

# The Influence of BMI on the PSA Status of Nigerian Men Affected By Prostate Cancer

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## ABSTRACT

**Background:** Data mostly from the Caucasian population is suggestive of an inverse influence of BMI on the PSA levels. Hence, this study was instituted to examine this relationship among Nigerian men of Negroid race with prostate cancer (PCa) disease.

**Materials and Methods:** This descriptive cross-sectional study was conducted prospectively in a tertiary health center in Nigeria among 220 males with treatment-naïve and histologically-confirmed PCa disease. Clinical, anthropometric and laboratory variables were obtained from each study participant and analyzed using SPSS software version 21. Laboratory analytical methods were carried out under standard protocols.

**Results:** The majority (n = 95; 43.2%) of the study population were within 70- 79 years of age bracket. The rates of ideal weight, overweight, and obese status among the study population were 23.2% (n = 51), 55.0% (n = 121), and 21.8% (n = 48) respectively. Increasing BMI trend was associated with a significant progressive decrease in the total serum PSA levels. An inverse relationship existed between PSA and BMI among the entire study cohorts (Beta: -0.709; SE: 0.198); p < 0.001), overweight cohorts (Beta: -0.268; SE: 0.671); p = 0.003) and among the obese cohorts (Beta: -0.384; SE: 0.223; p = 0.007).

**Conclusion:** The study affirms the inverse association between BMI and PSA in patients with PCa disease and this inverse relationship was more pronounced among the obese cohorts. This relationship should be considered in interpreting PSA results among obese individuals with prostate cancer disease.

**Keywords:** Nigeria; Prostate cancer; BMI; PSA.

## INTRODUCTION

At present, prostate cancer (PCa) disease has maintained a significant health burden among the middle-aged and the elderly males across the globe. [1] Data from Asia, Middle East, North America, Europe, and the African continents portray an increasing magnitude in the incidence, prevalence, morbidity and, mortality of the disease. [1,2] The World Health Organization (WHO) had reported a 4.0% prevalence rate of the disease in the developing countries. [3]

However, the report from a community-based study documented a 15.7% prevalence rate of the disease among Nigerian males. [4]

Co-existing with the rising trend of global PCa disease is the concomitant exponential upsurge of obesity disorder among the middle-aged and the elderly in different regions of the world. [5,6] Within the last two decades, the world had witnessed a substantially increased rate of obesity-related conditions such as coronary

heart disease, diabetics, hypertension, and cancer which have profound effects on the middle-aged and the elderly. [6]

Epidemiologic data seem to suggest a link between obesity and various prostate cancer disease characteristics. [7-11] Some investigators had posited that obesity inversely correlates with PCa disease incidence owing to its influence on the serum prostate-specific antigen (PSA) levels. [9-11] These investigators are of the opinion that obesity attenuates the normal serum PSA level which in turn delays the diagnosis of PCa disease in obese men, thereby influencing the disease incidence. [10]

However, most of these investigators had documented their findings among Caucasian men without PCa disease with conflicting and inconsistent findings. [8-10] To our knowledge, no study has been reported from our region of Negroid race on the influence of obesity on serum PSA levels among patients with PCa disease.

Hence, this present study had been instituted to investigate the influence of obesity defined using the body mass index (BMI) on serum PSA status among Nigerian men with PCa disease in Port Harcourt, Nigeria.

## **MATERIALS AND METHODS**

The study was a prospective cross-sectional in design, conducted in the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt, Nigeria over a 25 months period (November 2015 and January 2019).

Research approval was given by the UPTH Research Ethics Committee. Each participant gave individual written informed consent prior to recruitment. The study protocol was in accordance with the Declaration of Helsinki promulgated in 1964 and as amended.

The sample size was estimated using the formula for sample size determination for examining variables in a population >10,000 using a 15.7% prevalence of PCa disease in Nigeria, and a sample size of at

least 220 was obtained, including a 10% attrition rate. [12,13]

During the period of study, 389 males had presented to the Department of Urology of UPTH with clinical features of PCa disease. On subjecting the 389 males to detailed medical history review, clinical examinations (weight, height, blood pressure, and digital rectal examination), and investigations (serum total PSA, urinalysis, trans-rectal ultrasound scan of the prostate gland and trans-perineal prostate gland biopsy and subsequent histology), 343 were found to be positive for PCa disease. Following the applications of the eligibility criteria and using a simple random sampling technique, 220 were eventually enrolled in the study.

