Original Article

Relationship between Prostate Specific Antigen and Body Mass Index among Men in Lagos, South West Nigeria

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Abstract

B**ackground:** Obesity and overweight are health problems marked by excess adiposity which contribute to a number of preventable deaths and are significant risk factors for many chronic diseases including cancer. Prostate-specific antigen (PSA) has been used over the years to screen, diagnose, and monitor the treatment of prostate cancer. The aim of this study is to evaluate the relationship between body mass index (BMI) and PSA levels. **Materials and Methods:** A cross-sectional study of 125 overweight, 77 obese men and 78 controls aged 40–89 years was conducted in Lagos, South West Nigeria. The BMI, abdominal circumference (AC) serum total, and free PSA (tPSA; fPSA) were determined. Spearman correlation was used to determine the relationship between PSA and BMI and a significant level of $P < 0.05$ was used. **Results:** Participants with AC ≤102 cm had a higher median tPSA of 1.20 ng/ml (0.93, 1.55) than participants with AC >102 cm with a $P = 0.006$, but their median fPSA did not show any difference. The median tPSA among controls was higher than that of overweight and obese participants with $P = 0.008$ and $P = 0.000$, respectively. The control group had a higher median fPSA than the obese group ($P = 0.029$). There was also a significant negative correlation between tPSA and BMI ($r - 0.30$, $P = 0.00$) as well as between fPSA and BMI ($r - 0.14$, $P = 0.01$). **Conclusion:** The serum PSA levels in obese and overweight men are significantly lower than those of the controls. This can potentially prevent early detection of prostate cancer when using serum PSA as a screening tool in overweight and obese men.

Keywords: Obesity, overweight, prostate-specific antigen

Introduction

The discovery of serum prostate-specific antigen (PSA) and its extensive use over the past two decades has dramatically influenced the diagnosis and monitoring of prostate cancer before and after treatment, respectively.[1] Thus, PSA is currently the most common screening tool for prostate cancer with 58% of Caucasian men undergoing an annual test.[2] Early screening for prostate cancer includes testing for serum PSA which can help identify those who need to be followed up closely. PSA concentration has been noted to be lower in caucasian men compared to their negroid counterparts.[3,4]

Obesity marked by excess adiposity, on the other hand, is a growing global epidemic. One of the most recent global estimates found more than 650 million adults above 18 years were obese with about 42% of them being males.[5,6]

Previous studies have also suggested that components of metabolic syndrome are risk factors for the development of benign prostatic hyperplasia as well as prostate cancer.[7-10] However, much study has not been carried out to establish the relationship between individual components and the combined components of the metabolic syndrome, especially excess adiposity as seen in obesity and overweight and PSA in African blacks. It is imperative therefore, that with an increasing prevalence in prostate cancer in Nigerian men,[11] and a concurrent increase in the prevalence of obese and overweight patients,[12] there is a need to identify if there are possible associations between PSA, obesity, and overweight using the BMI and abdominal circumference as markers of excess adiposity. This knowledge will help to avoid errors in

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the assessment of prostate disorders using PSA concentrations for overweight and obese subjects and consider using additional diagnostic tools in them.

Materials and Methods

A cross-sectional study of 125 overweight, 77 obese men and 78 controls aged 40–89 years was conducted in Lagos, South West Nigeria. The study participants had no documented clinical and biochemical history of the prostate disorder, as well as no documented history of endocrine or metabolic diseases and who had not in the preceding 6 weeks used medications known to alter serum PSA like nonsteroidal anti-inflammatory drugs, statins, and thiazide diuretics.[13] Males who were not exposed to procedures or conditions likely to alter serum PSA levels such as digital rectal examination (DRE), transrectal ultrasound, sexual exposure, transurethral, or radiation procedures were also included in the study.

Questionnaires were administered to the participants recruited for the study to obtain basic demographic data.

Physical measurements were then taken by trained staff. The weight to the nearest 0.1 kg of each participant was taken. The height of each participant was measured to the nearest 0.1 m using a stadiometer; the abdominal circumference to the nearest 0.1 cm using a nonelastic tape rule at a point midway between the umbilicus and the iliac crest. The body mass index (BMI) was calculated from the weight and height using the formula BMI = weight/(height)^2.

