Prostate specific antigen in Africans: a study in Nigerian men

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Abstract

Background: Since the reference range of prostate specific antigen (PSA) that are used for the screening, diagnosis and management of prostate disease are based on studies of PSA range of Caucasians and African-Americans, they may not be applicable to other ethnicities, especially indigenous African populations.
Methods: In a hospital-based study, we measured total PSA levels using an immunoassay (DSL-10-9700 Active Enzyme-Linked Immusorbent Assay, Webster, TX) in patients with prostate disease (n = 48) and age-matched healthy controls (n = 64).
Results: The mean total PSA value for healthy Nigerians was significantly lower than the established values for African-Americans (2.22 ± 2.90 ng/ml versus 7.56 ± 1.11 ng/ml, respectively). PSA values in the controls did not increase with age. Severity of symptoms was not age-dependent; however, PSA levels did increase with severity of symptoms ($p = 0.002$).
Conclusion: The PSA range of healthy Nigerian men were significantly lower than those of African-American or Caucasian men. This underscores the need for a population-specific reference range for African men.

Keywords: Prostate specific antigen, benign prostatic hyperplasia, prostate cancer

Introduction

Prostate cancer is the commonest cancer in men and the second leading cause of male cancer deaths in the United States. [1] The disease may become a growing health problem as life expectancies of African populations increase. The incidence of

prostate cancer is two-thirds higher in African-Americans than Caucasian-Americans and twice as high as that for Asians. [2] Furthermore, African-Americans also have a higher mortality rate (53.7 per 100,000) from prostate cancer when compared to Caucasian-Americans (24.4 per 100,000). [3] Serum PSA levels are significantly higher in African-American men than in similarly aged Caucasian-American men without prostate cancer. [1] However, little is known about prostatic disease and PSA levels of African men in the African sub-continent.

In one report from, Cameroon, the incidence of prostate cancer in a hospital-based population was 98.8 per 100,000 while in a similar study in Lagos, Nigeria the incidence was 127 per 100,000. [4] Between 1980 and 1988, cancer of the liver was the most common cancer in Nigerian men. [5] However, from 1989 to 1996 prostate cancer accounted for 11% of all male cancers. This increase in incidence in prostate disease has occurred despite the absence of prostate screening in Nigeria. [5]

The use of prostate specific antigen (PSA) for the screening, diagnosis and management of prostate cancer is well established in the U.S. and other developed countries. As such, the PSA reference range is based on the PSA levels in Caucasian and African-American populations that may not necessarily be applicable to men of other ethnicities.

At the Jos University Teaching Hospital (JUTH) in Jos, Nigeria carcinoma of the prostate is the most common urological cancer seen in men, [6] and the disease is seen in younger age groups. The purpose of this study was to investigate the levels of PSA in an indigenous African population.

Method and Materials

Subjects

Men (n = 48) between 35 and 83 years of age who presented with benign prostatic hyperplasia (BPH) or prostate cancer were recruited from the Urology Unit of the Jos University Teaching Hospital. These conditions are associated with bladder neck outflow obstruction. Patients underwent a detailed history clinical examination including a digital rectal examination (DRE). Nine clinical and physical criteria were used to compute a severity score: frequency of micturition, hesitancy during urination, overflow/dribbling, retention, incomplete emptying, enlarged prostate, fixed overlying mucosa, obliterated sulcus and nodularity.

Age-matched control subjects (n = 64) were recruited from a population of asymptomatic men at the Jos University Teaching Hospital. Inclusion criteria were the following: no history of benign prostate hyperplasia, prostate cancer, or any other cancer, and no history of urological dysfunction. Many of the men were recruited from another study that sought healthy men for bone-density screening. This study was approved by the Ethics Review Committee of the Jos University Teaching Hospital in Jos, Nigeria and the Human Research Review Committee of the University of New Mexico Health Sciences Center in Albuquerque, NM. Informed consent was obtained from all subjects.

The ages of the subjects were recorded and height, weight, mid-arm circumference (MAC) and triceps skin fold (TSK) measurements were also obtained.

Sample collection

Blood was collected from each participant at the time of presentation and was allowed to clot at room temperature for at least 45 minutes. After separation of the serum, the samples were stored at -40°C until transfer to University of New Mexico Health Sciences Center, Albuquerque, New Mexico for analysis of total PSA.

PSA Determination

Total PSA from blood serum was measured using an immunoassay (DSL-10-9700 Active PSA Enzyme-Linked

Immunosorbent Assay, Webster, TX). This procedure is an enzymatically amplified "two-step" sandwich type immunoassay in which serum samples are incubated in microtitration wells that have been coated with anti-PSA antibody. The wells were then treated with anti-PSA detection antibody linked to horseradish peroxidase (HRP). After a second incubation with the substrate, tetramethylbenzidine (TMB), an acidic stopping solution was added and the degree of enzymatic turnover of the substrate was determined by dual wavelength absorbance measurement at 450 nm and 620 nm. The absorbance was directly proportional to the concentration of PSA present.

