

Establishment of Age Specific Reference Range of Serum PSA Level among Healthy Indian Hindu and Muslim Males

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Abstract

Aim: This study was aimed to investigate the racial and ethnic differences in age specific references range of serum Prostate Specific Antigen (PSA) among healthy Indian Hindu and Muslim males and its comparison with Asian population.

Method: The present study was done at Medanta-The Medicity on 1300 adult Indian male patients who were visiting in the executive health checkup package. Out of 1300 subjects, 1060 healthy subjects were Hindus and 193 were Muslims without any prostate disease ranging from age 19-97 years, while rest 47 were excluded due to some urological diseases. Statistical analysis was carried out. Mean + SD, median and the central 95 percentile were calculated for each age group.

Result: The age specific reference range of serum PSA values in healthy Hindu males is 0.69 ng/ml in those younger than 40 years; 0.83 ng/ml in 40-49 years; 1.13 ng/ml in 50-59 yrs group; 1.46 ng/ml in 60-69 yrs group; 1.83 ng/ml in men's older than 70 years age group. Whereas the age specific reference range of serum PSA values in healthy Muslim males is 0.86 in those younger than 40 years; 1.01 ng/ml in 40-49 years; 1.41 ng/ml in 50-59 yrs group; 1.70 ng/ml in 60-69 yrs group; 2.92 ng/ml in men's older than 70 years age group.

Conclusion: Present study highlighted the age-specific reference range of serum PSA in Healthy Hindu Males are on lower side as compared to Muslim males. The data also suggested that the PSA levels are associated with increasing age.

Keywords: Age-specific reference range; Prostate specific antigen; Hindu male; Muslim male

Introduction

Prostate cancer (PC) is the most frequently diagnosed visceral cancer and the second leading cause of cancer death of men [1]. Prostate Specific Antigen (PSA) is a serine protease produced by epithelial cells of normal, hyperplastic and cancerous prostatic tissues [2], is one of the valuable tools for the diagnosis of prostatic carcinoma [3].

Several studies have reported that important racial and ethnic differences exist in age specific reference range of serum PSA value among global populations [4-7]. African and American men have highest PSA values [6] while the PSA values are lower in Asian and Arabian men [4,5,8] and higher in European men [9]. Asian men living in different region have diverse PSA levels. Some information regarding PC in Asian – Indians suggests that the incidence in five major Indian metro cities appears to be rising [10]. In India it is the third commonest male cancer in Delhi, fourth in Mumbai, fifth in Bangalore and ninth in Chennai [11-12]. Several article considered that the effect of race and ethnicity, environmental factors, lifestyles, metabolic & physiological changes with advancing age can lead to changes in serum PSA levels [4,5].

In world literature, the 95 percentile value (upper limit of normal ranges) of Serum PSA is 4 ng/ml has been accepted as the Reference Range of serum PSA for all age groups [6-7]; however the incidences of prostate cancer detection in Asian population were 16.7% in low PSA group (2-4 ng/ml) and 23.7% in intermediates PSA group (4.1-10 ng/ml) [13]. Thus the concept of standard references range (4 ng/ml) for serum PSA does not compensate for healthy Indian males.

To our knowledge, no previous report is available to provide reference interval of serum PSA for healthy Hindu and Muslim-Indian males. The objective of the present study was a step to establish age specific reference range of serum PSA in healthy Indian Hindu and Muslim males and its comparison with other Asian- Indian population.

Materials and Methods

Study design

The present study was conducted recently in a Clinical Laboratory at MEDANTA, THE MEDICITY GURGAON over a period of two years from January 2010 to January 2012. The main purpose of this study was to identify racial and ethnic differences in age specific references range of serum PSA among Healthy Hindu and Muslim-Indian males.

Study Population

Approximately 1300 patients were enrolled in executive Health Checkup and were prescribed for serum PSA test. Out of 1300 subjects, 1060 were healthy Indian Hindu males and 193 were healthy Indian Muslim males without prostate diseases belonging to the age between 19-97 years and they were selected for the study after excluding the subjects as per appropriate exclusion criteria defined by International Federation of Clinical Chemistry (IFCC).

Data collection

The entire serum PSA values were obtained from medical charts of patients who were prescribed for PSA test and this chart were available in electronic format through IBA eHIS Medicity Applications. After this, subjects having some urological complication, post operation of prostate gland or pre-historical issues of prostate diseases were excluded from the present study. If patients taking any chemotherapy or radiotherapy were also be placed in exclusion criteria. Patients having puss cell more than 4 were also excluded from our study. Finally in total, 1253 Indian subjects met the eligibility criteria in which 1060 were Hindu males and 193 were Muslim males.

