

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 a 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) 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/m²) 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 that 1.6% of the sampled population had BMI <18.5Kg/m², 32.8% had BMI between 18.5 Kg/m² and 24.9 Kg/m², while 50.8% were noticed to have a BMI of between 25.0 Kg/m² and 29.9 Kg/m², and 14.8% had BMI of 30 Kg/m² 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.

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

34 **Introduction**

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

64 **Materials and methods**

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

73 digital rectal examination (DRE) and transrectal ultrasonography (TRUS) were performed. Two
 74 drops of whole blood collected from all 200 participants in attendance were tested by adding
 75 unto the test chamber of dry chemistry (Rapid Diaspot) one-step device for PSA assay along
 76 with a drop of diluent and was read after 5 minutes. However, only the samples of 61
 77 participants who met the inclusion criteria (abstinence from coitus or masturbation in past three
 78 days, not on the urethral catheter, did not have DRE before the presentation) were used as data
 79 for statistical analysis following the findings on DRE and TRUS procedures. Body mass index
 80 (BMI) was mathematically determined by dividing the weight in Kilograms (Kg) by the square
 81 of the height in square meters (m²). The PSAD was also mathematically determined by dividing
 82 the PSA by the prostate volume which was estimated with the means of the TRUS.

83 Results

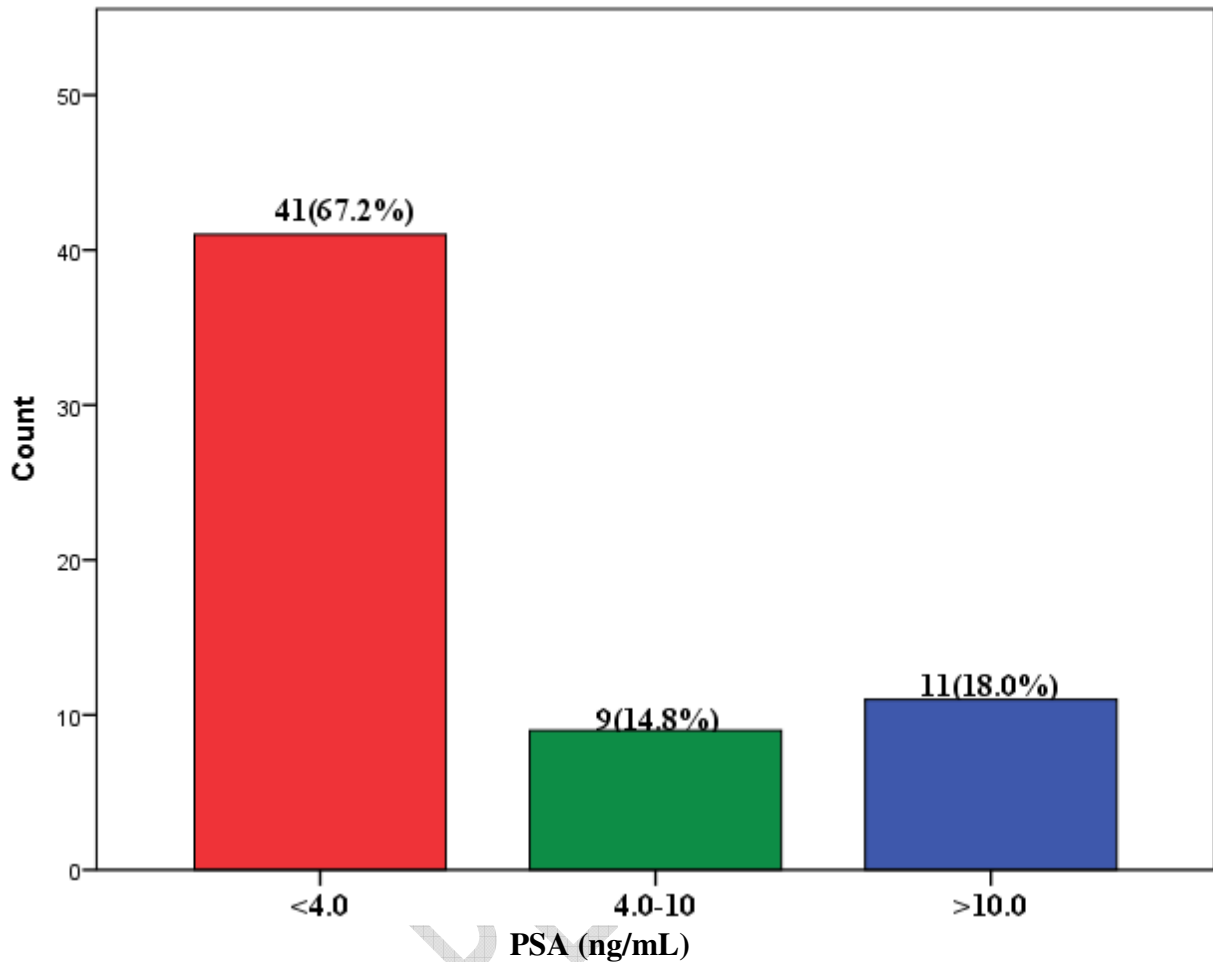
84 The socio-demographic findings are presented in Table 1. The ages of participants were grouped
 85 into 40-49 years, 50-59 years and 60 years and above with a range of 40-66 years and mean age
 86 of 52.03±7.5 years. The 40-49 years age grouping had a frequency of 22 representing 36.1% of
 87 the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

