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ORIGINAL ARTICLE

The likelihood of having serum level of PSA of ≥4.0 ng/mL and ≥10.0 ng/mL in non-obese and obese Nigerian men with LUTS

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Abstract *Objective:* This study was undertaken to determine the likelihood of having serum total prostate specific antigen (PSA) levels ≥4.0 ng/mL and ≥10.0 ng/mL among a cohort of non-obese and obese Nigerian men with lower urinary tract symptoms (LUTS).
Methods: This was a prospective cross-sectional survey among men who presented with benign prostatic hypertrophy to the urology clinic of the Ekiti State University Teaching Hospital, Ado-Ekiti with LUTS between January 1 and December 31, 2014. One hundred and forty men who presented in the urologic clinic with LUTS were recruited. PSA was analyzed using standard method while other clinical variables were collected using a clinical case form. Multivariate logistic regression was used to estimate the odds of an abnormal PSA of ≥4.0 ng/mL or ≥10.0 ng/mL in these men.
Results: The mean ages of obese and non-obese men were 64.8 and 64.0 years respectively. The mean total serum PSA were 14.8 and 13.2 ng/mL for obese and non-obese men respectively. Univariate analysis showed no difference ($p > 0.05$) in the proportion of obese and non-obese men with LUTS who had a PSA threshold of at least 4.0 ng/mL. Multivariate logistic regression showed that, at a PSA threshold of 10.0 ng/mL, obese men had a statistically significant proportion ($p < 0.05$). Although not significant, non-obese patients were less likely to have PSA level of ≥4.0 ng/mL (OR 0.701; 95% CI 0.301–1.630) compared to obese men. In

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the same vein, non-obese men were less likely to have a PSA level of 10.0 ng/mL (OR, 0.686; 95% CI, 0.318—1.478) in a simultaneous context of age.
Conclusion: Our study demonstrated that, in a sample population of predominantly native African men, there was a non-significantly higher likelihood of overweight/obese patients having a higher serum PSA level than the non-obese. A community based study is needed to further confirm this finding.

1. Introduction

Prostate specific antigen (PSA) was reported to have been first identified by researchers attempting to find a substance in seminal fluid that would aid in the investigation of rape cases [1]. It was subsequently found to be able to identify prostate cancer (PCa) in men not known to have the cancer [2]. Men with PCa generally have elevated PSA levels in their serum; this tumour marker is now frequently used for PCa screening, diagnosis and monitoring of response to therapy [3—8].

To improve treatment outcome, PSA has been developed which categorized patients into three; viz: (i) low risk disease (LRD), (ii) intermediate risk disease (IRD), and (iii) high risk disease (HRD) especially when combined with Gleason score and American Joint Commission on Cancer clinical tumour category so as to determine the outcome and suitability of various treatment modalities for PCa [9]. In such instances PSA level of $<$10.0 ng/mL was matched for LRD, PSA level of 10.0—20.0 ng/mL was matched for IRD while PSA of $>$20.0 ng/mL was matched for HRD [9]. The low specificity of PSA testing and questionable benefits of PSA screening on PCa mortality highlight the need for better detection strategies for PCa [10].

Some studies suggested that body weight (BW) and body mass index (BMI) have effect on serum PSA, while some other researchers hold contrary opinion [5—8,11]. The variation of PSA levels with obesity in contemporary times poses a great challenge in the utilization of the marker for diagnosis. Establishing the relationship between PSA levels and obesity will detect the influence of BMI in the interpretation and clinical evaluation of PSA results. Moreover, PSA levels differ between various ethnic groups and races [12]. It is uncertain whether findings from studies investigating the association between BMI and PSA conducted primarily in Western populations can be applied to other ethnic groups.

In our country where healthcare infrastructure is overstretched coupled with a rising prevalence of cardiovascular risk including obesity, knowledge of the influence of concomitant co-morbidities such as obesity on serum PSA concentrations may improve the discriminant value of this test for predicting PCa and reduce the number of unnecessary biopsies and subsequent over-diagnosis of indolent cancers. In this study we examined the likelihood of having a serum PSA of $\geq$4.0 ng/mL and $\geq$10.0 ng/mL in obese and non-obese Nigerian men presenting with lower urinary tract symptoms (LUTS).

2. Patients and methods

2.1. Study site

This was a prospective hospital based cross-sectional observational study conducted at the urology clinic of Ekiti State University Teaching Hospital (EKSUTH), Ado-Ekiti, South-Western Nigeria. The study covered a period between 1st January and 31st December, 2014.

2.2. Subject's selection

One hundred and forty consecutive patients aged 40 years and above, who presented to urology clinic with LUTS within the study period were recruited.

However, the following categories of patients were excluded:

(i) those who have had digital rectal examination (DRE);
(ii) those who have had sexual intercourse within 24 h of examination;
(iii) those who have had recent catheterization or any other form of urologic manipulations;
(iv) those on 5-α-reductase inhibitor;
(v) those with a diagnosis of PCa;
(vi) those who have had prostate surgery or prostatitis;
(vii) those who did not give their consent;
(viii) All patients who had suspicious DRE or had PSA of $\geq$10.0 ng/mL were subjected to prostate biopsy and were excluded if positive for cancer.