Data analysis

All serum samples were assayed by using an Immunometric Assay Technique [VITROS 5600 Clinical Chemistry Analyzer] based on chemiluminescence method and was analyzed in same laboratory to prevent the variation in measurement. The Vitros PSA Assay is an

equimolar assay for the detection of free and ACT- complexed PSA. PSA concentration is measured in nanogram per milliliter (ng/ml). All the data were entered into MS Excel 2007 and were divided as per age group of decade: <40 yrs ($n_H=100$, $n_M=26$); 40-49 yrs ($n_H=199$, $n_M=55$), 50-59 yrs ($n_H=318$, $n_M=59$), 60-69 yrs ($n_H=247$, $n_M=33$) and above 70 yrs ($n_H=196$, $n_M=20$). Finally statistical analysis was done using SPSS Package. Data are expressed as the mean + SD, median, Standard Error of Mean (SEM) and lower and upper 95% Confidential Interval (CI).

A comprehensive internal quality control program was followed and results were released after calibrating values between mean \pm 1SD. This internal quality control analysis was performed daily. Apart from this, lab was also participated in External Quality Assurance Scheme (EQAS) by BIORAD

Result

In total, 1253 healthy subjects (1060 Hindu males and 193 Muslim males) as per age group from <40 years to men older than 80 years were included in our study. The result that is expressed in mean + SD, median, 95% Confidential Interval (CI) for all age groups of 1060 healthy Hindu males were 1.11+1.08, 0.76 ng/ml, 1.17 ng/ml (Table 1) and for 193 healthy Muslim males were 1.15+1.01, 0.84 ng/ml, 1.29 ng/ml (Table 2). The min-max concentration of serum PSA in healthy Hindu males is 0.06-5.9 ng/ml and 0.09-5.3 ng/ml for healthy Muslim-Indian males.

PSA (ng/ml)	20-29	30-39	40-49	50-59	60-69	Above 70	All ages
N	18	82	199	318	247	196	1060
Mean \pm SD	0.47 \pm 0.30	0.65 \pm 0.38	0.76 \pm 0.50	1.01 \pm 0.96	1.31 \pm 1.22	1.63 \pm 1.43	1.11 \pm 1.08
Median	0.46	0.60	0.64	0.77	0.89	1.2	0.76
SEM	0.07	0.04	0.04	0.05	0.08	0.10	0.03
Lower 95% CI	0.33	0.57	0.69	0.90	1.15	1.43	1.04
Upper 95% CI	0.61	0.73	0.83	1.11	1.46	1.83	1.17
Min- Max	0.06-1.03	0.06-2.27	0.06-3.86	0.06-5.9	0.06-5.61	0.06-5.87	0.06-5.9

Table 1: Age specific serum PSA in healthy Indian Hindu males.

PSA (ng/ml)	20-29	30-39	40-49	50-59	60-69	Above 70	All ages
N	7	19	55	59	33	20	193
Mean \pm SD	0.46 \pm 0.23	0.82 \pm 0.34	0.86 \pm 0.60	1.15 \pm 1.00	1.30 \pm 1.18	2.24 \pm 1.56	1.15 \pm 1.01
Median	0.38	0.75	0.69	0.97	0.88	1.91	0.84
SEM	0.09	0.08	0.08	0.13	0.21	0.35	0.07
Lower 95% CI	0.29	0.67	0.70	0.90	0.90	1.55	1.00
Upper 95% CI	0.62	0.98	1.01	1.41	1.70	2.92	1.29
Min- Max	0.17-0.79	0.36-1.5	0.09-3.08	0.13-5.12	0.17-5.2	0.11-5.3	0.09-5.3

Table 2: Age specific serum PSA in healthy Indian Muslim males.

The 95% Confidential Interval (CI) values of serum PSA in healthy Hindu males is 0.69 ng/ml in those younger than 40 years; 0.83 ng/ml in 40-49 years; 1.13 ng/ml in 50-59 years group; 1.46 ng/ml in 60-69 years group; 1.83 ng/ml in men older than 70 years age group.

Whereas the age specific reference range of serum PSA values in healthy Muslim males is 0.86 in those younger than 40 years; 1.01 ng/ml in 40-49 years; 1.41 ng/ml in 50-59 years group; 1.70 ng/ml in 60-69 years group; 2.92 ng/ml in men older than 70 years age group.

The highest 95 percentile Confidence Interval (upper limit of normal range) was 2.92 and were seen in Indian Muslim men older than 80 years age group. Age wise distribution of serum PSA of the Healthy Hindu and Muslim groups are shown in the Figures 1 and 2. One of the interesting things noticed in both Hindu and Muslim males that there was a progressive increase in mean + SD and 95 % CI with advancing age groups from 20 years to above 80 years are shown in Table 3.