90 **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

91

92 Age range= 40-66



94

95

96

97

Figure 1: Bar chart showing PSA values of participants.

98

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

104

105

106 The association of age with prostate-specific antigen levels was captured in Table 2 and showed
 107 that out of the 22 participants that were within the 40-49 years age grouping 18 of them
 108 representing 81.8% had PSA values of less than 4.0ng/mL and only 2 participants had 4.0-
 109 10.0ng/mL and another 2 greater than 10.0ng/mL representing 9.1% of each group.

110 15 participants out of the 27 within the age grouping of 50-59 years representing 55.6% had PSA
 111 values of less than 4.0ng/mL, while 5 participants representing 18.5% had PSA values between

112 4.0 and 10.0ng/mL and 7 participants translating to 25.9% had PSA values greater than
113 10.0ng/mL.

114 Out of the 12 participants that fell within the age grouping of 60 years and above, 8 of them
115 representing 66.7% had PSA values below 4.0ng/mL, while 2 had PSA values between 4.0 and
116 10.0ng/mL and another 2 participants had PSA values greater than 10.0ng/mL, both representing
117 16.7% of each group.

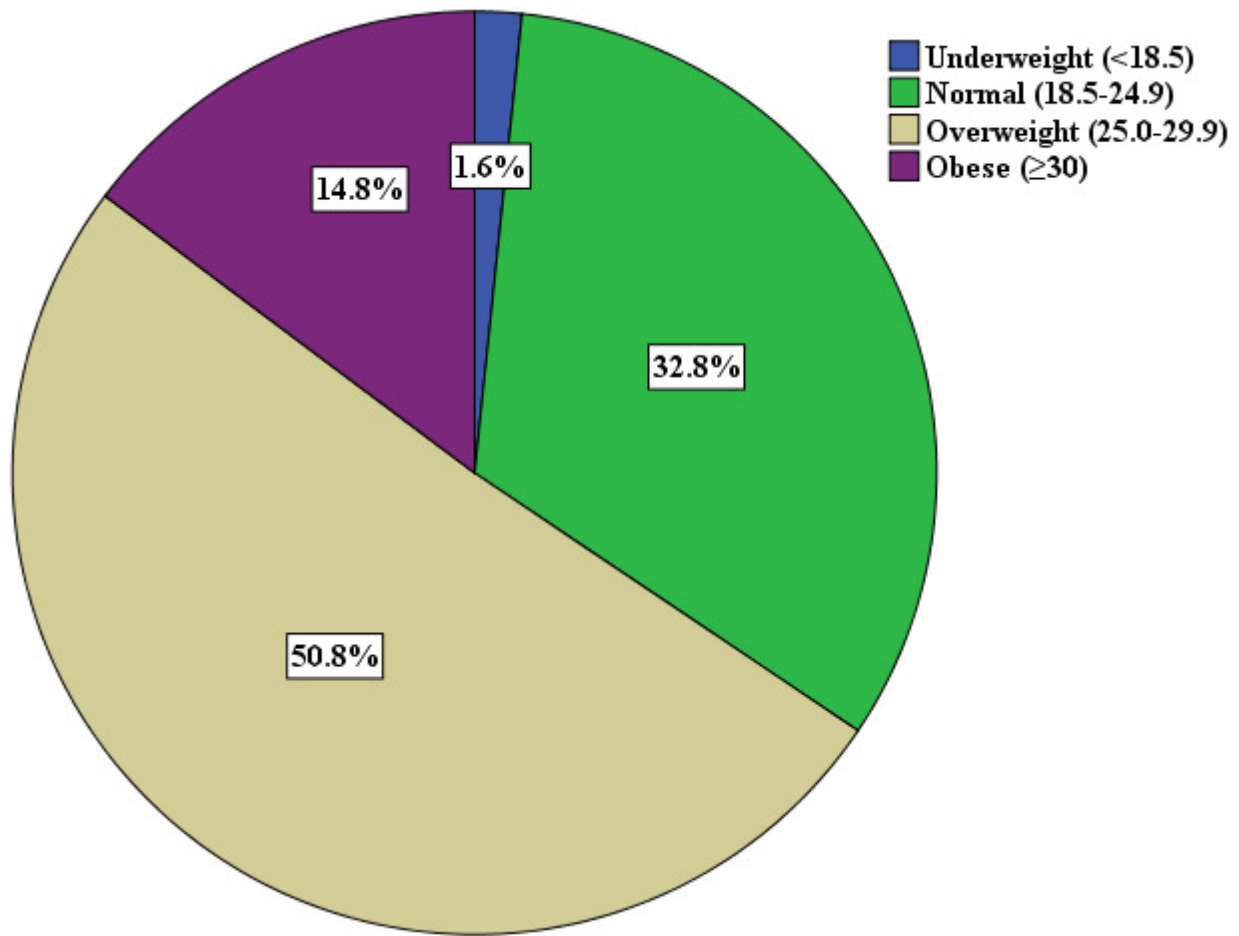
118

119 **Table 2: Association between PSA titre and age group of participants**
120

	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)

121 $X^2=3.933$, $df=4$, $p\text{-value}=0.415$

122



123
124

125

126 **Figure 2: BMI class of participants**

127 The body mass index (BMI) class of participants has illustrated in the pie chart in figure 2 above.
128 14.8% of the participants were obese while 50.8% were overweight. The remaining 32.8% and
129 1.6% were normal weight and underweight respectively.

130

131

132

133 The body mass index (BMI) and prostate-specific antigen (PSAD) were shown in table 3. The
134 mean BMI was $27.99 \pm 3.9 \text{ Kg/m}^2$ with a minimum of 20.54 Kg/m^2 and a maximum BMI of
135 35.43 Kg/m^2 . The median prostate-specific density (PSAD) was 0.01 ng/mL/cm^3 with the
136 minimum of 0.00 ng/mL/cm^3 and maximum value of 1.00 ng/mL/cm^3 .

