

Age-specific Serum Prostate Specific Antigen Ranges Among Apparently Healthy Nigerian Men Without Clinical Evidence of Prostate Cancer

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ABSTRACT

Introduction: Serum prostate specific antigen (PSA) levels increase with age and varies among different races and communities. The study was aimed at defining the age-specific reference ranges of serum PSA in our environment. **Methods:** We evaluated the relationship between age and serum PSA levels and the age-specific reference ranges of serum PSA among civil servants in Lagos, who underwent routine medical checkups. Criteria for inclusion were men who have no lower urinary tract symptoms, normal digital rectal examination and serum PSA ≤ 20 ng/ml. SPSS Statistic 21 was used for data evaluation and the mean, median, 95th percentile PSA levels were estimated. Pearson's correlation was used to examine the relationship, and $P < 0.05$ was considered significant. **Results:** 4032 men met the criteria for inclusion in the evaluation. The mean age was 51.6 (range 40–70) years, and there was a strong correlation between serum PSA levels and age ($r = 0.097$, $P < 0.001$). PSA ranges of 0–2.5, >2.5–4.0, >4.0–10, and >10 ng/ml were found in 3218 (80%), 481 (12%), 284 (7%), and 52 (1%) men, respectively. The mean, median and the 95th percentile PSA for the overall group were 1.84, 1.33, and 5.2 ng/ml respectively. However the 95th percentile PSA levels for men aged 40–49, 50–59, and 60–70 years were 4.78, 5.47, and 8.93 ng/ml respectively. **Conclusion:** The age-specific PSA levels among Nigerian men for each age group is higher than what was described for men in the Western world. These reference ranges of serum PSA should be considered for men aged ≥ 40 years in our environment.

KEYWORDS: Age, cancer, Nigerian, prostate specific antigen, reference

INTRODUCTION

Prostate cancer is the most common cancer among men in Nigeria.^[1–4] Currently, the prostate cancer screening is controversial as regards the relative hazards and benefits of screening.^[5] Screening for prostate cancer involves the use of the serum prostate-specific antigen (PSA), a serine protease discovered about 30 years^[6] and still remains a useful tool for the diagnosis of early and potentially curable prostate cancer.^[5,7] It is however not specific for carcinoma of the prostate and has a high false positive rate when used as a screening tool.^[8]

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It is known that serum PSA increases with age and varies among different races.^[9–15] The use of the standard absolute reference value of 0–4 ng/ml may have the potential of over-diagnosis or under-diagnosis and, therefore, unnecessary diagnostic procedures and treatment.^[16] In 1996, Oesterling described the age-specific serum PSA from a community-based population of 471 healthy American white men.^[9] There are concerns over the general applicability of those reference ranges. Different races have their own reference ranges because of the influence of geographic and ethnic differences.^[16] Although similar studies have been presented for a number of different groups of men and few studies have looked at the pattern of serum PSA among Nigerians^[17–20] but no such studies on normal serum PSA ranges and the age-specific pattern have been carried out among healthy Nigerian men.

This study was therefore performed to determine the appropriate age specific serum PSA cut-off value among Nigerian men without a diagnosis of prostate cancer.

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METHODS

The serum PSA levels of men aged ≥ 40 and ≤ 70 years in Civil Service in Lagos State, Nigeria, who underwent free medical checkup were evaluated. Only men who reported no lower urinary tract symptoms (LUTS) and had normal digital rectal examination (DRE) were included in the study. Serum PSA tests using chemiluminescence immunoassay (Beckman Coulter Access 2) were carried out on blood samples drawn from the participants before DRE as previously described.^[21] The same method was used for PSA measurements for all the participants. The serum PSA measurement was carried out in the same laboratory of General Hospital, Lagos. Men with outlier PSA values of >20 ng/ml were excluded in the evaluation because of the higher risk of prostate cancer.

The age of the men were classified into 40–49, 50–59, and 60–70 years. The serum PSA were also classified into 0–2.5 ng/ml, 2.6–4.0 ng/ml, 4.1–10.0 ng/ml, and >10 ng/ml. IBM-SPSS Statistics 21 (SPSS, Inc., Chicago, IL, USA) was used for data analysis. The mean, median and the 95th percentile values of the serum PSA for the different age categories were evaluated. The correlation between the age and serum PSA was evaluated using Person method and $P < 0.05$ was considered significant.