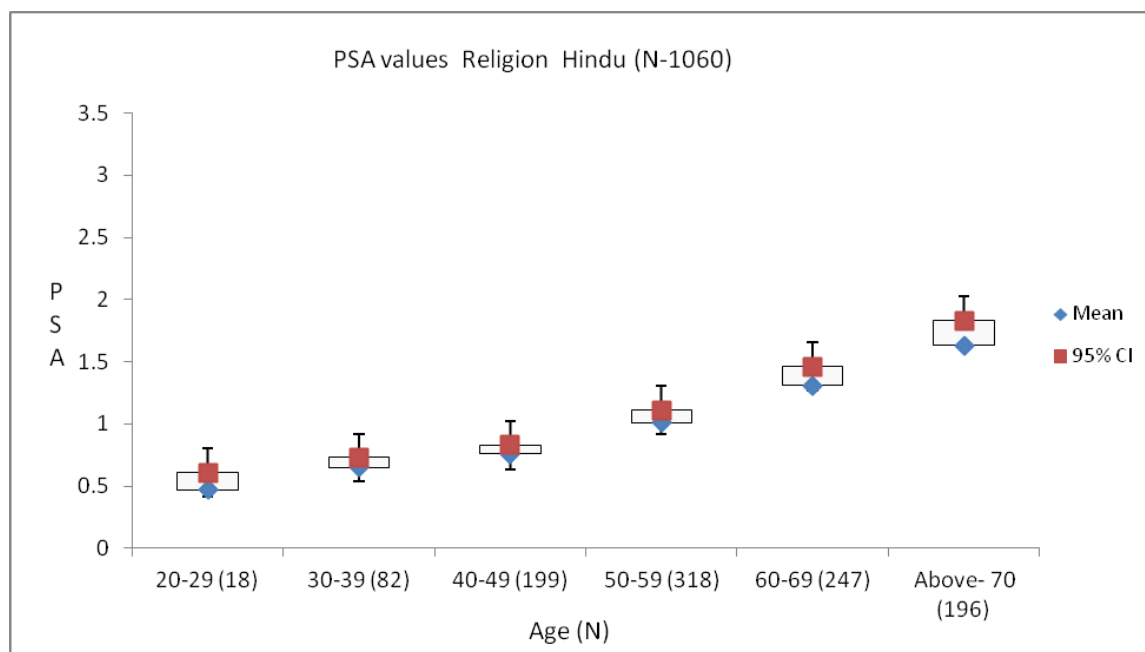


Figure 1: Mean and 95% Confidence Interval (CI) of Serum PSA values (ng/ml) in Healthy Indian Hindu Males (N-1060) with ascending age groups in years.

	Population (yrs)	<40 (Year, n)	40-49 (yrs)	50-59 (yrs)	60-69 (yrs)	>70 (yrs)
Lee et al. [13] (n=5805)	Korean	1.8	2	2.4	3.9	6.3
Liu et al. [21](n=8422)	Chinese	-	2.15	3.2	4.1	5.37
Oesterling et al. [7] (n=286)	Japanese	-	2	3	4	5
Mendez et al. [25] (n=63926)	Spanish	1.4	1.7	3.3	5.18	-
Saw et al. [26] (n=513)	Singaporeans	1.4	1.7	2.3	4	6.3
Kamal et al. [23]	Saudi Arabian	-	2.85	3.99	5.41	6.29
Mehrabi et al. [8] (n=650)	Iranian	-	1.35	1.85	3.2	4.4
Malti et al. [4] (n=583)	South Indians	0.9	1.3	1.48	1.6	2
Our series (nH=1060, nM=193)	Indian Hindus	0.69	0.83	1.11	1.46	1.83
	Indian Muslims	0.86	1.01	1.41	1.7	2.92

Table 3: Age specific serum PSA (ng/ml) in Asian populations.