Statistical analysis

Comparisons between subjects and controls were made using a two-sample t-test (NCSS, Kaysville, UT). Correlations between PSA, age and severity score were also determined. A p-value of <0.05 was considered statistically significant.

Results

A summary of the study population characteristics is given in Table 1. There were no significant differences in the mean ages of the patients (62.0 ± 10.6 years) and controls (59.0 ± 7.8 years). Although the mean body mass index (BMI) of the patients and controls were not significantly different, there were statistically significant differences in the mean MAC and TSK between subjects with prostate disease and controls ($p = 0.005$ and $p = 0.03$, respectively).

The mean total PSA level for the patients was significantly higher than for controls (35.5 ± 44.9 ng/ml vs. 2.22 ± 2.9 ng/ml, respectively, $p < 0.001$). Although the PSA level for 31 of 48 patients was above the upper limit of the U.S. reference range (10 ng/ml), 17 of the subjects with prostate disease had PSA levels at or below this concentration (Figure 1). Similarly, 26 of the 48 patients had serum PSA concentrations more than two standard deviations above the mean for the healthy Nigerian controls (8.0 ng/ml) and 22 patients had PSA values lower than 8.0 ng/ml. The PSA level was found to increase with severity of clinical and physical symptoms (Figure 2, $r^2 = 0.247$, $p = 0.002$). However, there was no significant correlation between age and PSA in the patients or controls or with severity of symptoms.

Table I. Anthropometric characteristics of Nigerian men with prostate disease and healthy controls

Characteristic	Subjects (n=48)	Controls (n=64)	P-value
Age (yrs)	62.0 ± 10.3	59.0 ± 7.8	NS
Weight (kg)	61.1 ± 11.6	64.8 ± 13	NS
Height (cm)	166.3 ± 5.9	168.3 ± 6.8	NS
BMI (kg/m^2)	22.0 ± 3.7	22.7 ± 4.0	NS
MAC (cm)	25.1 ± 3.2	27.3 ± 3.7	0.005
TSK (cm)	8.7 ± 4.9	11.6 ± 6.7	0.03
PSA (ng/ml)	35.5 ± 44.9	2.22 ± 2.9	<0.001

BMI: body mass index, MAC: mid-arm circumference, TSK: tricep skin fold thickness, PSA: prostate specific antigen, NS: not statistically significant.

Figure 1. Age and PSA levels in Nigerian men with prostate disease (O). (solid line represents the mean PSA level age for healthy controls and dashed line represents the 95th percentile for the distribution of PSA levels of healthy Nigerian men)

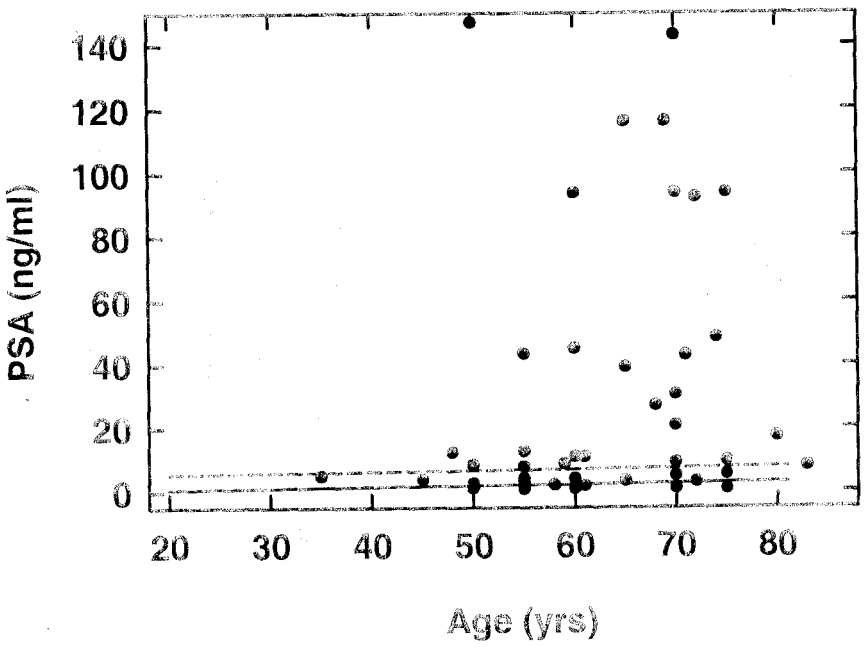
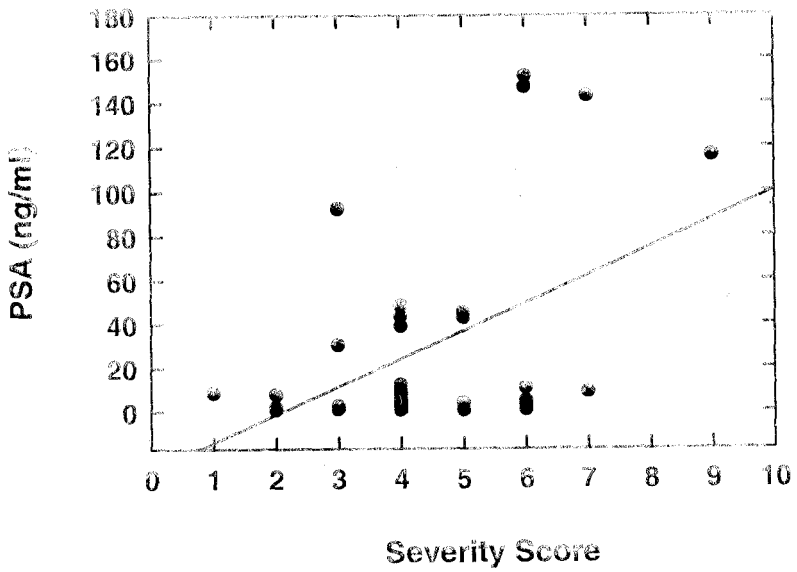