Following a 12 h overnight fast, 4 mm of venous blood was collected from the antecubital fossa into a serum separator tube. The blood was then centrifuged at 3000 rpm for 5 min. The supernatant (serum) was transferred into plain bottles and stored at −20°C in a nonself-defrosting freezer up to a maximum of 1 month before analysis.[14]

The total PSA was analyzed using an enzyme-linked immunosorbent assay (ELISA) kit from Teco Diagnostics, US. Accubind ELISA kit Monobind Inc., USA was used for the quantitative determination of free PSA. The reaction was read using microtiter well reader, (Acurex Diagnostics, USA). The minimum detectable concentration of free PSA in this assay is estimated to be 0.052 ng/ml.

Approval was obtained from the research and ethics committee of the hospital, and informed consent was obtained from the participants of this study. Anonymity and confidentiality of findings were ensured, and patients were free to withdraw from the study if they wanted to.

Data from completed questionnaires and results of both total and free PSA analysis were entered into Microsoft Office Excel 2010.

The statistical analysis was carried out with the IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp. Data were tested for normality using the Kolmogorov–Smirnov test and descriptive statistics with normal distribution were presented as mean and standard deviation while the ones without a normal distribution were presented as median and interquartile ranges. The mean and standard deviation for age, height, weight, BMI, and for total and free PSA (tPSA and fPSA), the median and interquartile ranges were computed. Association between anthropometry and PSA was assessed using Spearman's correlation. The *P* value was set at <0.05.

Results

Two hundred and eighty participants were recruited for this study consisting of 202 and 78 cases and controls, respectively. Table 1 shows characteristics of the study participants. More than a quarter (27.90%) of the participants had ideal BMI, 44.60% were overweight and 33.80% were obese. Among the obese group, 85.7% of them had an abdominal circumference >102 cm, 15.2% of the overweight group had AC >102 cm while none of the controls had AC above 102 cm.

The mean age of participants in the overweight class was 49.17 years; obese class 50.92 years; Ideal weight was 51.68 years which are similar to a *P* = 0.15.

Table 2 shows the mean AC and mean BMI for the controls, overweight, and obese participants.

Table 3 shows the serum tPSA and fPSA across the BMI groups as well as across the AC cutoff values within each group. The median tPSA in the control group was 1.40 ng/ml, 1.10 ng/ml in the overweight group with a *P* value of 0.01 while the obese participants had the lowest median serum PSA of 0.96 ng/ml with a *P* value of 0.00. The median fPSA among the Ideal weight participants was 0.45 ng/ml which was similar to 0.45 ng/ml among the overweight group with

Table 1: General characteristics of study participants

Variables	Number of participants and percentage
BMI class	
Ideal weight	78 (27.90)
Overweight	125 (44.60)
Obese	77 (33.80)
Age range	
40-49	152 (54.30)
50-59	80 (28.60)
60-69	36 (12.90)
70-79	9 (3.20)
80-89	3 (1.07)
Mean age (years)	50.35±9.49
Mean height±SD (m)	1.71±0.07
Mean weight±SD (kg)	79.19±16.04
Mean BMI±SD (kg/m^2)	27.12±4.70
Mean abdominal circumference±SD (m)	0.95±0.14
Median total PSA (IQR) (ng/mL)	1.13 (0.50-3.27)
Median free PSA (IQR) (ng/mL)	0.47 (0.05-1.17)

BMI: Body mass index, SD: Standard deviation, PSA: Prostate specific antigen, IQR: Interquartile range

a $P = 0.77$. The obese participants, however, had a lower free PSA of 0.39 ng/ml with a $P = 0.03$.

Among the men who had abdominal circumference above 102 cm, the median serum tPSA was 1.0 ng/ml (0.65, 1.45) while fPSA was 0.42 ng/ml (0.31, 0.61) [Table 3]. The participants with abdominal circumference of 102 cm and below had a median tPSA of 1.2 ng/ml (0.93, 1.6) and a free PSA of 0.45 ng/ml (0.36, 0.53).

The Spearman correlation analysis [Table 4] shows a significant positive correlation between age and serum tPSA ($r = 0.26$, $P = 0.00$) as well as serum-free PSA values ($r = 0.14$, $P = 0.02$). There is a significant negative correlation between serum tPSA, fPSA, and BMI. Total PSA is negatively correlated with abdominal circumference [Table 4].