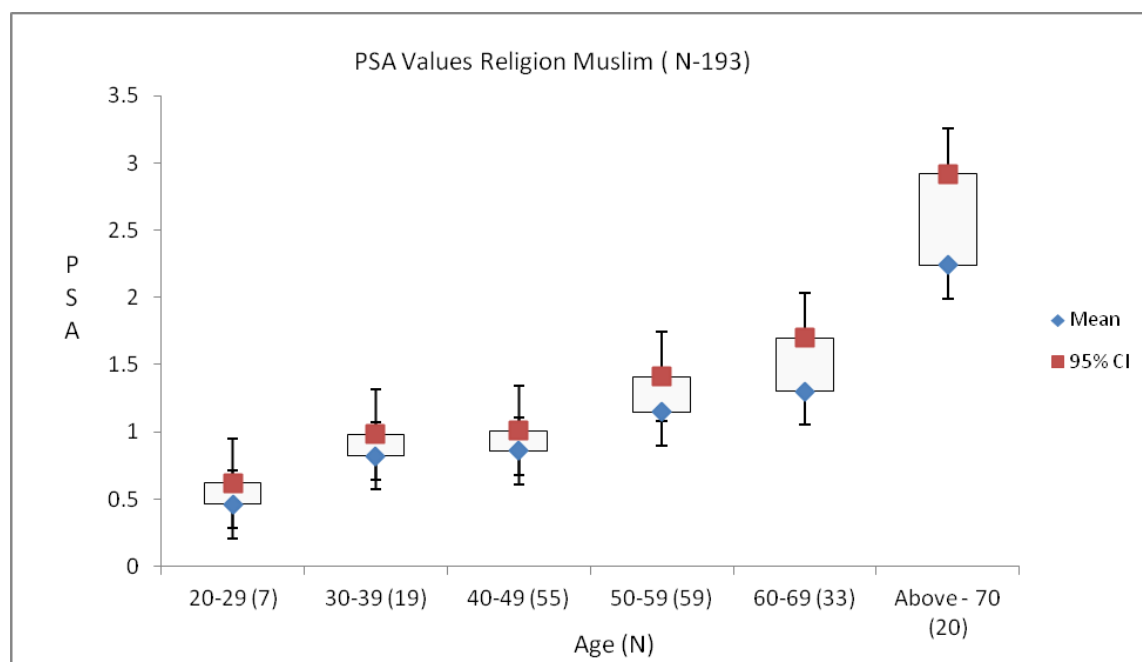


Figure 2: Mean and 95% Confidence Interval (CI) of Serum PSA values (ng/ml) in Healthy Indian Muslim Males (N=1060) with Ascending Age groups in years.

Discussion

India is a socioculturally and ethnically diverse country. Therefore, the prevalence of prostate disease varies markedly. But the reasons for such ethnic disparities are poorly understood. Serum PSA is the common oncogenic marker for prostate cancer (PC). Besides this its level can be affected by many factors like age, race, and ethnicity [4-6]. The main aim of this study was to identify racial and ethnic differences in age specific reference range of serum PSA among healthy Indian Hindu and Muslim males.

In our study 85% of the subjects were Hindus and 15% were Muslims in which Indian Muslim males have slightly higher serum PSA range than Indian Hindu males. The result of present study was compared with Asian population and suggests that the normal level of serum PSA in Indian subjects is lower than other Asian countries population (Table 3). Studies also suggest that Asian population have lower PSA levels than other races. It may be due to lower level of androgen. Androgens are required for the normal development of prostate, as well as its neoplastic transformation. Despite the widespread clinical use of PSA as a tumor marker; the relationship between androgen action and PSA concentration in men without prostate hyperplasia or cancer remain unclear.

Age is one of the key factors for the prostate disease, with the increment of the age; susceptibility towards the disease too increases [5]. Serum PSA was found to be elevated with age and was clearly shown in various studies conducted among Asian populations such as Chinese, south India, Koreans, Singaporeans, and Japanese [4,7,13-26]

Dubey concluded that in India there is no scientific rationale to advocate routine use of PSA for early detection of PC in Indian males due to low incidence of PC. But the importance to establish reference range of serum PSA for healthy south Indian males to interpret PSA

result in benign as well as malignant disorders of prostate was given by Malati and Kumari [4]. The study suggests that the reference range of serum PSA level increases with advancing age in south Indian males and are lower than global population. In the present findings, Muslim males have quite similar serum PSA range as in south Indian males but have slightly higher PSA than Hindu males.

The higher serum PSA in Indian Muslim males as compared to Indian Hindu males may be either due to inherited susceptibility associated with genetic factors or other factors that are influencing serum PSA level like race and ethnicity, environmental etiology, difference in life style characterized by dietary habits and physical exercise. But still there have not been any study investigating this variation of serum PSA level. PSA could be related to the specific dietary habits. Edward et al. reported that a lower intake of red meat and a higher intake of soya based food may reduce the risk of PC [27-30].

Studies have demonstrated a significant impact of diet on prostate cancer. East Asian diets have been traditionally vegetarian and low in fat content [31,32] A diet rich in phytoestrogens, which is found in vegetarian diets, and soy products has been associated with a protective mechanism against prostate cancer [33]. There is a growing evidence that curcumin (turmeric) and a diet rich in vegetables has a significant protective effect on prostate cancer growth [34-36] These dietary factors could be responsible for the low incidence of prostate cancer in India.

In conclusion, there is great racial and ethnical variation in age specific reference range of serum PSA among healthy Indian Hindu and Muslim males. The normal level of serum PSA in Indian males is lower than other Asian countries males. More research is needed to determine the factors that influence the serum PSA concentration in

Indian Muslim males. The study also indicates that serum PSA positively correlates with advancing ages

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