Original Research Article

Body mass index and age correlation with prostate-specific antigen density as prostate cancer risk indicators in a screened male University population in Nigeria: A pilot study

Abstract

Background: Prostate-specific antigen density (PSAD) is one of the means of improving PSA sensitivity as a marker of prostate cancer diagnosis. However, this ability is perceived to be obscured by certain factors such as high body mass index and age in Caucasian and western populations, which tends to reduce its sensitivity and lead to misclassification of at-risk patients for prostate cancer.

Aim: We studied the correlation of body mass index (BMI) and age with prostate-specific antigen density (PSAD) as indicators of prostate cancer risk in a screened male population(40 years and above) in the University of Calabar, Nigeria.

Study design: A cross sectional analytical study with consecutive participant recruitment.

Place and duration of study: The study was carried out in the University of Calabar Medical centre during a medical outreach.

Materials and method: The study involved sixty one (61) apparently healthy male participants. BMI was mathematically determined from the weight and height and was categorized as underweight, normal weight, overweight and obesity based on the WHO classification with values of <18.5, 18.5-24.9, 25.0-29.9, and ≥30 (Kg/m^2) respectively. Blood samples were collected and analyzed for PSA and transrectal ultrasound scan was done to estimate the prostate volume and was used to calculate the prostate-specific antigen density.

Results: Over 67% of participants had PSA values below 4.0ng/ml, 14.8% between 4.0-10.0ng/ml, and 18% above 10.0ng/ml. Body mass index (BMI) assessment revealed that1.6% of the sampled population had BMI <18.5Kg/m^2, 32.8% had BMI between 18.5 Kg/m^2 and 24.9 Kg/m^2, while 50.8% were noticed to have BMI of between 25.0 Kg/m^2 and 29.9 Kg/m^2, and 14.8% had BMI of 30 Kg/m^2 and above.

Conclusion: There was an inverse correlation of BMI with prostate-specific antigen density (PSAD) and a direct correlation of age with PSAD in this study of Nigerian men.

Key words: Age, body mass index, prostate-specific antigen, prostate-specific antigen density, University of Calabar

Introduction

Prostate cancer is top on the list among causes of cancer related deaths in men and ranks as the second most common cancer after lung cancer the world over.[1] In Nigeria there is a gradual trend of rising prostate cancer cases which is attributable to increasing urbanization and changing dietary habit as well as the increased awareness towards the use of health facilities leading to more cases being documented. Body mass index (BMI) has been linked with aggressive prostate cancer by some studies but its association still requires to be properly established as previous studies have disputed a clear pattern of relationship.[2] Some studies suggest that the effect of BMI on serum prostate-specific antigen levels is inversely related meaning that in obesity or high BMI there is decrease concentration of PSA.[1, 2]It is on this premise therefore that some investigators think that obesity as evidenced by high BMI might reduce the sensitivity of screening for prostate cancer with prostate specific antigen (PSA).[3]This apparent decrease in sensitivity or of PSA concentration was attributed to the dilution effect resulting from raised plasma volume in obese individuals.[3] High BMI as a strong indicator of obesity, is said to be responsible for myriad of co-morbidities, and is on the rise in transitioning economies like Nigeria.[1] Age and ageing have been associated with changes in prostate-specific antigen level, prostate volume and prostate-specific antigen density (PSAD) with elevations seen with increasing age.[4,5]PSAD is the means by which PSA secretion per unit volume of prostatic tissue is assessed.[6] Prostate-specific antigen density has also been used to improve the sensitivity of PSA at indeterminate concentrations to detect prostate cancer in men with negative digital rectal examination.[7]High BMI (obesity) has been associated with low prostate-specific antigen density and has high risk of prostate cancer due to the reduction in sensitivity of the test.[2, 8]Studies have also shown an association between PSAD status and aggressiveness of prostate cancer disease and its usefulness in selecting patients for biopsy and surveillance purposes.[9, 10] In men with high BMI (obesity) the PSAD is seen to be low and therefore are predisposed to the risk of developing prostate cancer disease without being detected early. PSAD and BMI are race-dependent and therefore vary along racial lines, [11] and since age also influences the levels of PSA, it is imperative to study these parameters in different ethnic communities, globally.[6, 12]This study therefore was conducted to determine the correlation of these prostate cancer influencing indices among apparently healthy men in the University of Calabar, Nigeria.

