The influence of bmi on the psa status of nigerian men affected by prostate cance...

Parts of the World, Africa

Introduction

At present, prostate cancer (PCa) disease has maintained a significant health burden among the middle-aged and the elderly males across the globe. 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. The World Health Organization (WHO) had reported a 4. 0% prevalence rate of the disease in the developing countries. However, the report from a community-based study documented a 15. 7% prevalence rate of the disease among Nigerian males.

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. 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.

Epidemiologic data seem to suggest a link between obesity and various prostate cancer disease characteristics. Some investigators had posited that obesity inversely correlates with PCa disease incidence owing to its influence on the serum prostate-specific antigen (PSA) levels. 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.

However, most of these investigators had documented their findings among Caucasian men without PCa disease with conflicting and inconsistent findings. 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.

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 ≥ 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, 5α-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. 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/m2), systolic and diastolic blood pressures (mmHg) and prostate volume (cm3). 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/m2), overweight (25 – 29. 9 kg/m2) or obese (> 30 kg/m2) based on the definition established by the World Health Organization.

Statistical analysis was done using statistical package for social science (SPSS) version. 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.

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. 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.

A number of investigators had proposed the pathophysiology behind the inverse association documented between BMI and PSA in the literature. The first proposition is that of hemodilution suggesting that the increasing BMI status occasions increased plasma volume which ultimately dilutes the PSA levels. 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.

Conclusion

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.