British Journal of Medicine & Medical Research
4(18): 3519-3528, 2014

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Effects of Body Mass Index and Age on Prostate Specific Antigen: A Study on Men Attending a Tertiary Hospital in Ghana

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Authors' contributions

This work was carried out in collaboration between all authors. Authors RKDE, DBA, BOA, DNMO and ED designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors ED, DNMO, JA and DLS managed the analyses of the study. Authors RKDE, DNMO, JA and DLS managed the literature searches. All authors read and approved the final manuscript.

Original Research Article

Received 26th October 2013
Accepted 23rd December 2013
Published 9th April 2014

ABSTRACT

Background: Prostate specific antigen (PSA) is useful in the diagnosis of prostate adenocarcinoma.
Aims: Our study sought to establish possible effect of age and BMI on serum PSA levels in Ghanaian men with genitourinary complaints.
Methods: In this non-randomized, cross-sectional study, we recruited 202 men from the Genitourology and pathology departments of the Korle-Bu Teaching Hospital (KBTH) and MDS-Lancet Laboratories Ghana, between July 2011 and February 2012. Height and weight were measured and body mass index (BMI) calculated for each participant. Serum PSA levels were measured and prostate biopsies from each of the participants were examined histologically for diagnosis.

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Results: The mean PSA level was 200 ng/ml, mean age of 66.33±8.90 years, and a BMI of 23 kg/m^2. The mean Gleason score of all participants was 3.38±3.58 years. There was a positive correlation between age and PSA levels (r=0.020; *P*=.78). A negative correlation was established between BMI and PSA (r=-0.068; *P*=.33). There was however a significant positive correlation (r=0.237; *P*=.001) between PSA levels and Gleason score. Linear regression analysis revealed no relationship between PSA and age (r=0.002; *P*=.98) and, PSA and BMI (r=-0.068, *P*=.36).
Conclusion: Serum PSA levels correlate with age and BMI, however these factors do not have an effect on the levels of serum PSA at measurement. We suggest that PSA values be used in the context of the clinical scenario and other PSA altering factors.

Keywords: Age; Body Mass Index (BMI); Prostate Specific Antigen (PSA); Ghana; obesity.

ABBREVIATIONS

BMI: Body Mass Index; r: Co-effcient of correlation; BPH: Benign Prostate Hyperplasia; ACP: Adenocarcinoma of the Prostate.

1. INTRODUCTION

Prostate cancer is one of the leading cancers in older men of today. Prostate specific antigen (PSA) has over the years been very useful in the diagnosis of prostate malignancies. It was first discovered in 1971, known then as γ-seminoprotein. It has since 1979, when the protein was purified from prostate tissue, been known as Prostatic Specific Antigen (PSA) [1]. PSA screening is still uncommon in most parts of Sub-Saharan Africa, with reported prevalence of 2.5% in Ghana (unpublished data).

Since its introduction into clinical practice, PSA has been of immense benefit to both patients and health practitioners in the diagnosis, staging, management, and treatment of prostate malignancies. However, unknown to most users of the marker, it may be affected by several other factors, such as age, obesity and prostate volume.

Overweight and obesity is increasingly an issue of concern in the world over and has been linked to the development of various cancers and several other chronic metabolic diseases [2]. The question still remains however, on the potential association of obesity and prostate cancer [3-5]. Some studies have revealed that PSA levels are significantly lower amongst healthy but obese men compared to non-obese men [6,7]. Meanwhile other studies have reported no associations between Body Mass Index (BMI) and PSA levels [8,9]. On the contrary, studies conducted by Freedland et al. [8], attributed increases in prostate volume to obesity, another condition under which PSA levels may differ. However, this assertion has been debunked by the work of Nichols et al. [10]. Similarly, age has been shown to vary with serum PSA levels [11].

The variation of PSA levels with age and obesity in contemporary times poses a great challenge in the utilization of the marker for diagnosis. Establishing the relationship between PSA levels, age and obesity will establish the influence of age and BMI in the interpretation and clinical evaluation of PSA results. Moreover, PSA levels differ between various ethnic groups and races [12]. Hence the fact that established relationships between age, BMI and PSA levels can be used in the world over, especially Ghana remains a debate. The objective

of this study is to determine the effect of age and BMI on serum PSA levels among Ghanaian men with genitourinary complaints.