Discussion

This study investigated the levels of serum PSA in overweight and obese healthy Nigerian men aged 40 years and above to assess the effect of BMI on PSA. The study focused more on men who are 40 years and above without including men in the younger age group because PSA has been noted to increase with advancing age. We found a median PSA among the controls which were slightly higher than a previous study done in the same region which studied 214 Nigerians aged 22–76 years and reported a median PSA value of 0.7 ng/ml (0.1, 4.3) among the healthy participants.[15] Their findings of low PSA value among controls can be traced to the fact that the age distribution of the study participants in their study was lower than our study and they recruited fewer participants as controls than our study.

We used the measurement of BMI and AC as the measures of excess adiposity in the participants. More than 80% of the obese participants had AC greater than the desirable cutoff while about 15% of the overweight group had AC more than the desirable cutoff according to the National Cholesterol Education Programme.[16] This follows that most of the obese participants had abdominal adiposity. However, median PSA in the participants with increased AC was significantly higher than those with the desirable abdominal circumference. All the controls had desirable AC values. The difference in fPSA between the two groups was, however, not statistically significant. The apparently healthy controls had a statistically significant higher median PSA than the obese and overweight groups. We also found significant lower levels of serum tPSA concentration in the obese and overweight participants when compared to the control participants of similar age groups. We believe this reflected the true state of the participants since those with possible interferences that affect PSA concentrations including medications such as nonsteroidal anti-inflammatory drugs and statins were excluded from the study. The overweight participants had higher tPSA concentrations than their obese counterparts thus supporting the fact that BMI is inversely related to PSA concentration. In addition, the serum fPSA was also found to follow a similar pattern with tPSA, i.e., control participants having a higher serum free PSA than their obese counterparts.

According to a study, men who are obese were found to have lower PSA levels than their nonobese counterparts, and this was attributed to decreased testosterone concentration and plasma hemodilution, which is the dilution of soluble tumor markers by increased plasma volumes.[17]

Since most prostate cancers are signaled by an abnormal PSA test, it, therefore, follows that if the baseline serum PSA were reduced, obese men with early disease will be at increased risk for having serum PSA levels lower than the cutoff values.[18] To this end, a previous study reported obesity to be positively associated with increased risk of prostate cancer-specific mortality rate.[19]

Despite these findings, the relation of BMI to PSA has however not received much attention in populations of African origin.[20]

Fowke *et al*.[21] in their study reported decreasing PSA levels with increasing BMI. They reported that race, BMI, and height were independently associated with PSA. Their values in the

Table 2: Body mass index and abdominal circumference of participants

	Overweight	Obese	Ideal	*P*
Mean BMI±SD	26.70±1.41	33.12±3.20	21.87±1.54	0.01
Mean AC±SD	92.18±9.55	111.08±8.66	82.99±5.95	0.01

BMI: Body mass index, SD: Standard deviation, AC: Abdominal circumference

Table 3: Total and free prostate specific antigen by body mass index and abdominal circumference

	Overweight	Obese	Ideal	*P*
Median tPSA (IQR)	1.10 (0.90-1.55)	0.96 (0.63-1.23)	1.40 (1.10-1.60)	0.00
Median fPSA (IQR)	0.45 (0.36-0.60)	0.39 (0.30-0.58)	0.45 (0.38-0.54)	0.03
For AC ≤102 cm				
Median tPSA (IQR)	0.94 (0.74-1.32)	0.82 (0.57-1.14)	0.90 (0.76-1.18)	0.01
Median fPSA (IQR)	0.44 (0.35-0.52)	0.38 (0.33-0.65)	0.37 (0.44-0.53)	0.53
AC >102 cm				
Median tPSA (IQR)	1.30 (0.78-2.42)	0.94 (0.56-1.45)	-	0.01
Median fPSA (IQR)	0.50 (0.38-0.81)	0.46 (0.31-0.68)	-	0.03

AC: Abdominal circumference, IQR: Interquartile range, tPSA: Total PSA, fPSA: Free PSA, PSA: Prostate specific antigen

Table 4: Spearman correlation analysis

	tPSA	fPSA
Age	r=0.26**; P=0.00	r=0.14**; P=0.02
Weight	r=−0.28; P=0.00	r=−0.15; P=0.01
Height	r=−0.13; P=0.03	r=−0.09; P=0.13
BMI	r=−0.30; P=0.00	r=−0.14; P=0.01
AC	r=−0.20; P=0.00	r=0.12; P=0.04

**Correlation is significant at 0.01 level (two-tailed). BMI: Body mass index, AC: Abdominal circumference, tPSA: Total PSA, fPSA: Free PSA, PSA: Prostate specific antigen

African American and Caucasian were comparably lower to findings in our study but had a similar inverse relationship between PSA and BMI.