Materials and methods

This was a cross sectional analytical study involving sixty one (61) apparently healthy participants recruited consecutively in a medical outreach carried out in the University of Calabar Medical Center for members of the University community. The participants had already been prepared through instructions on fliers and other media outlets to abstain from sexual intercourse and ejaculation for at least 3 days prior to the exercise. Informed consent was collected from participants who were 40 years and above and had no previous history of prostate cancer or benign prostatic hyperplasia. The height and weight of all the participants were measured with a stadiometer device and 1 mL of blood samples collected for prostate-specific

antigen (PSA) assay before digital rectal examination (DRE) and transrectal ultrasonography (TRUS) were performed. Two drops of whole blood collected from all 200 participants in attendance were tested by adding unto the test chamber of a dry chemistry (Rapid Diaspot) one-step device for PSA assay along with a drop of diluent and was read after 5 minutes. However, only the samples of 61 participants who met the inclusion criteria (abstinence from coitus or masturbation in past three days, not on urethral catheter, did not have DRE before presentation) were used as data for statistical analysis following the findings on DRE and TRUS procedures. Body mass index (BMI) was mathematically determined by dividing the weight in Kilograms (Kg) by the square of the height in square meters (m^2). The PSAD was also mathematically determined by dividing the PSA by the prostate volume which was estimated with the means of the TRUS.

Results

The socio-demographic findings are presented in Table 1. The ages of participants were grouped into 40-49 years, 50-59 years and 60 years and above with a range of 40-66 years and mean age of 52.03±7.5 years. The 40-49 years age grouping had a frequency of 22 representing 36.1% of the participating population while the age grouping of 50-59 years had a frequency of 27 which represented 44.3% of the participants and a frequency of 12 was noted for those 60 years and above which represented 19.7% of the sampled population.

Table 1 showing socio-demographics of the participants

Variable	Frequency (n=61)	Percentage
Age group (years)		
40-49	22	36.1
50-59	27	44.3
≥60	12	19.7
Mean±SD	52.03±7.5	
Marital status		
Single	12	19.7
Married	49	80.3
Level of education		
Primary	8	13.1
Secondary	15	24.6
Tertiary	38	62.3