RESULTS

After excluding 23 men with PSA >20 ng/ml, 4035 men who reported no LUTS and had normal DRE were evaluated for the relationship between age and serum PSA. There was a strong correlation between age and serum PSA ($P = 0.000$, $r = 0.097$). The mean age of the entire cohort was 51.1 years. The mean

ages among the PSA groups 0–2.5 ng/ml, 2.6–4.0 ng/ml, 4.1–10.0 ng/ml, and >10 ng/ml were 50.9, 51.4, 52.1, and 53.4 years respectively. This showed the increasing PSA value with increasing age.

The majority of the men had PSA value in the range of 0–2.5 ng/ml as shown in Figure 1. There were 3218 (80%), 481 (12%), 284 (7%), and 52 (1%) men in the PSA groups of 0–2.5 ng/ml, 2.6–4.0 ng/ml, 4.1–10.0 ng/ml, and >10 ng/ml respectively [Table 1]. The overall mean (and median) PSA value was 1.84 (1.33) ng/ml. The mean and the median PSA increased with age as demonstrated in Table 2. The result of the 75th and the 95th percentile PSA for the overall group and the different age groups are also depicted in Table 2. The 95th percentile PSA

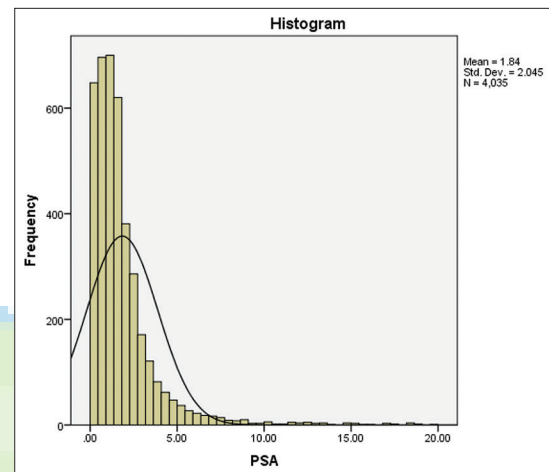


Figure 1: Histogram showing the distribution of the serum PSA in the population

Table 1: Distribution of the serum PSA among the age group

Serum PSA (ng/ml)	Frequency (%) of age groups (years)				Mean age (SD)
	40-49	50-59	60-70	Total	
0.0-2.5	1326 (33)	1841 (46)	51 (1.3)	3218 (80)	50.9 (4.4)
>2.5-4.0	177 (4)	281 (7)	13 (0.3)	481 (12)	51.4 (5.0)
>4.0-10.0	96 (2)	178 (4)	10 (0.3)	284 (7)	52.1 (4.9)
>10.0	12 (1)	37 (1)	3 (0.1)	52 (1)	53.4 (6.5)
Total	1611 (40)	2347 (58)	77 (2)	4035 (100)	51.1 (4.6)

Table 2: Mean, median, 75th and 95th percentile PSA among the population and comparison of the normal PSA ranges with Caucasian and US back men

Serum PSA (ng/ml)	Age-groups (years)			
	40-49	50-59	60-70	All
Mean PSA (95% CI)	1.68 (1.58, 1.78)	1.93 (1.84, 2.00)	2.73 (2.27, 3.18)	1.84 (1.79, 2.27)
Median PSA	1.26	1.40	1.83	1.33
75 th percentile PSA	2.10	2.30	3.51	2.24
95 th percentile PSA	4.78	5.47	8.93	5.22
Age-reference PSA range	0-4.8	0-5.5	0-8.9	0-5.2
US Blacks PSA range ^[12]	0-2.7	0-4.4	0-6.7	
US Whites PSA range ^[10]	0-2.5	0-3.5	0-4.5	