Figure 2. The correlation of PSA levels with severity score for prostate disease



Discussion

When a DRE reveals a normal prostate, the finding of a PSA level of 4 ng/ml or less is usually indicative of an absence of prostate disease, whereas levels between 4 and 10 ng/ml and above 10 ng/ml increase the likelihood of prostatic disease. Until recently, efforts to establish a PSA reference range have involved study populations that have included few men of African descent (7,8). Serum PSA levels are significantly higher in African-American men than in similarly aged Caucasian-American men (7.97 ± 0.95 ng/ml and 4.3 ± 2.4 ng/ml respectively). Kulbricht and coworkers in another study also found PSA levels to be statistically different between age-correlated healthy African-Americans and Caucasian-Americans (7.56 ± 1.11 ng/ml and 5.06 ± 0.32 ng/ml, respectively) (9). It is therefore possible that these PSA reference ranges may not be appropriate for men of African descent. Since little data is available regarding PSA levels of African men, it has not been possible to draw a comparison between PSA levels in African and African-American men.

The mean PSA value for the healthy Nigerian men in the present study was significantly lower than PSA values reported for healthy African-American men in the previously mentioned studies. The control sample from our study had a mean PSA level range of 2.22 ± 2.90 ng/ml, whereas healthy African-American men in other studies had PSA levels range of 7.97 ± 0.95 ng/ml and 7.56 ±1.1 ng/ml. [1,9]

We sought to establish a population-specific reference range for the healthy Nigerian men. As shown in Figure 1, 26 out of 48 patients had PSA levels that were above the upper limit of the range we determined using data for the healthy control subjects. While a number of patients had PSA values that fell between the median value for the population and the 95 percent confidence interval, several patients had PSA values below the median value.

When we compared anthropometric data for patients and controls, several statistically significant differences emerged. The mean MAC was higher in the control subjects than in the patients, indicating that the controls had more muscle mass than the patients. The mean TSK was also significantly higher for the controls. In addition to showing that the controls had more body fat than the patients, together, these observations suggest that the controls were better nourished than the patients with prostatic disease

It has been widely reported that PSA values are age-dependent. [3,7,8,10-12] In our study, however, we found that the PSA level did not increase with age and that severity of symptoms was not age-dependent. These data suggest that if men in their forties have similar symptoms and PSA levels as men in their seventies, the onset of prostate cancer or BPH may occur earlier in Nigerian men than in African-American men. However, due to the small population size in the present study, further investigation into PSA levels, age and severity of symptoms for African men are needed.

The limitations of this study are substantial and should be acknowledged. The number of patients and controls recruited for this study were low. Increasing the study population would be helpful for establishing a PSA reference range. Because the average life span for individuals in sub-Saharan African countries is generally lower than that of Americans, recruiting control subjects over the age of 50 years with no medical condition was problematic.

Prostate disease constitutes a major health problem for African men. Prostate cancer is associated with a higher morbidity and mortality rate since Nigerian men usually present to the hospital later and at a much lower age than men in developed countries. Due to the increasing

incidence in a population that is growing increasingly older, a screening strategy should be implemented to reduce the number of metastatic cases of prostate cancer. The availability of Nigerian-specific control values should aid in the diagnosis and monitoring the course of prostatic diseases in this population. This study serves as a useful first step towards establishing an index of suspicion for prostate cancer among African men.

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