Those included were only the incident, treatment-naïve, and histologically-confirmed PCa patients with Gleason score  $\geq 6$  based on the recommendations of the International Society of Urological Pathology (ISUP). Criteria for exclusion from the study were as follows: non-consenting patients, those who had undergone prostatectomy or vasectomy, and those with any other malignant conditions. Excluded also were those on medications or with disease conditions known to influence serum PSA levels such as the followings: diabetes mellitus, chronic renal disease, chronic liver disease, statins, nonsteroidal anti-inflammatory drugs, thiazide medications, calcium supplements, aspirin, 5 $\alpha$ -reductase inhibitors, and exogenous testosterone medications. Questionnaires were administered to extract clinical, medical, demography and drug intake histories and each participant subsequently examined.

A10-hour fasting venous blood specimen was acquired for analysis of serum total PSA and fasting plasma glucose (FPG) prior to DRE exploration. Thereafter, each participant underwent a trans-rectal ultrasound scan (TRUS) of the prostate. The prostate volume (PV) was computed with the ellipsoidal formula [0.524 x L (cm) x H(cm) x W (cm)] using the TRUS-derived

dimensions [cephalocaudal length (L), anteroposterior height (H) and transverse width (W)] of the prostate. [14,15] Total serum PSA was determined using Enzyme-linked Immunosorbent Assay (ELISA) method while FPG was determined using the glucose oxidase method. The laboratory analytical procedures were done in duplicates and the average obtained.

Data obtained were age (years), total PSA (ug/l), FPG (mmol/l), weight (kg), height (m), calculated BMI (kg/m<sup>2</sup>), systolic and diastolic blood pressures (mmHg) and prostate volume (cm<sup>3</sup>). Age was arbitrarily categorized as < 50 - 59, 60 - 69, 70 - 79 and > 80 years. BMI was categorized as ideal weight (18.5 - 24.9 kg/m<sup>2</sup>), overweight (25 - 29.9 kg/m<sup>2</sup>) or obese (> 30 kg/m<sup>2</sup>) based on the definition established by the World Health Organization. [16]

Statistical analysis was done using statistical package for social science (SPSS) version 21. The distribution of the continuous data was evaluated for normality using the Shapiro-Wilk test. The non-parametric distributed data were log-transformed prior to analysis. The continuous variables were presented as mean ± standard deviations and compared with one-way analysis of variance test. The categorical variables were presented in numbers and percentages. Multivariable linear regression analysis was utilized to evaluate the direction and magnitude of the relationship between BMI and PSA while adjusting for confounders. An alpha value of < 0.05 was taken as being significant.

## RESULTS

The majority (n = 95; 43.2%) of the study population were within the 70 - 79 years of age bracket, while those who are above 80 years of age constituted the minority (n = 18; 8.3%) in the age groups (Table 1). The frequency of obesity, overweight, and ideal weight BMI status were 21.8% (n = 48), 55.0% (n = 121), and 23.2% (n = 51) respectively among the study population (Table 1).

A statistically significant difference (p < 0.001) in the mean values of weight, BMI, FPG, total PSA, and prostate volume was observed between the obese, overweight, and the ideal weight cohorts (Table 2).

With increasing BMI status (Ideal weight: 23.43 ± 1.42 kg/m<sup>2</sup>; Overweight: 27.70 ± 1.30 kg/m<sup>2</sup>; Obese: 32.38 ± 1.50 kg/m<sup>2</sup>), there was a corresponding attenuation in the mean levels of total PSA values (Ideal weight: 49.13 ± 13 µg/l; overweight: 40.24 ± 9.94 µg/l; Obesity: 20.09 ± 2.09 µg/l). The least mean PSA value was documented among the obese cohorts, while the highest mean PSA value was observed among the ideal weight cohorts (Table 2).

Within the entire study cohorts (n=220), an inverse relationship existed between BMI and total serum PSA levels on linear regression analysis (Beta: -0.709; SE: 0.198); p < 0.001). A unit increase in BMI status on linear regression analysis resulted in a decrease in serum total PSA by 0.709 units among the entire study cohorts (Table 3). The magnitude of this inverse relationship was mildly attenuated but remained significant following adjustment for potential confounders (Table 3).

An inverse relationship also existed between BMI and serum total PSA among the ideal weight (Beta: -0.108; SE: 1.131); p = 0.450), overweight (Beta: -0.268; SE: 0.671); p = 0.003), and the obese (Beta: -0.384; SE: 0.223; p = 0.007) cohorts on linear regression analysis with decreasing unit in PSA values as the BMI status increases (Table 3).