2.3. Ethical consideration

This study was approved by the Health Research and Ethics Committee of EKSUTH. All the participants were adequately informed through written notice before the data were collected.

2.4. Data collection

2.4.1. Anthropometric variable

Height without shoes was measured to the nearest centimetre with a stadiometer (seca, Birmingham, UK) and weight in light clothing was measured to the nearest 0.1 kg, with a bathroom scale (Zhongshan Camry Electronic, Guangdong, China). BMI was calculated as a ratio of weight

(kg) to height squared (m^2). All anthropometric measurements were made by trained observers. The subjects were then classified as non-obese (BMI <25 kg/m^2) or obese [BMI ≥ 25 kg/m^2] according to Asian-Pacific classification more suited for African community [13].

2.4.2. PSA assay

Normal laboratory procedures were complied with in carrying out PSA analysis. About 5 mL of blood sample was taken into the screwed cap plain specimen bottle for the laboratory analysis of PSA. The blood sample was left to retract for about 30 min. Each set of sample was centrifuged at 2500 *g* for 5 min after which serum was separated into another screwed cap plain specimen bottle. The serum was later kept frozen till analysis of that batch. Serum PSA was determined using ready-to-use enzyme immunoassay commercially manufactured kit (Teco Diagnostic Laboratory, USA). This was based on the principle that PSA molecule was sandwiched between solid phase (rabbit anti-PSA antibody) and enzyme linked antibodies (monoclonal anti-PSA conjugated to Horse raddish peroxidise) [14].

2.5. Statistical analysis

The mean and standard deviation were used as appropriate to describe normally distributed continuous data. Median and inter-quartile (IQ) ranges and Mann–Whitney *U*-test were employed in analysing between group differences for skewed variables. A *p*-value was calculated using the independent *t*-test for continuous variables and the Pearson Chi-square test for categorical variables. Two separate PSA thresholds, ≥ 4.0 and ≥ 10.0 ng/mL, were used to categorize PSA values as "normal" or "abnormal" for the analyses. To describe the association between age, obesity and the likelihood of a certain serum total PSA level, multivariate analysis was used after dichotomising men as having a PSA level ≥ 4.0 or ≥ 10.0 ng/mL, respectively. The odds ratio (OR) of having an 'abnormal' PSA level for each threshold was then calculated, using overweight/obese men as the reference. The OR of having normal or abnormal PSA was also dichotomised between ages ≥ 65 years and <65 years with ≥ 65 years as the reference. The SPSS 17.0 software (SPSS Inc., Chicago, IL, USA) was used for the statistical analyses and $p < 0.05$ was considered statistically significant for all analyses.

3. Results

Table 1 shows the demographic characteristics of patients with LUTS. The mean ages of overweight/obese and non-obese men with LUTS were 64.00 ± 11.26 and 64.80 ± 10.88 years respectively. There was no statistical difference between the mean ages ($p > 0.05$). The median (IQ range) of the PSA level was 13.2(160.2) ng/mL for non-obese patients and 14.8(145.1) ng/mL for overweight/obese group. The number of overweight/obese patients with PSA level ≥ 10 ng/mL was 64(61.5%) while 19(52.8%) non-obese patients had PSA ≥ 10.0 ng/mL. This was not statistically significant even though greater proportion of obese patients had PSA ≥ 10 ng/mL.

Table 2 shows the multivariate logistic regression analysis of the relationship between age and BMI on serum PSA threshold of ≥ 4.0 ng/mL and ≥ 10.0 ng/mL.

Although there was no statistically significant difference, non-obese patients were less likely to have PSA level of ≥ 4.0 ng/mL (0.701) as shown in Model 1. Also, Model 1 shows that patients aged <65 years were 1.395 times likely to have a PSA ≥ 4.0 ng/mL compared to older patients. This finding was also not statistically significant. Model 2 shows that patients aged <65 years were less likely to have a PSA value of ≥ 10.0 ng/mL compared with older patients, while non-obese patients were less likely to have a PSA ≥ 10.0 ng/mL.

Table 1 The demographic and clinical characteristics of patients with LUTS.

