The likelihood of having serum level of PSA of \( \geq 4.0 \, \text{ng/mL} \) and \( \geq 10.0 \, \text{ng/mL} \) in non-obese and obese Nigerian men with LUTS

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Lower urinary tract symptoms; Men; Nigeria; Overweight; Obesity

Abstract  Objective: This study was undertaken to determine the likelihood of having serum total prostate specific antigen (PSA) levels \( \geq 4.0 \, \text{ng/mL} \) and \( \geq 10.0 \, \text{ng/mL} \) 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 \( \geq 4.0 \, \text{ng/mL} \) or \( \geq 10.0 \, \text{ng/mL} \) 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 \( \geq 4.0 \, \text{ng/mL} \) (OR 0.701; 95% CI 0.301–1.630) compared to obese men.

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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 ≥4.0 ng/mL and ≥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 ≥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 (m²). All anthropometric measurements were made by trained observers. The subjects were then classified as non-obese (BMI <25 kg/m²) or obese (BMI ≥25 kg/m²) 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 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 with 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/Obes (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/m²               | 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.
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 increase in the use of PSA as screening marker for PCa associated with increasing risk of PCa and this has driven logistic regression analysis. 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.

References

[1] Chia SE, Lau WK, Chin CM, Tan J, Ho SH, Lee J, et al. Effect of ageing and body mass index on prostate-specific antigen levels among Chinese men in Singapore from a community-based study. BJU Int 2009;103:1487–91.
[2] Catalona WJ, Smith DS, Ratliff TL, Dodds KM, Coplen DE, Yuan JJ, et al. Measurement of prostate-specific antigen in serum as a screening test for prostate cancer. N Engl J Med 1991;324:1156–61.
[3] Oesterling JE. Prostate specific antigen: a critical assessment of the most useful tumor marker for adenocarcinoma of the prostate. J Urol 1991;145:907–23.
[4] Consedine NS, Morgenstern AH, Kudadjie-Gyamfi E, Magai C, Neugut AI. Prostate cancer screening behavior in men from seven ethnic groups: the fear factor. Cancer Epidemiol Biomarkers Prev 2006;15:228–37.

Table 2  Multivariate logistic regression showing predictors of PSA values of \( \geq 4.0 \) ng/mL and \( \geq 10.0 \) ng/mL.

| Variables                      | B coeff | SE    | OR    | 95% CI          | p-Value |
|--------------------------------|---------|-------|-------|-----------------|---------|
| **Model 1 (PSA \( \geq 4.0 \) ng/mL)** |          |       |       |                 |         |
| BMI (reference is overweight/obesity) | −0.356  | 0.431 | 0.701 | 0.301–1.630     | 0.409   |
| Age (reference is age \( \geq 65 \) years) | 0.333   | 0.390 | 1.395 | 0.649–2.995     | 0.394   |
| **Model 2 (PSA \( \geq 10.0 \) ng/mL)** |          |       |       |                 |         |
| BMI (reference is overweight/obesity) | −0.377  | 0.392 | 0.686 | 0.318–1.478     | 0.336   |
| Age (reference is age \( \geq 65 \) 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.
[5] Banez LL, Hamilton RJ, Partin AW. Obesity-related plasma hemodilution and PSA concentration among men with prostate cancer. JAMA 2007;298:2275-80.

[6] Kubota Y, Seike K, Maeda S. Relationship between prostate-specific antigen and obesity in prostate cancer screening: analysis of a large cohort in Japan. Int J Urol 2011;18:72-8.

[7] Grubb III RL, Balck A, Izmirlian G. Serum prostate-specific antigen hemodilution among obese men undergoing screening in the prostate, lung, colorectal, and ovarian cancer screening trial. Cancer Epidemiol Biomarkers Prev 2009;18:748-51.

[8] Wright JL, Lin DW, Stanford JL. The effect demographic and clinical factors on the relationship between BMI and PSA levels. Prostate 2011;71:1631-7.

[9] D’Amico AV, Whittington R, Malkowicz SB, Schultz D, Blank K, Broderick GA, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. JAMA 1998;280:969-74.

[10] Schroder FH, Hugosson J, Roobol MJ, Tammela TL, Clatto S, Nelen V, et al. Screening and prostate-cancer mortality in a randomized European study. N Engl J Med 2009;360:1320-8.

[11] Baillargeon J, Pollock BH, Kristal AR, Bradshaw P, Hernandez J, Basler J, et al. The association of body mass index and prostate-specific antigen in a population-based study. Cancer 2005;103:1092-5.

[12] Ekman P. Genetic and environmental factors in prostate cancer genesis: identifying high-risk cohorts. Eur Urol 1999;35:362-9.

[13] Kanazawa M, Yoshiike N, Osaka T, Numba Y, Zimmet P, Shuji I. Criteria and classification of obesity in Japan and Asia-Oceania. World Rev Nutr Diet 2005:94:1-12.

[14] Stowell L, Sherman I, Hamel K. An enzyme-linked immunosorbent assay [ELISA] for prostate specific antigen. Forensic Sci Intern 1991;50:125-38.

[15] Loeb S, Yu X, Nadler RB, Roehl KA, Han M, Hawkins SA, et al. Does body mass index affect preoperative prostate specific antigen velocity or pathological outcomes after radical prostatectomy? J Urol 2007;177:102-6.

[16] Culp S, Porter M. The effect of obesity and lower prostate-specific antigen levels on prostate cancer screening results in American men. BJU Int 2009;104:1457-61.

[17] Baillargeon J, Pollock BH, Kristal AR, Bradshaw P, Hernandez J, Basler J, et al. The association of body mass index and prostate-specific antigen in a population-based study. Cancer 2005;103:1092-5.

[18] Kim YJ, Han BK, Hong SK, Byun SS, Kim WJ, Lee SE. Body mass index influences prostate-specific antigen in men younger than 60 years of age. Int J Urol. 2007;14:1009-12.

[19] Yang WJ. The likelihood of having a serum PSA level of ≥2.5 or ≥4.0 ng/mL according to obesity in a screened Korean population. Asian J Androl 2013;15:770-2.

[20] Naito M, Asai Y, Mori A, Fukuda Y, Kuwabara M, Katase S, et al. Association of obesity and diabetes with serum prostate-specific antigen levels in Japanese males. Nagoya J Med Sci 2012;74:285-92.

[21] Banez LL, Hamilton RJ, Partin AW, Vollmer RT, Sun L, Rodriguez C, et al. Obesity-related plasma hemodilution and PSA concentration among men with prostate cancer. JAMA 2007;298:2275-80.

[22] Muller H, Raum E, Rothenbacher D, Stegmaier C, Brenner H. Association of diabetes and body mass index with levels of prostate-specific antigen: implications for correction of prostate-specific antigen cutoff values? Cancer Epidemiol Biomarkers Prev 2009;18:1350-6.

[23] Thompson IM, Leach R, Troyer D, Pollock B, Naylor S, Higgins B. Relationship of body mass index and prostate specific antigen in a population-based study. Urol Oncol 2004;22:127-31.

[24] Kang JS, Maygarden SJ, Mohler JL, Pruthi RS. Comparison of clinical and pathological features in African-American and Caucasian patients with localized prostate cancer. BJU Int 2004;93:1207-10.