Age range= 40-66

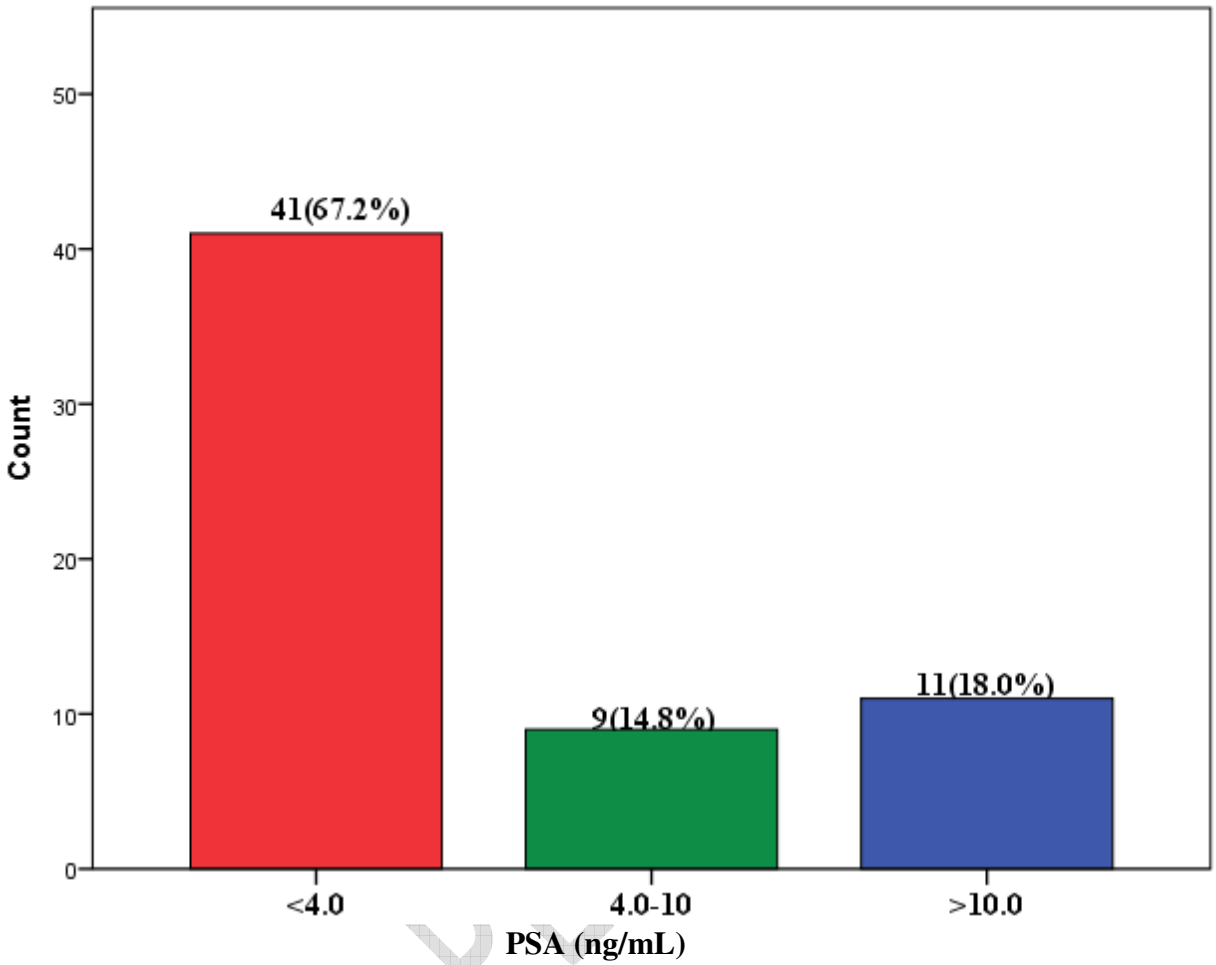

Figure 1: Bar chart showing PSA values of participants.

The values of PSA concentration were presented in Figure 1. Forty one (41) participants representing 67.2% of the sampled population had PSA concentration less than 4.0ng/mL (< 4.0 ng/mL), while nine (9) of the participants representing 4.8% had PSA values of 4.0-10.0 ng/mL and 11 of the participants had values greater than 10.0 ng/mL (>10.0 ng/mL) representing 18.0% of the sampled population.

The association of age with prostate-specific antigen levels was captured in Table 2 and showed that out of the 22 participants that were within the 40-49 years age grouping 18 of them representing 81.8% had PSA values of less than 4.0ng/mL and only 2 participants had 4.0-10.0ng/mL and another 2 greater than 10.0ng/mL representing 9.1% of each group.

15 participants out of the 27within the age grouping of 50-59 years representing 55.6% had PSA values of less than 4.0ng/mL, while 5 participants representing 18.5% had PSA values between

4.0 and 10.0ng/mL and 7 participants translating to 25.9% had PSA values greater than 10.0ng/mL.

Out of the 12 participants that fell within the age grouping of 60 years and above, 8 of them representing 66.7% had PSA values below 4.0ng/mL, while 2 had PSA values between 4.0 and 10.0ng/mL and another 2 participants had PSA values greater than 10.0ng/mL, both representing 16.7% of each group.