Parameters	Non-obese ($N = 36$)	Overweight/Obese ($N = 104$)	*p*-Value
Age (mean ± SD), year	64.00 ± 11.26	64.80 ± 10.88	0.708
Marital status, *n*(%)			
Single	2(5.6)	5(4.8)	0.895
Married	34(94.4)	99(95.2)	
Occupation, *n*(%)			
Public servant	8(22.2)	38(36.5)	0.104
Business	13(36.1)	20(19.2)	
Retired	7(19.5)	29(27.9)	
Others	8(22.2)	17(16.4)	
Comorbidity, *n*(%)			
Hypertension	10(27.8)	35(33.6)	0.292
Diabetes	3(8.3)	14(13.5)	0.417
Alcohol	18(50.0)	55(52.9)	0.765
BMI (mean ± SD), kg/m^2	22.62 ± 2.28	28.59 ± 2.40	<0.001
IPSS score	2.22 ± 0.76	2.19 ± 0.66	0.107
Bother's score	3.92 ± 0.28	3.85 ± 0.58	0.182
PSA (median, IQ range), ng/mL	13.2, 160.2	14.8, 145.1	0.334
PSA ≥ 4.0 ng/mL, *n*(%)	25(69.4)	79(76.0)	0.441
PSA ≥ 10.0 ng/mL, *n*(%)	19(52.8)	64(61.5)	0.359

95% IC, 95% confidential interval; IQ, inter-quartile; LUTS, lower urinary tract symptoms; PSA, prostate specific antigen; SD, standard deviation.

Table 2 Multivariate logistic regression showing predictors of PSA values of ≥4.0 ng/mL and ≥10.0 ng/mL.

Variables	B coeff	SE	OR	95% CI	*p*-Value
Model 1 (PSA ≥4.0 ng/mL)					
BMI (reference is overweight/obesity)	−0.356	0.431	0.701	0.301−1.630	0.409
Age (reference is age ≥ 65 years)	0.333	390	1.395	0.649−2.995	0.394
Model 2 (PSA ≥10.0 ng/mL)					
BMI (reference is overweight/obesity)	−0.377	0.392	0.686	0.318−1.478	0.336
Age (reference is age ≥ 65 years)	−0.233	0.248	0.792	0.400−1.567	0.502

B coeff, B coefficient; SE, standard error; OR, odd ratio; 95% CI, 95% confidential interval; BMI, body mass index; PSA, prostate specific antigen.

4. Discussion

Having a serum PSA level of above 10.0 ng/mL has been associated with increasing risk of PCa and this has driven the increase in the use of PSA as screening marker for PCa [10]. We sought to establish the effect of obesity on the likelihood of having serum PSA of 4.0 ng/mL (normal 0−4.0 ng/mL and indicative of PCa ≥10.0 ng/mL) among Nigerian men with LUTS. When PSA thresholds of 4.0 ng/mL and 10.0 ng/mL were compared between non-obese and overweight/obese, we found that PSA threshold of 4.0 ng/mL and 10.0 ng/mL were prevalent among overweight/obese patients. Although this difference did not reach statistical significance.

Our multivariate logistic analysis showed a non-statistically significant trend towards a higher likelihood of overweight/obese men having a total serum PSA level ≥4.0 ng/mL and ≥10.0 ng/mL. When this threshold was considered, a trend of increasing PSA level with increasing BMI was noted. This is similar to the findings of Loeb et al. [15] who found that total PSA increased with an increasing BMI in a cohort of nearly 600 men who underwent radical prostatectomy (RP) by a single surgeon [15].

Besides, when our threshold was considered, a trend of decreasing PSA level with increasing BMI could not be established. This finding is contrary to that of Curp and Porter [16] and some researchers who found a decreasing level of point estimates of abnormal PSA level with increasing BMI although the authors' studies were better powered. However, most of these studies were amongst men of cross-cultural origins, ranging from Hispanics to Koreans [17−19]. In spite of this, Naito et al. [20] found that there was an increased serum PSA with Japanese men with higher normal BMI even though they also reported a lower PSA among the overweight/obese. Although the exact mechanism for lower PSA has not been fully elucidated, their findings were based on the theory of hormonal hypothesis that suggested a possible interaction between body adiposity and steroid hormone metabolism [19]. Other contributory postulation is that, men with a higher BMI could have larger plasma volumes, which could decrease serum concentrations of soluble tumour markers [21]. All the above postulations are still subject of debate.

Moreover, it should be noted that PSA levels are influenced by a number of demographic, lifestyle, and health characteristics, all of which deserve careful attention in the interpretation of test results [22]. The association between BMI and PSA may vary according to population characteristics [12,23], and this may explain why this study is different from those conducted outside Africa. Therefore, the explanation for the finding in this study may be due to racial differences as a result of larger prostate size and higher mean PSA typical of the African race compared to others [24]. However, our study is hospital based and less powered. Therefore, additional studies are needed to further clarify the relationships between BMI and PSA and determine whether weight reduction could lead to improved outcomes.

Our findings imply that overweight/obesity could create a false positive screening cut-off level of PSA as a screening test for PCa. We suggest interpretation of PSA levels with clinical findings and other diagnostic methods such as histopathology, DRE and imaging studies.

5. Conclusion

Our study demonstrated that in a sample population of predominantly native African men, there was a higher likelihood of overweight/obese patients of having higher PSA level; however, this association was washed off in a logistic regression analysis. Additional studies are needed to further clarify the links between BMI and PSA and to determine whether weight reduction could lead to improved level of serum PSA.

Conflicts of interest

The authors declare no conflict of interest.

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