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Original Article

Serum PSA levels in the Indian population: Is it different?

Lt Col Amit Agrawal^{a,*}, Brig Shailesh Chandra Karan (Retd)^b^aClassified Specialist (Surgery) & Urologist, Command Hospital (Southern Command), Pune 411040, India^bConsultant (Urology & Renal Transplant), Columbia Asia Hospital, Ghaziabad, UP, India

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ABSTRACT

Background: Serum prostate-specific antigen (PSA) is an important tumour, marker which is widely used to trigger trans-rectal ultrasound (TRUS)-guided prostate biopsy. However, the PSA levels vary with race and ethnicity. Therefore, there is a need to have an Indian reference range.

Methods: All adult male patients meeting the inclusion and exclusion criteria were enrolled in this study. They were subjected to assessment of serum total PSA, digital rectal examination and trans-abdominal ultrasound. If any one or more of these were found abnormal, then a TRUS-guided 12-core prostate biopsy was done. Patients who were detected to have prostatic cancer were excluded from the final analysis. The data so obtained was grouped among the following three age groups: 40–49, 50–59 and 60–70 years, and the age-specific PSA values, prostatic volume and PSA density were found.

Results: A total of 1772 patients were analysed. The mean serum total PSA was 1.76 ng/ml with a standard deviation of 2.566 ng/ml. Group-wise age distribution of the mean serum total PSA was 1.22, 1.97 and 2.08 ng/ml in 40–49, 50–59 and 60–70 years age groups.

Conclusion: The mean total PSA and the age-specific PSA range tend to be lower in the Indians than the Western population.

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Introduction

Prostate-specific antigen (PSA) is a serine protease elaborated by the prostate gland. This antigen was originally sought to be used as a forensic tool to identify semen in rape victims.¹ Since then, PSA has travelled a long way through numerous

refinements and researches. And just before the turn of the century, PSA became an invaluable tool for detection of prostatic cancer.² However, this stature became debatable soon. Researchers found that PSA alone is not good enough to diagnose prostatic cancer and various PSA derivatives became the new object of their focus.^{3,4} Nevertheless, whatever the current status of PSA may be, in the absence of any other

* Corresponding author. +9971664222.

E-mail address: majoramitagrawal@gmail.com (A. Agrawal).

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reliable tumour marker for prostate cancer, this antigen would continue to be used for detecting prostate cancers early in its course.

Although numerous studies exist on the ability of PSA and its usage as a tumour marker, there are very few studies that have looked into the normal values of PSA in a native population.^{2–5} Workers have shown that the levels of PSA not only differ with the diseases of the prostate but there also existed a racial difference in their serum levels.⁶ Numerous studies from various countries have documented the normal levels of PSA in their population, but the Indian data on the subject is scarce. Thus, we carried out this study with an aim to seek the serum levels of PSA in a healthy, male, Indian population within the age-specific ranges thereby adding to the Indian data bank on the subject.

Materials and methods

The study was designed as a cross-sectional analytical study with an aim to estimate the levels of serum total PSA in the Indian population and also the age-specific ranges. The Institutional Review Board clearance was taken prior to the conduct of the study. Before the participants were enrolled in the study, a written informed consent was obtained from each one of them. The study was conducted for a period of two years from July 2013 to June 2015.

Inclusion criteria

All male patients reporting to the Urology outpatient department, during the study period, who were

1. between the ages of 40 and 70 years and
2. willing to enroll in the study and be on follow-up, if required.

Exclusion criteria

1. Patients who had known prostatic disease and/or were on treatment for the same (BPH, prostatitis, prostate cancer, etc.).
2. Documented urinary tract infection on urine culture.
3. History of urinary tract instrumentation within the last one month prior to the presentation, including catheterization.
4. Fever at the time of presentation.
5. Patients who were diagnosed to harbour prostatic malignancy during the study (proved on TRUS-guided prostate biopsy) were also excluded from the final analysis.

Methods

All patients enrolled in the study were subjected to the following:

1. A serum sample was collected to estimate the total PSA value. All serum PSA estimations were carried out with radiometric assay technique (Diagnostic system Laboratory, Texas, United States). The PSA estimation was done in our

institute's pathology laboratory. The serum sample was collected prior to any manipulation on the prostate.