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

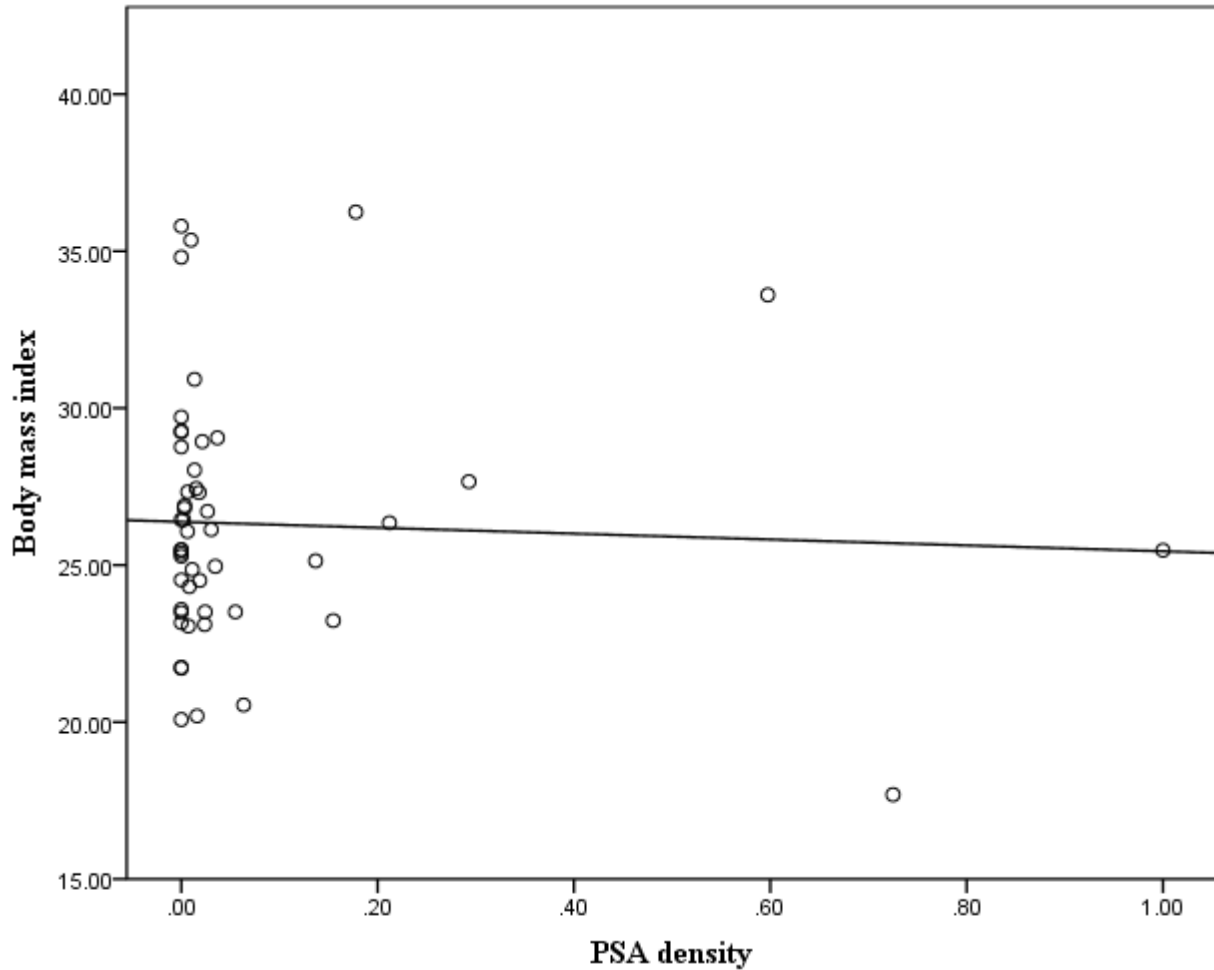
	Mean±SD	Minimum	Maximum
Height (m)	1.66±0.62	1.48	1.77
Weight (Kg)	73.10±13.4	45	111
BMI (Kg/m²)	27.98±3.9	20.54	35.43
	Median	Minimum	Maximum
Total PSA (ng/mL)	0.20	0.00	20.80
Prostate volume (cm³)	22.85	7.70	105.02
PSA density (ng/mL/cm³)	0.01	0.00	1.00