Table 2: Association between PSA titre and age group of participants

	Prostate-specific antigen		
	<4.0	**4.0-10.0**	**>10.0**
Age group (years)			
40-49	18(81.8)	2(9.1)	2(9.1)
50-59	15(55.6)	5(18.5)	7(25.9)
≥60	8(66.7)	2(16.7)	2(16.7)

X^2=3.933, df=4, p-value=0.415

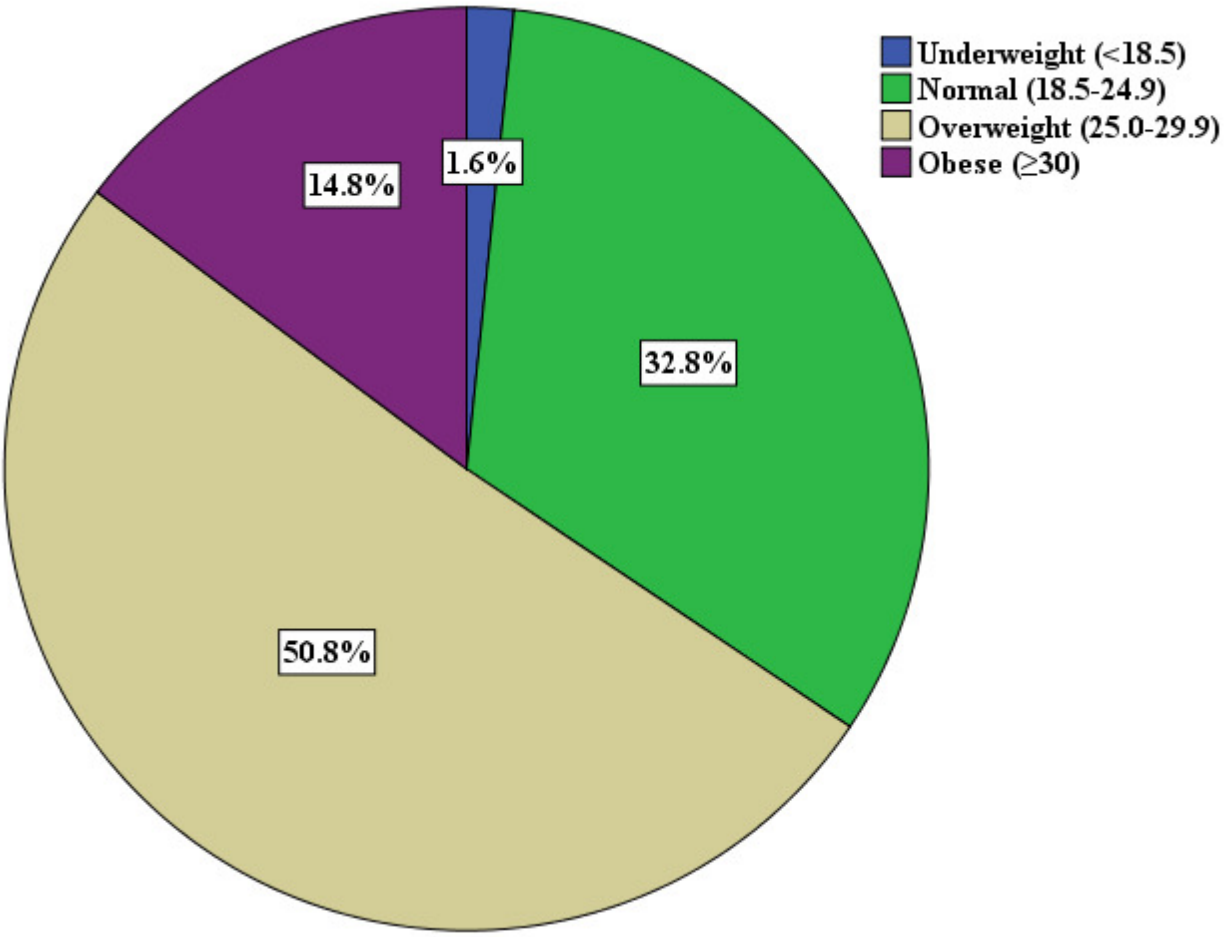

Figure 2: BMI class of participants

The body mass index (BMI) class of participants is illustrated in the pie chart in figure 2 above. 14.8% of the participants were obese while 50.8% were overweight. The remaining 32.8% and 1.6% were normal weight and underweight respectively.