No statistical significance (p = 0.450) was observed among the ideal weight cohorts following the evaluation of the relationship between BMI and PSA on crude and adjusted regression analysis. While among the overweight and the obese cohorts, the magnitude of the inverse relationship was also mildly attenuated but remained statistically significant on adjustments for potential confounders. Among the obese cohorts, the magnitude of

the inverse relationship was amplified on adjusting for systolic and diastolic blood pressures (Table 3).

On crude linear regression analysis, a unit increase in the BMI status resulted in the attenuation of the serum total PSA level by 0.268 units among the overweight cohorts (Table 3). The greatest attenuation of PSA levels was observed among the obese cohorts, with a unit increase in the BMI status attenuating the serum total PSA level by 0.385 units among the obese cohorts, without any significant influence by

the potential confounders in the adjusted regression models (Table 3).

**Table 1: Descriptive characteristics of the categorical variables**

Strata of Study Variables	n	%
Age group (years):		
< 59	27	12.3
60 - 69	80	36.4
70 - 79	95	43.2
>80	18	8.3
BMI Status (kg/m <sup>2</sup> ):		
18.5 - 24.9 (Ideal Weight)	51	23.2
25 - 29.9 (Overweight)	121	55.0
>30 (Obese)	48	21.8

\*Statistically significant; BMI: Body Mass Index  
NA: No Response

**Table 2: Comparison of mean values of the non-categorical variables based on BMI status**

Variables	Ideal Weight n = 51 Mean ± SD	Overweight n = 121 Mean ± SD	Obese n = 48 Mean ± SD	p-value
Age (years)	71.60 ± 7.09	70.18 ± 7.40	71.73 ± 8.30	0.163
Weight (kg)	64.89 ± 4.74	77.13 ± 4.74	89.68 ± 4.90	< 0.001*
Height (m)	1.66 ± 0.03	1.67 ± 0.03	1.67 ± 0.24	0.467
BMI (kg/m <sup>2</sup> )	23.43 ± 1.42	27.70 ± 1.30	32.38 ± 1.50	< 0.001*
SBP (mmHg)	133.52 ± 10.92	133.22 ± 9.76	135.20 ± 6.83	0.467
DBP (mmHg)	82.54 ± 7.16	84.04 ± 7.24	83.33 ± 7.24	0.475
FPG (mmol/l)	4.40 ± 0.50	4.29 ± 0.48	4.04 ± 0.07	< 0.001*
tPSA	49.13 ± 13	40.24 ± 9.94	20.09 ± 2.09	< 0.001*
PV(cm <sup>3</sup> )	33.98 ± 2.08	34.46 ± 2.21	35.42 ± 2.96	< 0.001*
Gleason scores	7.62 ± 1.82	7.27 ± 1.37	7.08 ± 1.51	0.128

BMI: Body Mass Index; WC: Waist Circumference; PV: Prostate volume  
SBP: Systolic Blood pressure; DBP: Diastolic Blood Pressure;  
FPG: Fasting Plasma Glucose; tPSA: Total Prostate-specific Antigen.  
SD: Standard Deviation

**Table 3: Linear regression models of the relationship between BMI and PSA based on the BMI strata with PSA as the dependent variable while adjusting for potential confounders.**

	Entire study cohorts n = 220	Ideal Weight n = 51	Overweight n = 121	Obese n = 48
Regression Models	Beta (SE); p-value	Beta (SE); p-value	Beta (SE); p-value	Beta (SE); p-value
Model 1	-0.709(0.198); < 0.001*	-0.108(1.131); 0.450	-0.268(0.671); 0.003*	-0.384(0.223); 0.007*
Model 2	-0.684(0.208); < 0.001*	-0.019(1.118); 0.895	-0.239(0.706); 0.011*	-0.376(0.241); 0.014*
Model 3	-0.702(0.213); < 0.001*	-0.026(1.138); 0.857	-0.247(0.663); 0.006*	-0.367(0.242); 0.017*
Model 4	-0.699(0.215); < 0.001*	-0.042(1.155); 0.775	-0.246(0.669); 0.006*	-0.368(0.261); 0.026*
Model 5	-0.654(0.211); < 0.001*	-0.035(0.984); 0.781	-0.251(0.665); 0.005*	-0.366(0.257); 0.024*
Model 6	-0.659(0.213); < 0.001*	-0.031(1.022); 0.812	-0.253(0.679); 0.005*	-0.406(0.252); 0.012*