According to analyzed data from the USA 2001/2004 National Health and Nutrition Examination Survey involving whites, blacks, and Mexican Americans. It reported that White and Mexican American men had a trend of decreasing PSA levels with increasing BMI. The median PSA levels for BMI group of <25 kg/m^2 had higher PSA values than the 25–30 kg/m^2 group.[22]

Obesity has been observed to be the most influencing factor on serum PSA concentration among the components of metabolic syndrome by reducing serum PSA concentration, and it is also the most common cause of insulin resistance.[7,8] A higher BMI was positively associated with risk of death from 12 different types of cancer among men, including prostate cancer. Class I obese men were 20% more likely to die from prostate cancer than ideal weight men, whereas men who were Class II obese were 34% more likely to die from prostate cancer.[19] Various explanations have been given for the relationship between obesity and prostate cancer, and these include alterations in serum hormone concentrations (e.g., testosterone, estrogen, and insulin), diet and lack of physical activity.[23] Testosterone is a key prostate growth factor, and obesity has been found to be associated with decreased testosterone levels.[23] Recent data from retrospective studies suggested that testosterone may exert a differentiating effect on prostate cancer and decreased serum testosterone levels have been associated with more advanced and poorly differentiated tumors at presentation.[24] It has even been suggested that maintaining a normal serum testosterone level may prevent prostate cancer.[25] In addition to alterations in serum testosterone levels, obese men have increased serum estradiol levels due to peripheral conversion of testosterone to estradiol by aromatase in adipocytes; although, the exact role it plays is still unclear.[26] Beyond alterations in the sex steroid hormones of testosterone and estradiol, obesity is associated with altered levels of several other serum hormones including insulin, leptin, and adiponectin.[27] When focusing on the prostate, periprostatic (PP) adipose tissue represents the first structure outside the organ capsule; its infiltration by tumor cells has a detrimental effect on the prognosis of patients with prostate cancer.[28] While growing evidence suggests an important link between obesity and several human malignancies, the mechanisms underlying this relationship are still poorly understood.[29]

Furthermore, several genes were differentially expressed and identified in the PP adipose tissue of obese patients (for example, FADS1, LEP, and ANGPT1) in a study by Lugezzani while working on the PP adipose tissue of 18 obese/overweight patients. These genes were mainly related to anti-lipolytic, lipogenic, proliferative, and anti-apoptotic activities. Genes linked to the inflammatory response (for example, NPY1R and FADS1), were also differentially expressed in the PP adipose tissue of obese patients, thus determining a favorable environment for disease progression.[29]

In addition to having a low PSA, obese men are also at the risk of having the highest rate of undetected cancer due to the technical difficulty of adequately sampling an enlarged prostate by needle biopsy.[30]

Our findings revealed that participants with a higher AC also had a lower tPSA and fPSA. The underweight group had a significant elevation above the obese group who had lower PSA values. Ukoli *et al*.,[31] reported that central adiposity may be a more important predictor of elevated PSA than BMI in the population they studied. The findings in this study, however, suggest that both abdominal circumference and BMI are important anthropometric indices to be considered. Serum PSA has been reported to be negatively associated with obesity as measured by BMI or waist circumference. In this study, we found a negative correlation between abdominal circumference and serum tPSA, but a positive correlation with fPSA.[18]

A study conducted in Nigeria, however, reported that an inverse relationship has not been proven in all ethnic groups and that although overweight and obesity is common among Nigerian men, there was no associated tendency toward lower serum total PSA among them.[32] There is, therefore, a need to replicate similar studies in other ethnic groups or geographical regions in Nigeria.

A limitation of the present study is that prostate biopsy was not carried out to ascertain the true state of health of the prostate gland in the apparently healthy study participants.

Conclusion

This study found that both serum total and free PSA are lower in overweight and obese Nigerian men as well as men with the higher abdominal circumference. It is recommended that additional clinical tools such as DRE and transrectal ultrasonography of the prostate be combined with PSA assay in overweight and obese men. A failure to detect the true status of the level of PSA during prostate cancer screening can potentially prevent early detection of prostate cancer when using serum PSA alone as a screening tool in overweight and obese men.

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Conflicts of interest

There are no conflicts of interest.

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