

Research Article

Prostate Specific Antigen Values of Geriatric Individuals Visiting a Tertiary Care Hospital in Southern India for Comprehensive Check Up

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Abstract: Prostate Specific Antigen (PSA) has become the most commonly used tumour marker for prostate cancer. Studies have suggested that age specific cutoff values for PSA screening are better than the currently used standard cutoff of 4.0ng/ml and different races have their own reference ranges. The objective of this study was to measure the PSA values of elderly individuals attending a tertiary care centre in southern India and postulate the possible normal values of PSA in different age groups of elderly. A total of 1038 males over the age of 60 years presenting to the Elderly Comprehensive Health clinic at the Department of Geriatrics of a tertiary hospital in Southern India between March 2009 and February 2011 were studied. 4ml blood was collected and PSA was estimated by Chemiluminiscent Micro-particle Immunoassay. PSA values were analyzed in terms of mean, standard deviation and 5th and 95th percentiles. Results showed that 5th and 95th percentile values were 0.27 and 3.82 among those who were 60-69 years, 0.28 and 3.43 among those who were 70-79 years and 0.26 and 3.95 among those who were more than 80 years. 10 % of the elderly population in all age subsets had PSA values over the normal. This study showed that the PSA values from South India are similar to the expected. The age specific Indians being ethnically distinct, need to have separate PSA reference ranges which need to be established with large community-based multicentre Indian studies.

Keywords : Prostate Specific Antigen, prostate cancer, tumour marker

1. INTRODUCTION

Prostate Specific Antigen (PSA) has become the most commonly used tumour marker for prostate cancer. PSA is a serine protease produced by the epithelial cells of normal, hyperplastic, and cancerous prostatic tissue. Because the enzyme is not specific for prostate cancer, the PSA test has a high false positive rate when used as a screening tool. Roughly one in four of men with serum PSA levels between 4.1 and 9.9 ng per ml have prostate cancer on biopsy.^[1-4] In men without prostate cancer, PSA levels increase with age, mainly because of increases in prostate volume due to benign prostatic hyperplasia. PSA is a continuous marker, there has been controversy about what threshold should be used to refer men for biopsy.^[5-7] Cross-sectional population data suggest that the serum PSA increases 4% per mL of prostate volume, and that 30% and 5% of the variance in PSA can be accounted for by prostate volume and age, respectively.^[8] Initial studies set the upper limit of normal for PSA at 4 ng/mL, with levels greater than 10 ng/mL being suspicious for malignancy and levels of 4 to 10 ng/mL being indeterminate. Oesterling et al. developed age-specific reference ranges for white men from Olmsted County, Minnesota.^[9] Later multiple studies have suggested that age specific cutoff values for PSA screening are

better than the currently used standard cutoff of 4.0ng/ml and the fact that different races have their own reference ranges.^[10-13] Nonetheless, serum PSA screening is a powerful tool for the detection of prostate cancer in both blacks and whites, and when properly applied on an individual basis, the use of age-specific reference ranges can improve the clinical value of such screening.^[10-13]

The objective of the current study was to study the PSA values of elderly individuals attending a tertiary care centre in southern India and postulate the possible normal values of PSA in different age groups of elderly.

2. MATERIALS AND METHODS

Amrita Institute of Medical Sciences (AIMS) is a 1400 bedded premier teaching hospital and tertiary care centre located in central Kerala, Southern India. AIMS hosts a separate Geriatric Department with a team of healthcare personnel trained in Geriatric care - Geriatricians, Gerontological Nurses, Medical Social Workers, Gerontological Physiotherapists and Nutritionists. Comprehensive geriatric health checkup program is being conducted where elderly

people from all over the state visit to get comprehensive full check-up and screen for diseases. PSA is being routinely offered for all geriatric patients visiting the comprehensive geriatric check up program. 4ml blood was collected in red vacutainer and was estimated by Chemiluminiscent Micro-particle Immunoassay with micro-particle and Acridinium labeled conjugate as the reagent. All the patient clinical information is registered in a fully computerized and networked Hospital Information System (HIS).

A total of 1038 males over the age of 60 years presenting to the Elderly Comprehensive Health clinic at the Department of Geriatrics of Amrita Institute of Medical Sciences and Research Centre, Kochi, Kerala between 1st March, 2009 to 28th February, 2011 were studied. All patients who had a Digital Rectal Examination (DRE) in the past 3 months, patients who have been catheterized in the past 3 months, those who are known cases of prostatic diseases – carcinoma prostate, BPH, patients on 5- α -reductase inhibitors were excluded.

Normative values were defined from individuals with a PSA value of less than 4 ng/ml and individuals with a PSA value of more than 4 ng/ml on whom biopsy was done and reported as normal. PSA values were analyzed in terms of mean, standard deviation and 5th and 95th percentiles.

3. RESULTS AND DISCUSSION

Data of 1038 elderly male were retrieved. 668 individuals (64.35%) were in the age group 60-69 years, 340 (32.75%) were in the age group 70-79 years and 30 individuals (2.8%) were above 80 years.

Among them, 70.7% had PSA values 2 or less, 81% had values 3 or less, 89.8% had values 4 or less and 10.62 % had PSA values greater than 4.(Table2) PSA values ranged between 0.038 to 21.30 in age group 60-69 years group; 0.019 to 11.0 in the 70-79 years group and 0.23 to 4.23 in the above 80 years age group. 78 individuals (7.5%) had values higher than 4 but less than 10 and 27 individuals (2.6 %) had values higher than 10.