\*Statistically significant; Beta: Standardized regression coefficient; SE: Standard Error;

CI: Confidence Interval

Model 1: Crude

Model 2: Adjusted for age

Model 3: Adjusted for age and prostate volume

Model 4: Adjusted for age, prostate volume and Gleason scores

Model 5: Adjusted for age, prostate volume, Gleason score and fasting plasma glucose

Model 6: Adjusted for age, prostate volume, Gleason score, fasting plasma glucose, systolic and diastolic blood pressures

## DISCUSSION

We had examined the relationship between BMI and PSA among the ideal weight, overweight and obese males with histologically-confirmed PCa. We meticulously excluded those PCa patients with any medical, surgical or present drug intake history known to influence the PSA

levels. The most significant finding was the progressive decrease of total plasma PSA levels as the BMI status increases which were more pronounced among obese patients. In addition, an inverse relationship existed between BMI and PSA among the entire study cohorts, the overweight and obese patients which was also marked

among obese patients. The inverse relationships were not significantly influenced by potential confounders among the entire study population, the overweight, and the obese cohorts.

The findings of this present series are in agreement with a number of documented reports. [17-19] In a similar study documented by Tulloch-Reid and colleagues, the investigators had evaluated the relationship between BMI and PSA among Jamaican men with PCa and observed a significant negative association between BMI and PSA (BMI difference = -0.51(0.13);  $p < 0.001$ ) which remained significant after adjusting for age, sexual activity, smoking, statin use, and Gleason score. [17] In another study which was conducted by Banez and colleagues, the investigators had examined the association between BMI and pre-operative PSA levels of about 14,000 American men who underwent radical prostatectomy for PCa and observed a significant association between BMI and PSA after adjusting for confounders. [18] However, the report of Chaine and colleagues, which was limited by its retrospective design, is at variance with the findings of this present study. [20]

A number of investigators had proposed the pathophysiology behind the inverse association documented between BMI and PSA in the literature. [21-24] The first proposition is that of hemodilution suggesting that the increasing BMI status occasions increased plasma volume which ultimately dilutes the PSA levels. [21] The second proposition is based on the steroid hypothesis suggesting that the increased BMI status is usually associated with low testosterone levels with secondary high estrogen levels due to the improved aromatase activity in the abundant adipose tissues. [22] The attendant low testosterone level diminishes the biologic growth influence of testosterone on the prostate, resulting in low serum PSA levels. [22,23] The third proposition is based on the derangements of some prostate gland growth factors (leptin, insulin and insulin-

like growth factor-1) which adversely affects prostate growth, thereby reducing the PSA levels. [24]

The strength of this study is inherent in its prospective structure and the recruitment of only the treatment-naïve and histologically-confirmed patients with PCa disease. However, this study was also limited to a certain degree. These limitations are worthy of mentioning. First, all of our study cohorts were of Negroid race, therefore findings may not be applicable to men of other races. Secondly, the histologic reports of the prostate biopsy tissues were documented by different histopathologist in the study setting. This may have created some degree of the tendency towards inter and intraobserver variations in the reporting and documentation of the tumor Gleason score grades. However, there was general agreement on the histologic diagnosis of PCa disease among the histopathologist on all the prostate biopsy tissues of the PCa cases in this present study. Finally, the conclusion of this study was a single-center hospital-based prospective finding which might not necessarily be representative and reflective of the entire general populace within the study region.

## CONCLUSION

PSA is the most common biomarker employed to aid prostate biopsy decisions in the diagnostic protocols of PCa disease. The low PSA levels occasioned with worsening BMI status is likely to delay diagnostic decision and impact on the incidence of the PCa disease.<sup>18</sup> In addition, high BMI status which is associated with increased prostate volumes, also present technical difficulties during digital rectal exploration and biopsy procedures in patients with PCa. [7-8] These relationships could partly explain the inverse association between increased BMI status and the high rate of PCa disease mortality, aggressiveness and advanced disease stage at diagnosis of PCa disease. [25] Hence, it is necessary that this inverse association and the challenges overweight and the obese status presents in PCa be

considered during management of the disease.

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#### Declarations

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**Conflict of interest:** None

**Ethical approval:** The UPTH Research Ethical Committee gave approval for this study.

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