138

139

140

141



142
143

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

145 **Spearman correlation (r) =0.019, p=0.898**

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

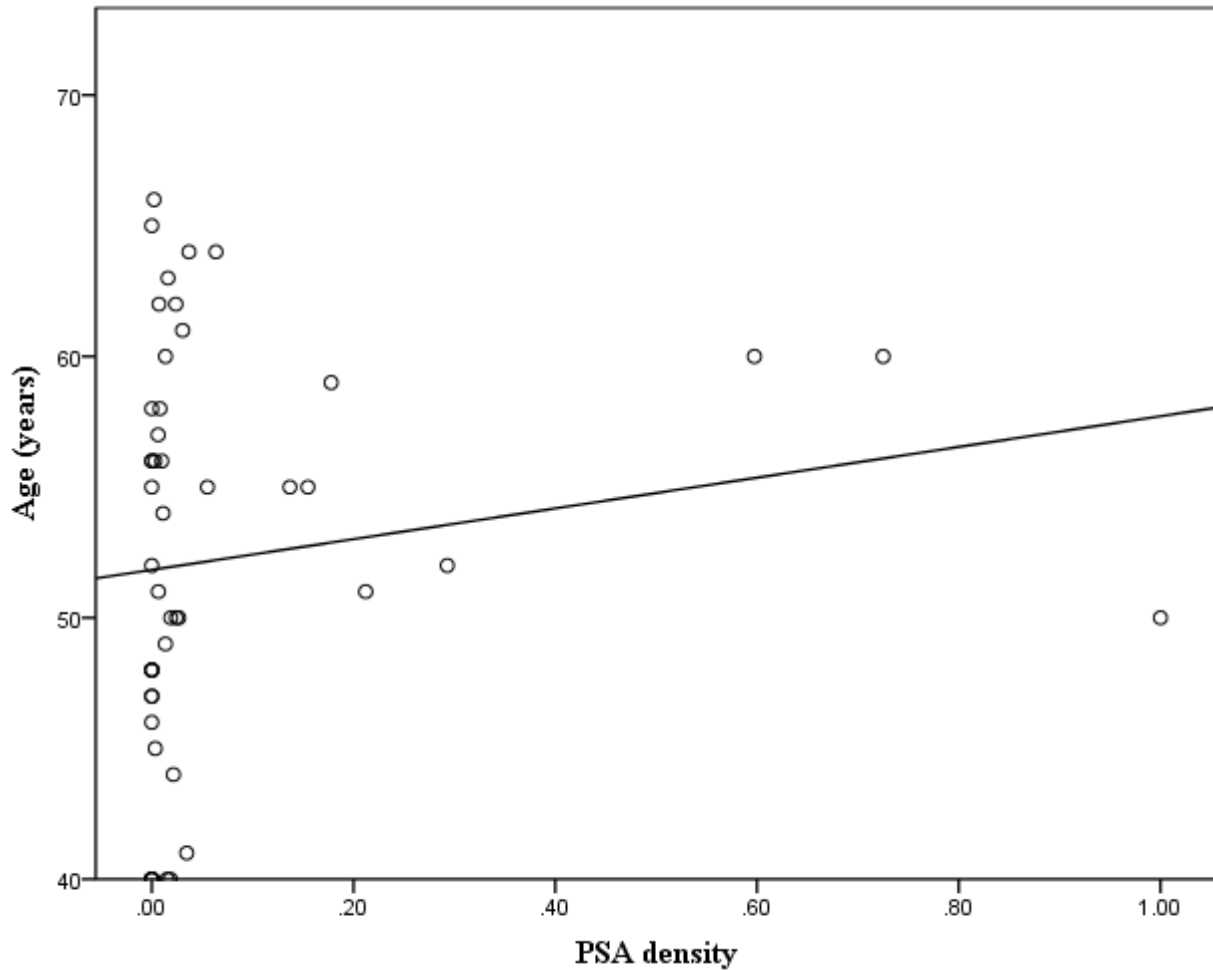
148

149

150

151

152



153

154

155

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

156

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

157

The relationship of age with PSAD has illustrated in figure 4 above in a scatter plot that showed

158

a moderate direct monotonic spearman's correlation. There was an increase in PSAD with

159

increasing age. P = 0.017

160

161 **Discussion**

162 The benefits of early diagnosis of prostate cancer include early commencement of treatment,
163 deferred complications and promotion of good quality of life. Some of the indices that reduce the
164 sensitivity of PSA as a marker of early detection of prostate cancer are body mass index (BMI)
165 and age among Caucasians and western populations. Their correlation with prostate-specific
166 antigen density (PSAD) was assessed in Nigerian men in this study. Our study which was in a
167 healthy population revealed our study group to have predominantly high BMI with over 65%
168 being either in the overweight or obese category. Bonn and colleagues² studied the association
169 between high BMI, serum PSA as well as a prostate cancer risk in 15,827 men, and during
170 follow up 735 men were diagnosed with prostate cancer with 38.4% being high-grade cancers.