CI: Confidence interval

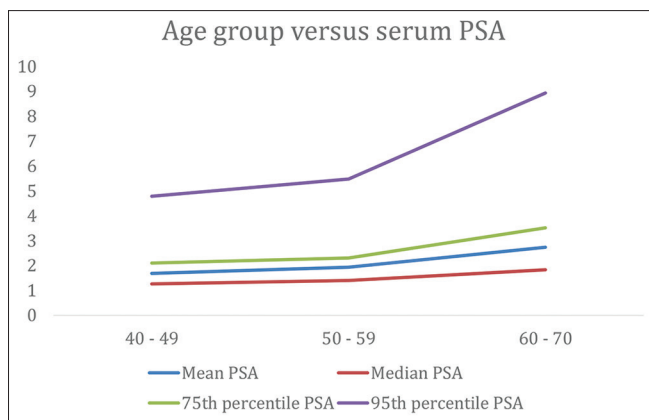


Figure 2: Mean, median, 75th percentile and 95th percentile PSA among the age groups

was 5.22 ng/ml for the overall group. Men in the age groups of 40–49, 50–59, and 60–70 years had 95th percentile PSA values of 4.78, 5.47, and 8.93 ng/ml respectively.

Defining normal serum PSA level with the 95th percentile values as done in previous studies, the normal PSA range for men of age groups 40–49, 50–59, and 60–70 years would be 0–4.78, 0–5.47, and 0–8.93 ng/ml respectively. In addition, the normal PSA value for the overall group of men would be 0–5.22 ng/ml.

DISCUSSION

Serum PSA estimation still remains a standard test in the diagnosis and management of prostate cancer.^[5] Our study to our knowledge is the first to describe the age-related serum PSA level in our environment. Although, the total serum PSA value, as well as the age-specific serum PSA values described for men in the western world, is generally used in the evaluation of men with prostate cancer, we think these may not be the appropriate values for our community.

Age-specific serum PSA had been introduced to improve the sensitivity and specificity of the PSA test.^[22] The age-specific reference ranges for serum PSA would therefore possibly detect potentially curable early organ-confined prostate cancer in younger men, while also detecting less clinically insignificant cancers in older men who might have life expectancy of <10 years. The mean, median and the 95th percentile PSA values are noted in our study to rise steadily with age. However, the rise only became more prominent among men 50 years and above as compared with men who were aged 40–49 years [Figure 2]. The recommended age-specific reference ranges, Oesterling proposed based on the Olmsted County data for serum PSA were 0–2.5 ng/mL, 0–3.5 ng/mL, 0–4.5 ng/mL, 0–6.5 ng/mL for men aged 40–49, 50–59, 60–69, and 70–79 years respectively.^[22] In our study, men older than 70 years did not participate. Therefore we could not calculate the predicted PSA for men above the age of

70 years. However, our predicted PSA values for the different age group were higher than previously reported by Oesterling.^[9,10] In addition, a previous study also reported a higher age-specific PSA of 0–2.7, 0–4.4, 0–6.7, and 0–7.7 ng/ml for African American men aged 40–49, 50–59, 60–69, and 70–79 years respectively.^[12] In our study, the age-specific serum PSA were 0–4.8, 0–5.5, and 0–8.9 ng/ml for men aged 40–49, 50–59, and 60–70 years respectively. Our study, therefore, suggests that men in our environment have higher total PSA and age-specific PSA values than those of US black men.

As men age, their prostates increase in volume and become more permeable due to the breakdown of the normal physiological barriers thereby allowing PSA to leak into the general circulation.^[13,23] Higher prevalence of subclinical prostatitis, prostatic ischemia/infarction as well as prostate cancer undetectable by current methods may also explain why the serum PSA increases with age.^[23] It is not clear why black men have higher PSA values than their Caucasian and Asian counterparts. It is possible that the black men may have larger prostate size, increase the prevalence of prostatitis in the community or generally a more leaky prostate thereby permitting higher levels of PSA in the circulation.^[17] Therefore using the appropriate age-specific PSA values for our community would improve the sensitivity and specificity of the PSA among men older than 40 years.

CONCLUSION

Our study has demonstrated that the total serum PSA and the age-specific serum PSA values are higher than described for Caucasian men as well as American blacks. We suggest that this PSA reference ranges should be used for men in our environment.

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Conflicts of interest

There are no conflicts of interest.

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