The body mass index (BMI) and prostate-specific antigen (PSAD) were shown on table 3. The mean BMI was 27.99±3.9Kg/m^2 with the minimum of 20.54Kg/m^2 and a maximum BMI of 35.43Kg/m^2. The median prostate-specific density (PSAD) was 0.01ng/mL/cm^3 with the minimum of 0.00ng/mL/cm^3 and maximum value of 1.00ng/mL/cm^3.

138 **Table 3: Descriptive statistics of anthropometry and PSA parameters**

	Mean±SD	Minimum	Maximum
Height (m)	1.66±0.62	1.48	1.77
Weight (Kg)	73.10±13.4	45	111
BMI (Kg/m^2)	27.98±3.9	20.54	35.43
	Median	**Minimum**	**Maximum**
Total PSA (ng/mL)	0.20	0.00	20.80
Prostate volume (cm^3)	22.85	7.70	105.02
PSA density (ng/mL/cm^3)	0.01	0.00	1.00

139

140

141

142

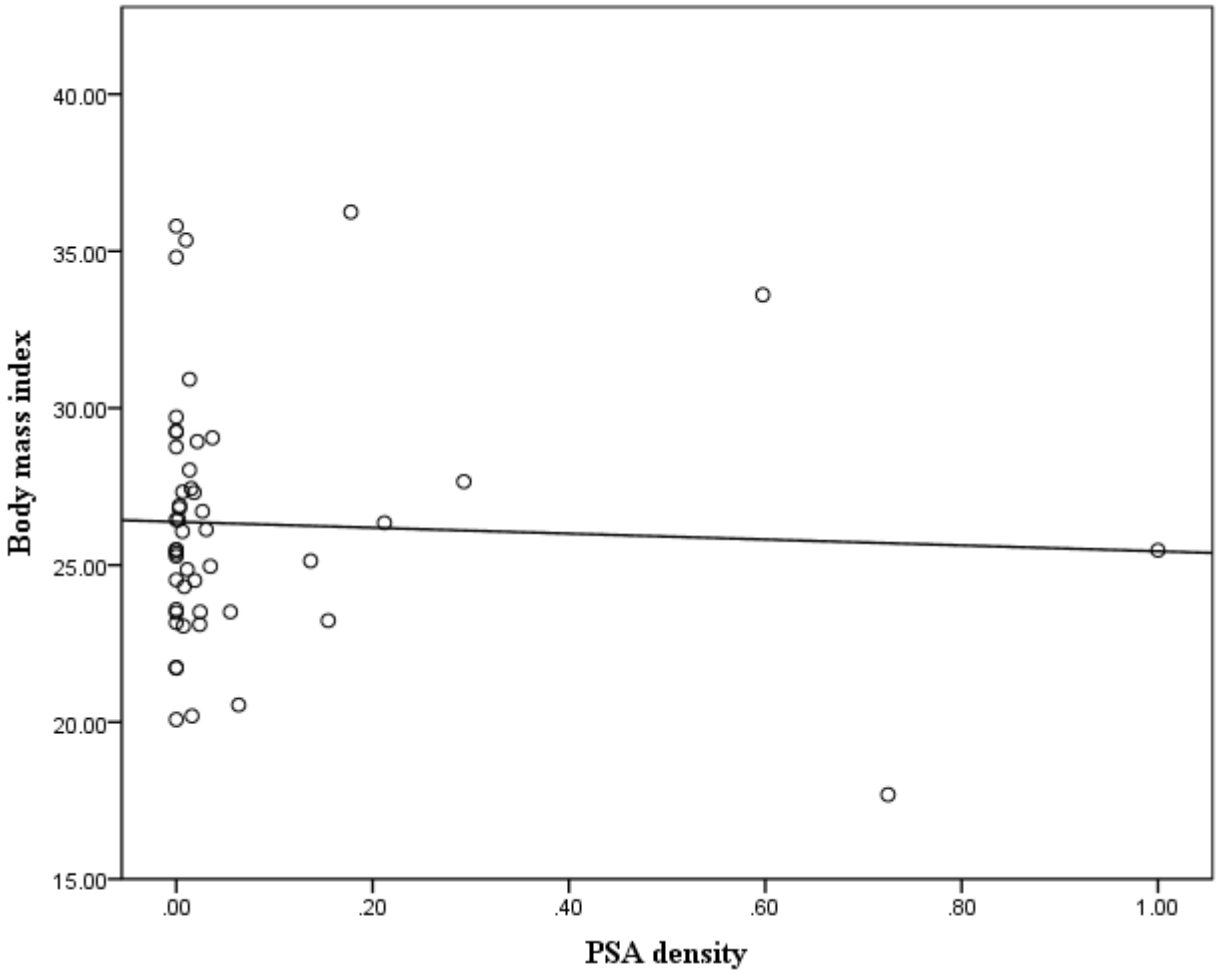

Figure 3: Scatter plot showing relationship between PSA density and BMI

Spearman correlation (r) =0.019, p=0.898

There was an inverse monotonic Spearman correlation of BMI with PSAD as shown in figure 3 above. PSAD decreased with increased BMI, P = 0.898.