171 Even though the association was not statistically significant, they concluded BMI was important
172 in risk stratification for prostate cancer. PSAD is known to improve the sensitivity of PSA as a
173 marker of prostate cancer and by extension, factors that affect PSA would affect PSAD. Body
174 mass index (BMI) had an inverse correlation with PSAD (PSAD was observed to decrease with
175 increased BMI). This observation conforms with a previous study in Northwestern Chinese
176 population.¹The decrease in PSAD masks the detection of patients at risk of prostate cancer due
177 to misclassification. Available literature shows that testosterone is known to improve the normal
178 differentiation of prostatic epithelial tissue and when reduced could lead to poor differentiation
179 that may promote carcinogenesis.¹³High BMI (obesity) is associated with a reduction in
180 testosterone level which suggests that patients with high BMI and low PSAD as was established
181 in this study are prone to the risk of poorly differentiated prostatic epithelial tissue and
182 aggressive prostate cancer. The PSAD was seen to have a direct monotonic correlation with age,
183 by subtly increasing with an increase in age. This was in keeping with published literature in
184 India that showed a similar pattern in PSAD in which there was an increase in PSAD with
185 increasing age and which was attributed to a corresponding increase in prostate volume with
186 age.¹¹PSAD is a function of PSA and prostate volume which are seen to increase with the
187 increase in age and therefore is affected by ageing.