2. METHODOLOGY

2.1 Study Site/Design

This non-randomized, cross-sectional study was conducted at the Genitourology and Pathology departments of the Korle-Bu Teaching Hospital (KBTH) the main referral hospital in Ghana, and MDS-Lancet laboratories, Dansoman-Accra, Ghana.

2.2 Study Participants

Between July 2011 and February 2012, 202 males, visiting the KBTH with various genitourinary complaints were recruited. Males aged 40 years and above who have been reporting to the genitourinary department, for the first time, and on no prior treatment were considered eligible for the study. All those who did not meet these criteria were excluded. Ethical clearance was obtained from the Institutional Review Board of the University of Cape Coast (IRB/UCC) and the facilities concerned. Informed consent was obtained from each participant prior to commencement of the study.

2.3 Data Collection

2.3.1 Anthropometric variables

Height to the nearest centimeter without shoes was measured with a stadiometer (seca 217, 40 Barn Street B5 5QB Birmingham, United Kingdom) and weight to the nearest 0.1 kg, in light clothing, was measured with a bathroom scale (Zhongshan Camry Electronic Co. Ltd, Guangdong, China). Body mass index (BMI) was calculated as a ratio of weight (kg) to height squared (m^2). This was used to categorize participants as underweight (<18Kg/m^2), normal (18-24 Kg/m^2), overweight (25-29.9 Kg/m^2) and obese (>30 Kg/m^2) according to WHO criteria [13].

2.3.2 Sample collection/Determination of serum PSA levels

Three milliliters (3 ml) of venous blood was drawn from each participant, allowed to clot and centrifuged at 1500g for 3-5 minutes. The serum obtained was aliquoted into cryovials and stored at -80^{o}C. The PSA levels of the study participants were measured using micro particle enzyme immunoassay method (Abbott IXM).

2.3.3 Preparation and examination of prostate biopsies

The prostate biopsies of the individual subjects were obtained and cut-ups of representative sections were done. These were then processed in an automated tissue processor, sectioned through to the slide stage and auto-stained with haematoxylin and eosin (H &E). The final mounted slides were presented to a qualified pathologist for histological diagnosis.

2.3.4 Estimation of Gleeson score

The severity of prostate adenocarcinoma was graded based on established criteria [14,15].

- Scores from 2 to 4 are very low on the cancer aggression scale.
- Scores from 5 to 6 are mildly aggressive.
- A score of 7 indicates that the cancer is moderately aggressive.
- Scores from 8 to 10 indicate that the cancer is highly aggressive.

2.4 Statistical Analysis

All data were entered into Microsoft Excel (Microsoft Corporation) and analysed with SPSS version 16.0 (SPSS Inc. Chicago). All categorical variables were compared with Chi-square and Fisher's exact test. All continuous variables were analyzed using independent samples t-test. Spearman's rho Correlation was used to determine the association between the various parameters. Linear regression analysis was used to determine the independent effect of age and BMI on PSA levels.

3. RESULTS

The mean age, height, weight and BMI of study participants was 66 years, 167cm, 65kg, and 23 kg/m^2. The mean Gleason score of all participants was 3.38±3.58. Most of the participants were in the age range 60-69 years (34.7%) followed closely by those of the ages 70-79 (30.2%). Only one participant was aged between 40-49 years (0.5%). More than half (60.9%) of the participants had normal BMI with less than 20% of the participants being underweight and overweight. Overweight was recorded in 7.9% of the participants. Close to 70% of participants had PSA levels of >10 ng/ml whereas 27.2% of participants had PSA levels >4 but ≤10 ng/ml. Only 3% of participants had normal PSA levels (O-4). Histological examination diagnosed 52.0% of the participants with prostate carcinoma whereas 45.5% were diagnosed with benign prostate hyperplasia (BPH) (Table 1).

The characteristics of study participants according to BMI categorization is shown in Table 2. Of participants histologically diagnosed with BPH, 69.6% had normal weight, 13.0% were underweight and 16.3% were overweight. However, only 1% was obese. Amongst those who had both BPH/ACP there was an equal distribution (40%) of normal and overweight participants. Of those with prostate adenocarcinoma, about (54.3%) were of normal weight. This category recorded the highest number of obese participants (14.3%). There was a significant association (P =.02) between BMI and histological diagnosis (Table 2).