2. A digital rectal examination (DRE) was carried out with the patient lying in the left lateral position.
3. A trans-abdominal ultrasound examination was done to assess the size and the echo-texture of the prostate gland apart from assessing the upper tracts and the urinary bladder with the pre- and post-void urine residue.
4. If any of the above three was found to be abnormal (i.e. abnormal echo-texture or a suspicious nodule on trans-abdominal ultrasound, abnormal DRE finding: hard nodule suspicious of malignancy, or raised serum PSA, which was defined as a value ≥ 4 ng/ml⁵), then the patient was taken up for trans-rectal ultrasound (TRUS) guided 12-core (6 + 6) prostate biopsy. The biopsy was done under local anaesthesia as an outpatient procedure after a single dose of pre-procedure intravenous antibiotic (Inj Magnex 1 g (sulbactam sodium/cefoperazone sodium 1:1; Pfizer). A standard biopsy scheme was employed, consisting of 12 cores of tissue targeting the peripheral zone at the apex, mid gland and base, as well as laterally directed cores on each side of the prostate. The cores obtained were sent in separate marked containers. A written consent was obtained prior to the prostate biopsy. The biopsy specimen was processed at our Pathology Lab and reported by one of the institutional pathologists.

The data so collected (age, DRE findings, prostate size on trans-abdominal sonography, serum PSA levels and prostate biopsy reports) were tabulated. For ease of tabulation, the patients were further divided into groups based on the ages, i.e. age groups 40–49 years, 50–59 years and 60–70 years. Men below 40 and above 70 years were excluded as per the study protocol.

Statistical analysis

The descriptive statistics is presented using mean (with SD) and median for quantitative variables and categorical variables are presented in frequencies along with respective percentages. The statistical comparisons for quantitative variables were done by using ANOVA. For bivariate correlations, Spearman's correlation coefficients were calculated and scatter plots were made for visual presentation.

Confidence interval gives the range where true value of parameter lies. 95% confidence interval was calculated as $\text{Statistic} \pm 1.96 \sqrt{\text{SE (statistic)}}$.

Data were entered and coded in MS Excel (Version, 2007) and all statistical analyses were performed by using SPSS software (Version 16, SPSS Inc, Chicago, IL, USA). The p value less than 0.05 was considered statistically significant.

Results

2124 patients met the inclusion and exclusion criteria and were enrolled in the study. However, 204 patients did not complete their workup, and 10 patients were not willing to participate after the initial consent and hence were excluded from the study. In the end, a total of 1910 patients were

Fig. 1 – The enrolment and distribution of patients in the study.

analyzed for the study. 294 patients were found to have raised PSA and/or suspicious nodule on DRE or USG. They were biopsied as per the protocol. Out of these, 138 patients were found to have malignancy and were excluded from the final analysis. This is depicted in Fig. 1.

The group-wise age distribution of the patients along with the mean serum total PSA values and the prostatic size on USG are tabulated in Table 1. PSA density (PSAD) was calculated as serum total PSA/prostate size in ng/ml/ml and is presented in the same table.

Out of 1772 participants, 1647 had PSA of ≤ 4 ng/ml while 125 participants had PSA of > 4 ng/ml. The mean serum total PSA level was 1.76 ng/ml (95% confidence Interval – 1.68–1.92) and a standard deviation of 2.566 ng/ml. The age-specific ranges are also depicted in Table 1. The mean serum total PSA in the 40–49 years age group was 1.22 ng/ml (95% CI: 1.17–1.39); in 50–59 years age group, it was 1.97 ng/ml (95% CI: 1.71–2.23) and in the 60–70 years age group, it was 2.08 ng/ml (95% CI: 1.88– 2.36) (Table 1). It was seen that the serum PSA levels increased with increasing age of the patients. There was a statistically significant difference in the serum PSA levels between the

three age groups (p value = 0.000). The serum total PSA was also plotted against the age of the participants and there was a significant correlation of higher serum PSA with increasing age of the population under study (Spearman's $Rho = 0.36$ and $p < 0.01$). This is depicted in the scatter diagram (Fig. 2) for a visual representation.

The size of the prostate was also found to be increasing along with the age of the patients in our study (p value = 0.000) (Table 1). A scatter diagram was also plotted, which also revealed a linear correlation between the two, i.e. as the age increases, the volume of prostate also increases (Spearman's $Rho = 0.44$ and $p < 0.01$, which was statistically significant) (Fig. 3). A similar correlation was also seen in the distribution of the PSAD in the study groups (p value = 0.005) (Table 1).

Discussion

PSA has been found to vary with the ethnicity and race. Oesterling et al. found a lower age-specific range of PSA in Japanese men when compared to the western population.⁷

Table 1 – Group-wise age distribution of the serum PSA, prostate size, and PSA density.