188 **Conclusion:**

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

193 **Recommendation:**

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

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

198 **Consent :**

199 Informed and written consent was collected from participants and preserved by author(s).

200 **Ethical :**

201 As per international standard written ethical approval has been collected and preserved by the
202 author(s).

203

204 **References**

205

- 206 1. Zhang J, Ma M, Nan X, Sheng B. Obesity inversely correlates with prostate-specific
207 antigen levels in a population with normal screening results of prostate cancer in
208 northwestern China. *Brazilian Journal of Medical and Biological Research*. 2016;49(8).
- 209 2. Bonn SE, Sjölander A, Tillander A, Wiklund F, Grönberg H, Bälter K. Body mass
210 index in relation to serum prostate-specific antigen levels and prostate cancer risk.
211 *International journal of cancer*. 2016;139(1):50-57.
- 212 3. Kubota Y, Seike K, Maeda S, Shinohara Y, Iwata M, Sugimoto N. Relationship
213 between prostate-specific antigen and obesity in prostate cancer screening: Analysis of
214 a large cohort in Japan. *International Journal of Urology*. 2011;18(1):72-75.
- 215 4. Mario BO, Manuel V, Renata M, Simona C, Giovanni C, Fabrizio F. Relationship
216 between prostatic specific antigen (PSA) and volume of the prostate in benign prostatic
217 hyperplasia in the elderly. *Critical Reviews in Oncology/Hematology*, 2003; 47(3):
218 207-211.
- 219 5. Abdo AK, Mehdi S, Seyyed MTA, Mehrzad L, Mehrdad A, Ali A et al. Age specific
220 reference levels of serum prostate-specific antigen, prostate volume and prostate-
221 specific antigen density in healthy Iranian men. *Iranian Journal of Immunology*, 2009;
222 6: 40-48.
- 223 6. Emeka IU, Ikenna IN, Francis OO, Fred OU, Adesina SO, Samuel RO, et al. Prostate-
224 specific antigen density values among patients with symptomatic prostatic enlargement
225 in Nigeria. *World Journal of surgical oncology*, 2016; 14:174.
- 226 7. Lujan M, Paez A, Llanes L, Miravalles E, Berenquer A. Prostate specific antigen
227 density. Is there a role for this parameter when screening for prostate cancer? *Prostate*
228 *cancer and prostatic diseases*. 2001;4:146-149.
- 229 8. Kim JH, Doo SW, Yang WJ, Song YS, Kwon S-S. Prostate-specific antigen density: a
230 better index of obesity-related PSA decrease in ostensibly healthy Korean men with a
231 PSA < 3.0 ng/mL. *Urology*. 2013;81(4):849-852.
- 232 9. Loeb S. Prostate Health Index (PHI): golden bullet or just another prostate cancer
233 marker? *European urology*. 2013;63(6):995-996.
- 234 10. Khezri AA, Shirazi M, Ayatollahi SMT, Lotfi M, Askarian M, Ariaifar A, et al. Age
235 Specific Reference Levels of Serum Prostate-Specific Antigen, Prostate Volume and
236 Prostate Specific Antigen Density in Healthy Iranian Men. *Iranian Journal of*
237 *Immunology*. 2009;6(1):40-48.

- 238
239
240
241
242
243
244
245
246
247
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. *Indian 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 Biomarkers Prev* 2007; 16 (1):63-69.

UNDER PEER REVIEW