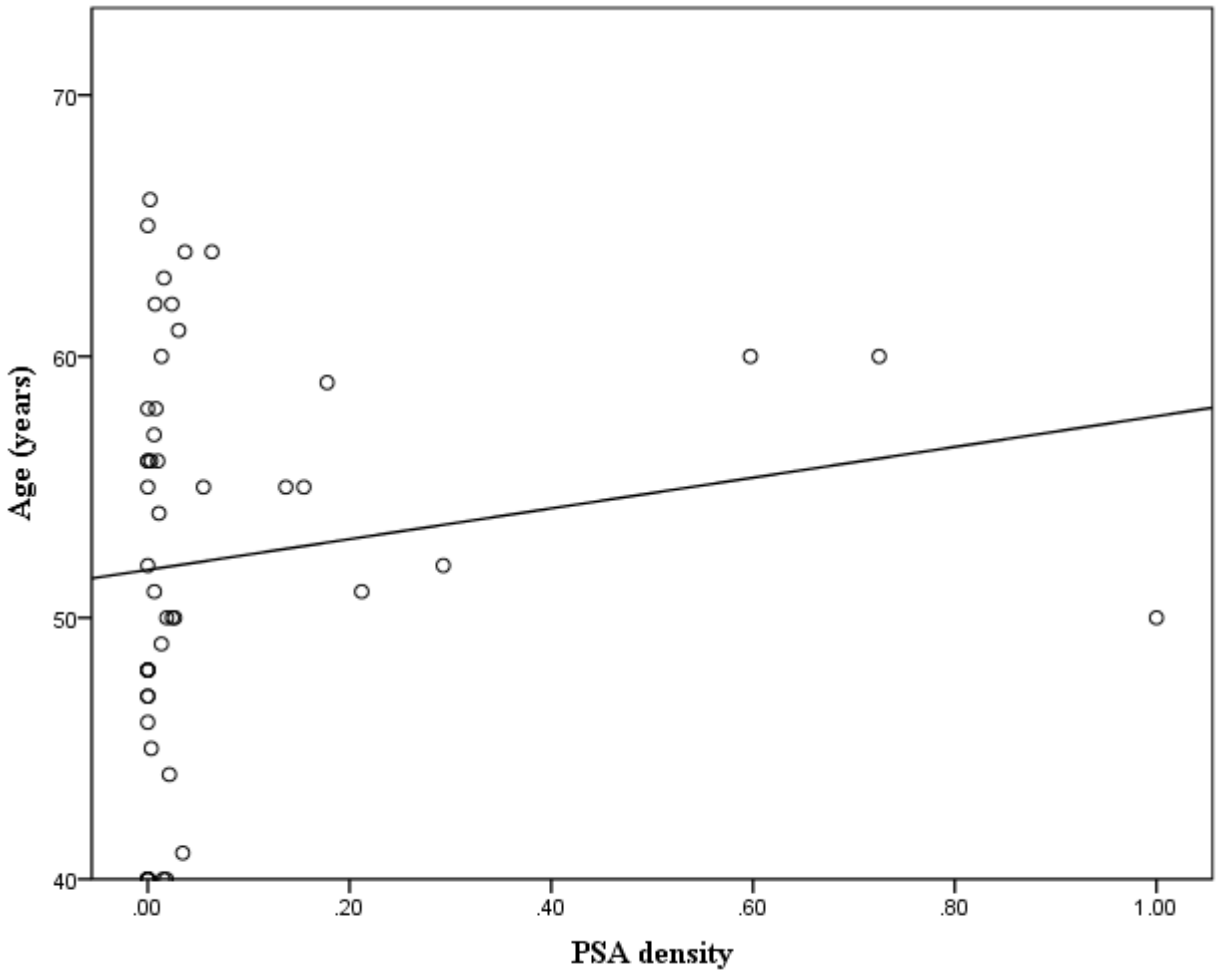

Figure 4: Scatter plot showing relationship between PSA density and Age

Spearman correlation (r) =0.337, p=0.017* (significant)

The relationship of age with PSAD was illustrated on figure 4 above in a scatter plot that showed a moderate direct monotonic spearman's correlation. There was increase in PSAD with increasing age. P = 0.017

Discussion

The benefits of early diagnosis of prostate cancer include early commencement of treatment, deferred complications and promotion of good quality of life. Some of the indices that reduce the sensitivity of PSA as a marker of early detection of prostate cancer are body mass index (BMI) and age among Caucasians and western populations. Their correlation with prostate-specific antigen density (PSAD) was assessed in Nigerian men in this study. Our study which was in an apparently healthy population revealedour study group to have predominantly high BMI with over 65% being either in the overweight or obese category. Bonn and colleagues[2]studied the association between high BMI, serum PSA as well as prostate cancer risk in 15,827 men, and during follow up 735 men were diagnosed with prostate cancer with 38.4% being high-grade cancers. Even though the association was not statistically significant, they concluded BMI was important in risk stratification for prostate cancer. PSAD is known to improve the sensitivity of PSA as a marker of prostate cancer and by extension, factors that affect PSA would affect PSAD. Body mass index (BMI) had an inverse correlation with PSAD (PSAD was observed to decrease with increased BMI). This observation is in conformity with a previous study in Northwestern Chinese population.[1]Thedecrease in PSAD apparently masks the detection of patients at risk of prostate cancer due to misclassification. Available literature shows that testosterone is known to improve the normal differentiation of prostatic epithelial tissue and when reduced could lead to poor differentiation that may promote carcinogenesis.[13]High BMI (obesity) is associated with a reduction in testosterone level which suggest that patients with high BMI and low PSAD as was established in this study are prone to the risk of poorly differentiated prostatic epithelial tissue and aggressive prostate cancer. The PSAD was seen to have a direct monotonic correlation with age, by subtly increasing with increase in age. This was in keeping with published literature in India that showed a similar pattern in PSAD in which there was increase in PSAD with increasing age and which was attributed to a corresponding increase in prostate volume with age.[11]PSAD is a function of PSA and prostate volume which are seen to increase with increase in age and therefore is affected by aging.

