 ng/d;l conferred a high risk.

In the present study, almost all the cases of cancer had PSA levels which were above 10ng/ml. Ellis et al., [8] reviewed the Sr PSA levels in BPH and PIN and found that a majority of the men with BPH had other pathological processes like inflammations, PIN or occult cancer with serial increases in the PSA levels. In the present study, we did not get any case with raised PSA levels which were due to any inflammation or any other cause apart from malignancy, which could be due to the difference in the sample size. Speight et al., [9] compared the traditional normal ranges of Sr PSA to the age specific normal ranges and concluded that the age specific normal ranges were helpful in increasing the specificity of PSA by eliminating some eliminated values of PSA in men who were in the 60s and 70s. In the present study, the age specific reference range was very much useful in categorizing these lesions as the serum PSA was near the traditional normal range, but clearly above the age specific normal range. Arista et al., [10] reported high levels of PSA in BPH and in cancer, which were attributed to the source of the reagent kits which were used for the PSA assay. Bains et al., [11] found a significant association between the PSA levels and the glandular proliferation. Chronic prostatitis and glandular proliferation are the two most important factors which contribute to the sr PSA elevation in hyperplastic prostates. Laris et al., [12] suggested that PSA screening had decreased the incidence of stage T1b prostate cancer and that PSA had been universally accepted as a marker for the progression of established prostate carcinoma. Catalona et al., [13] evaluated the usefulness of measuring the sr PSA levels in the detection and staging of prostate cancer in patients who underwent needle biopsies because of abnormal digital rectal examinations and inferred that sr PSA provided a better method of detecting prostate cancer by non-invasive methods, which is proven by the present study in the absence of other non-invasive methods. Brawer et al., [14] screened 1249 patients for prostate carcinoma on the basis of their serum PSA levels and concluded that PSA represented an important adjunct to DRE for the early detection of prostate carcinoma. Guthman et al., [15] studied 100 patients with biopsies and correlated the findings with the pre biopsy sr PSA levels and ultrasound findings and found that a significant percentage of patients with a benign DRE and an elevated sr PSA value harboured a clinically significant but potentially curable prostatic malignancy. Richie et al., [16] studied the efficacy of sr PSA in the early detection of prostatic carcinoma in men who were aged >50 yrs and found that the sensitivity of PSA was 75% and that its specificity was 87%. Smith et al., [17] studied the nature of the prostate cancer which was detected through a PSA based screening and concluded that a majority of the tumours which were detected through the PSA based screening had medically important prostate cancer. Aus et al., [18] observed that the cancer detection rate was significantly higher in the patients who had 5 or more biopsies than in those had 4 or less and with sr PSA levels which were <10ng/dl, while the detection rate was unaffected by the number of biopsies which were taken if the serum PSA alone was above 10ng/dl. Smart et al., [19], while documenting the facts and fiction of prostate cancer in USA, observed that an annual PSA blood test and DRS which were done on all the men who were over 50 yrs of age, followed by the appropriate treatment, had decreased the number of deaths which was caused by prostate cancer. In all the studies which have been mentioned, there was a considerable overlap of the Sr PSA levels in the cases with benign and malignant prostatic lesions. Joshua et al., [20] determined the normal age specific reference ranges for PSA in young men to increase the sensitivity in young men. They studied 1123 men who were between 30 and 59 yrs of age and concluded that the mean PSA level was 0.74ng/ml in the 40-49 yrs age group and that it was 2.3ng/ml in the 50-59yrs age group. They suggested that a lower threshold of 2 – 2.5ngml for younger men was reasonable to dictate the further evaluation. In the present study, there were two cases in which the sr PSA levels were in the higher limit of the normal, but which on FNAC and HPE turned out to be malignant, emphasizing the fact that the age specific reference range of sr PSA was a better tool for screening prostatic malignancies than the traditional reference range. The diagnostic accuracy of Sr. PSA in the present study was 95.6%, which was mainly due to the use of the age specific reference range for serum PSA. Chadwick et al., [21] assessed the value of serum PSA as a screening test and found it to be better than a digital rectal examination. Ferrero et al., [22] however suggested that the results of PSA must be interpreted cautiously, as they could be elevated in cases of prostatitis, prostate infarction, lithiasis and abscess formation. Gustafsson et al., [23]

found that the positive predictive value had increased to 4% when only a digital rectal examination was used and that it had increased to 71% when serum PSA was used along with DRE. Nadler et al., [24] concluded that the prostatic volume and inflammation were the most important factors which contributed to the serum PSA elevation in men without clinically detectable prostate cancer. Ronnett et al., [25] found that in patients with high grade prostatic intraepithelial neoplasia on the biopsy material and elevated serum PSA values, BPH may account for the elevated serum PSA levels. More likely, because of the association between the high grade prostatic intraepithelial neoplasia and carcinoma, these patients have an undiagnosed carcinoma as the source of the elevated serum PSA values.

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 progression of prostate carcinoma. They can be used as a marker of choice in the primary diagnosis of a prostatic enlargement, when an early diagnosis is required or when invasive methods like FNAC/Biopsy are not possible due to the patients' conditions. They can also be used as a marker for a prostatic malignancy in cases of disseminated unknown primary malignancies. The age specific reference ranges are better than the traditional reference range for screening for prostate cancer in patients with an enlarged prostate and in those with urinary complaints and for planning the management.

The age specific reference ranges have the potential to make serum PSA a more discriminating marker for detecting clinically significant cancers in older men (increasing specificity) and to find more potentially curable cancers in the younger men (increasing sensitivity).

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