Fifth and 95th percentile values were 0.27 and 3.82 among those who were 60-69 years, 0.28 and 3.43 among those who were 70-79 years and 0.26 and 3.95 among those who were more than 80 years.(Table3)

Out of the 1038 patients who presented for the Comprehensive Checkup Program at our hospital, 105 patients were found to have an elevated PSA level and were subsequently referred to the Urology Department for further evaluation which included a Digital Rectal Examination (DRE) and prostatic biopsy if required, depending on the DRE findings. 22 of these patients went to Urology Department, where a DRE was done and were advised to review in three months with repeat PSA values. DRE revealed suspicious findings in 7 (30.4%) patients and non-suspicious features in 15 (69.6%). Amongst the 7 patients who had suspicious DRE findings, 3 were lost to follow up and the remaining 4 were proven to be malignant.

Amongst the non-suspicious group, 2 were lost to follow up and biopsy was done in 8 patients – of which 2 had malignancy. 18 of these patients reviewed with repeat PSA values and of which PSA rose in 12 patients - of which 3 were proven to be malignant. Amongst the 6 patients who did not reported a rise a PSA – malignancy was proven in 3 patients.

Age specific reference ranges of PSA is essential in interpreting PSA of elderly and our study showed values that are similar to the expected. Interestingly, there is a fall in the mean values of PSA in higher age brackets but this is not statistically significant. The study also demonstrated that roughly 10 % of the elderly population in all age subsets had PSA values over the normal. This is comparable to other studies and conveys that routine PSA testing puts roughly 1 in 10 patients at risk for biopsy.^[15-19] Total number of patients who had an elevated PSA more than 4 ng/ml in our study were higher when compared to other studies – 8.4% with more than one-third of them being more than 10ng/ml.^[15-19]

Annual PSA screening was recommended both by the American Urological Association and the American Cancer Society for all men over the age of 50. Age specific PSA estimation studies have been done extensively in the West – predominantly amongst African Americans and in Asia, studies have been predominantly been done in the Far East but very few in the Indian subcontinent.^[15-19] One of the largest studies done in Asia on age related reference levels of PSA by Kuo-Jen Lin et al, revealed that median PSA values in the age groups 60-69, 70-79 and 80-89 were 1.15, 1.62 and 1.75 respectively.^[15] Arvind Ganpule et al in 2007, in their study involving 1787 patients, revealed values of 1.5 and 1.9 respectively.^[20] Punglia et al showed that the reference range for serum prostate specific antigen (PSA) in a group of healthy men older than 60 yr with normal digital rectal examination is 0.21–7.34 ng/ml (mean 1.23, standard deviation [SD] 2.48).^[21] They also showed that the mean PSA level among men with prostate cancer aged 60 yr, also with normal digital rectal examination, is 2.66 ng/ml.^[21] A meta-analysis of age specific analysis of PSA in elderly by Hans-Joachim et al in the European Urology Update 2007, that delved into multiple similar studies assessing age specific PSA reference values, have all demonstrated an increase in PSA values in patients aged 70-79 when compared to patients in the 60-69 age group with very few studies done on patients aged over the age of 80.

The established normal range limit of 4.0ng/mL for PSA was initially proposed in a 1986 study by Hybritech Inc., San Diego, CA, in a small population of 472 men without a history of prostate cancer.^[12] Later studies of larger and more clinically relevant populations to define the optimum cutoff value with both sensitivity and specificity for cancer detection fluctuated between 2.8 and 4.0 ng/mL.^[22] The scening study of 6630 men aged 50-74, which led to the first US Food and Drug Administration (FDA) approval for early detection, assessed the efficacy of the cut off and derived at an upper limit of 3.9 in the 5054 age group. [^{23,24}].At the time,

recommendation of a biopsy for men with PSA > 4.0ng/mL was considered to be an aggressive position because PSA values greater than 10ng/mL were often viewed as the biopsy decision point.

The study had all limitations of a retrospective record study based. This was done in a private tertiary care hospital and so itself is not representative of general population. Biopsy was done only for patients who had very high PSA values or suspicious DRE findings and we could not obtain follow up information on all subjects with elevated PSA. There could have been prostate cancers in patients with PSA values less than 4ng/ml and this could only have been evaluated if biopsy was done in all patients, irrespective of their PSA levels – which is not the accepted medical norm.

Table 1. DISTRIBUTION OF SUBJECTS WITH HIGH PSA VALUES BY AGE GROUPS

PSA VALUES	60-69 YEARS	70-79 YEARS	80+ YEARS	TOTAL
≤ 4ng/ml	597 (57.5%)	309 (29.7%)	27 (2.6%)	933(89.8%)
> 4ng/ml	71 (6.84%)	31 (2.98%)	3 (0.28%)	105(10.1%)

Table 2. DETAILS OF PSA VALUES IN THE STUDY SUBJECTS

AGE GROUPS	SAMPLE SIZE	MEAN	STANDARD DEVIATION	P value
60-69	668	1.5560	1.840419	0.333
70-79	340	1.4080	1.331744	
80+	30	1.2055	1.065599	
Total	1038	1.4971	1.6716	

Table 3. AGEWISE PERCENTILE DISTRIBUTION OF PSA VALUES

AGE GROUP	5 TH PERCENTILE	95 TH PERCENTILE
60-69 years	0.27	3.82
70-79 years	0.28	3.43
80+ years	0.26	3.95
Total	0.25	3.69

4.CONCLUSION

Age specific reference ranges of PSA is essential in interpreting PSA of elderly and our study in Southern India showed that the values are similar to the expected. The age specific Indians being ethnically distinct, need to have separate PSA reference ranges which need to be established with large community-based multicentre Indian studies.

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