Conclusion:

There was an inverse correlation of BMI with PSAD and a direct correlation of age with PSAD in this study of Nigerian men. Therefore, high BMI and increasing age affect PSAD by reducing its value consequently leading to misclassification of at-risk patient for prostate cancer disease.

Recommendation:

The use of prostate-specific antigen density (PSAD) as an adjunct tool in the diagnosis of prostate cancer should be used with caution and in conjunction with other parameters, especially in the obese and the elderly.

Further studies on this subject are required with a larger sample size to affirm these findings.

References

1. Zhang J, Ma M, Nan X, Sheng B. Obesity inversely correlates with prostate-specific antigen levels in a population with normal screening results of prostate cancer in northwestern China. Brazilian Journal of Medical and Biological Research. 2016;49(8).
2. Bonn SE, Sjölander A, Tillander A, Wiklund F, Grönberg H, Bälter K. Body mass index in relation to serum prostate-specific antigen levels and prostate cancer risk. International journal of cancer. 2016;139(1):50-57.
3. Kubota Y, Seike K, Maeda S, Shinohara Y, Iwata M, Sugimoto N. Relationship between prostate-specific antigen and obesity in prostate cancer screening: Analysis of a large cohort in Japan. International Journal of Urology. 2011;18(1):72-75.
4. Mario BO, Manuel V, Renata M, Simona C, Giovanni C, Fabrizio F. Relationship between prostatic specific antigen (PSA) and volume of the prostate in benign prostatic hyperplasia in the elderly. Critical Reviews in Oncology/Hematology, 2003; 47(3): 207-211.
5. Abdo AK, Mehdi S, Seyyed MTA, Mehrzad L, Mehrdad A, Ali A et al. Age specific reference levels of serum prostate-sppecific antigen, prostate volume and prostate-specific antigen density in healthy Iranian men. Iranian Journal of Immunology, 2009; 6: 40-48.
6. Emeka IU, Ikenna IN, Francis OO, Fred OU, Adesina SO, Samuel RO, et al. Prostate-specific antigen density values among patients with symptomatic prostatic enlargement in Nigeria. World Journal of surgical oncology, 2016; 14:174.
7. Lujan M, Paez A, Llanes L, Miravalles E, Berenquer A. Prostate specific antigen density. Is there a role for this parameter when screening for prostate cancer? Prostate cancer and prostatic diseases. 2001;4:146-149.
8. Kim JH, Doo SW, Yang WJ, Song YS, Kwon S-S. Prostate-specific antigen density: a better index of obesity-related PSA decrease in ostensibly healthy Korean men with a PSA< 3.0 ng/mL. Urology. 2013;81(4):849-852.
9. Loeb S. Prostate Health Index (PHI): golden bullet or just another prostate cancer marker? European urology. 2013;63(6):995-996.
10. Khezri AA, Shirazi M, Ayatollahi SMT, Lotfi M, Askarian M, Ariafar A, et al. Age Specific Reference Levels of Serum Prostate-Specific Antigen, Prostate Volume and Prostate Specific Antigen Density in Healthy Iranian Men. Iranian Journal of Immunology. 2009;6(1):40-48.
11. Arvind PG, Mahesh RD, Manohar T and Sharad B. Age-specific prostate specific antigen and prostate specific antigen density values in a community-based Indian population. Indain J Urol. 2007 Apr-Jun; 23(2): 122-125.
12. Shanggar K, Kia FQ, Retnagowri R Azad HAR, Norman D. Revisiting prostate specific antigen density (PSAD): A prospective analysis in predicting the histology of prostate biopsy. Int J Clin Exp Med, 2018; 11(4): 3873-3879
13. Carmen R, Stephen JF, Anusila D, Eric JJ, Marjorie LM, Alpha VP et al. Body mass index, weight change, and risk of prostate cancer in the cancer prevention study ii nutrition cohort.Cancer Epidemiol BiomarkersPrev 2007; 16 (1):63-69.