Age groups (years)	Serum total PSA (ng/ml)					Size of prostate (ml)				PSA density (ng/ml/ml)			
	Number of subjects (N)	Mean	SD	F statistics (ANOVA)	p value	Mean	SD	F statistics (ANOVA)	p value	Mean	SD	F statistics (ANOVA)	p value
40–49	570 (32.17%)	1.22	1.19	17.402	0.000	31.22	12.89	185.920	0.000	0.04	0.04	5.295	0.005
50–59	745 (42.04%)	1.97	3.17			42.85	11.89			0.05	0.07		
60–70	457 (25.79%)	2.08	2.63			43.41	11.38			0.05	0.06		
Total	1772 (100%)	1.76	2.57			39.25	13.29			0.04	0.06

Fig. 2 – Scatter diagram of PSA plotted against Age showing a linear correlation (Spearman's Rho = 0.36; p value <0.01).

Fig. 3 – Scatter diagram showing the linear relation between Age and the prostate volume (Spearman's Rho = 0.44; p value <0.01).

Table 2 – Age-specific PSA reference range in the western population.

Age range (years)	PSA reference range (ng/ml)		
	Oesterling et al. ⁶	Oesterling et al. ⁷	Dalkin et al. ⁸
40–49	0.0–2.5	–	0.0–2.4
50–59	0.0–3.5	0.0–3.5	0.0–3.8
60–69	0.0–4.5	0.0–5.4	0.0–5.6
70–79	0.0–6.5	0.0–6.3	0.0–6.9

Table 3 – Age-specific PSA in the Indian population, including that of this study.

Age groups (years)	PSA (ng/ml)		
	DeAntoni et al. ⁹ (Mean) N = 184	Agarwal et al. ¹⁰ (Mean) N = 1899	Our study (Mean) N = 1772
≤40	1.06	–	–
41–50	2	1.0	1.22
51–60	2.56	1.2	1.97
61–70	3.5	1.5	2.08
71–80	3.74	1.9	–
>80	5.7	–	–

The age-specific ranges from the western population are depicted in Table 2.^{6,8,9} It is seen that the PSA rises with age across all studies.

However, there is a paucity of literature from the Indian subcontinent on the subject. There are only a few studies that discuss about the age-specific PSA ranges in the Indian population. These are depicted in Table 3.^{10,11} The table also compares the data of this study with the others. Agrawal et al. had carried out a hospital-based study, in which they calculated the age-specific values. They found a lesser value in the Indian population. Ganpule et al., from a community-based study in Gujarat on 1899 participants, found a value that was even lesser than that reported by Agrawal et al. earlier. Our figures on 1772 participants are higher than those by Ganpule et al. probably because our population was again hospital-based as in the study by Agrawal et al. However, the age-specific PSA values were found to be lower than the western population in our study as well as other studies from the Indian subcontinent. This fact was also brought out by Richardson et al. who also found a higher age-specific PSA range in western population.¹²

With the zeal to detect prostate cancer at an earlier stage, the PSA cut-off values as a trigger for biopsy are being revisited. One such way to improve sensitivity and specificity is to adjust the “threshold” PSA level to a lower value for younger men and a higher value for older men, respectively (age-specific or age-adjusted PSA). Recently, a cut-off value of 2.6 ng/ml is being suggested for biopsy in younger patients to detect early organ-confined cancers. This lowered value in young patients translates to a higher number of biopsies in them. This means that the sensitivity increases in younger men when the PSA

value is lowered at the cost of specificity, and the specificity increases in the older men when the PSA value increased at the cost of sensitivity. Partin et al.¹³ reviewed the records of 4597 men with clinically localized prostate cancer from the extensive Johns Hopkins surgical series. They found that age-specific reference ranges would lead to 18% more cancer detection in men less than 60 years of age and 22% fewer cancers in men 60 years of age or more.¹³ Hence, there is a need to have a robust Indian data with large multi-centric studies, which would help in determining the age-specific ranges of the Indian population and thus reduce the number of biopsies performed.

The prostate volume in our study population was higher as compared to the published literature.¹¹ This may again be explained by the hospital-based population chosen for this study. But in accordance with the available studies, the prostate volume showed a linear correlation with the increase in age.

Conclusion

It is seen that the PSA varies with the race and ethnicity. The Indian ranges are seen to be lower than those in the western population, and hence the data available from the west cannot be extrapolated to the Indian patients. Age-specific PSA ranges of the Indian population are not currently available and this study is a step in that direction. We require a larger multi-centric study to firmly establish the Indian age-specific PSA ranges.

Conflicts of interest

The authors have none to declare.

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