There was a significant association between PSA levels and BMI categories. Across the PSA categories, more than half of the participants had normal weight whereas about 20% of overweight participants had PSA levels of 4-10 ng/ml and >10 ng/ml. The highest number of obese participants was recorded amongst those with PSA levels between 4-10 ng/ml (Table 2).

Age was significantly associated with BMI categories. Participants aged 40-49 were of normal weight (100.0%). There was an equal weight distribution of normal and overweight amongst those aged 50-59 (21.2%), 60-69 (22.9%) and 70-79 (18.0%) and 80-89 (5.6%). The highest number of obese participants was recorded amongst those aged 50-59 years.

Table 1. General characteristics of study participants

Variables	N (%)
Mean (SD) Age	66.33±8.90
Mean (SD) PSA (ng/ml)	200.27±1077.8
Mean (SD) BMI	23.10±4.15
Mean (SD) Height	166.57±12.72
Mean (SD) Weight	64.62±12.18
Mean (SD) Gleason	3.38±3.58
No. age (%)	
40-49	1 (0.5)
50-59	52 (25.7)
60-69	70 (34.7)
70-79	61 (30.2)
80-89	18 (8.9)
No. BMI ranges (%):	
Underweight	24 (11.9)
Normal	123 (60.9)
Overweight	39 (19.3)
Obese	16(7.9)
No. PSA levels (%):	
0-4	6 (3.0)
4-10	55 (27.2)
>10	141 (69.8)
No. Histological diagnosis (%):	
BPH	92 (45.5)
BPH/ACP	5 (2.5)
Carcinoma	105 (52.0)

SD=Standard Deviation; BMI=Body Mass Index; PSA=Prostate Specific Antigen; ACP=Adenocarcinoma of the Prostate; BPH= Benign Prostate Hyperplasia, No. =Number

Table 2. Participant Characteristics according to BMI category

Patient Characteristics	BMI Category			
	Underweight	Normal	Overweight	Obese
No. Histological diagnosis (%):				
BPH	12(13.0)	64(69.6)	15 (16.3)	1(1.1)
BPH/ACP	1(20.0)	2(40.0)	2(40.0)	0
Carcinoma	11(10.5)	57(54.3)	22(21.0)	15(14.3)
P -value for association*	.02			
No. PSA levels (%):				
0-4	0	3(50.0)	2(33.3)	1(16.7)
4-10	4 (7.3)	28(50.9)	11(20.0)	12(21.8)
>10	20(14.2)	92(65.2)	26(18.4)	3(2.1)
P -value for association*	.000			
No. age (%):				
40-49	0	1(100.0)	0	0
50-59	7(13.5)	11(21.2)	11(21.2)	13(25.0)
60-69	11(15.7)	16(22.9)	16(22.9)	3(4.3)
70-79	4(6.6)	11(18.0)	11(18.0)	0
80-89	2(11.1)	1(5.6)	1(5.6)	0
P -value for association*	.000			

BMI=Body Mass Index, PSA=Prostate Specific Antigen; ACP=Adenocarcinoma of the Prostate; BPH= Benign Prostate Hyperplasia, No.=Number; p <0.05 is significant

A Pearson correlation analysis is demonstrated in Table 3. There was a positive correlation between age and PSA levels (P=.78, r=0.020). A negative correlation was established between BMI and PSA levels (P=.33). There was however a significant correlation (r=0.237; P=.001) between PSA levels and Gleason score.

Table 3. Pearson correlation analysis of demographic, anthropometric and biochemical characteristics of study participants

Variables	Pearson's Correlations						
		PSA (ng/ml)	Age	BMI	Height (cm)	Weight (kg)	Gleason Score
PSA (ng/ml)	Pearson Correlation	1	.020	-.068	.033	-.052	.237**
	P-value		.78	.33	.64	.46	.001
Age	Pearson Correlation		1	-.262**	.010	-.315**	.027
	P -value			.000	.89	.000	.70
BMI	Pearson Correlation			1	-.165*	.933**	.118
	P -value				.02	.000	.09
Height (cm)	Pearson Correlation				1	-.021	.007
	P -value					.77	.92
Weight (kg)	Pearson Correlation					1	.105
	P -value						.14
Gleason Score	Pearson Correlation						1
	P -value						

***. Correlation is significant at the 0.01 level (2-tailed).*. Correlation is significant at the 0.05 level (2-tailed). BMI=Body Mass Index, PSA=Prostate Specific Antigen*

We used a linear regression model to determine the effect of age and BMI on PSA levels. There was a positive and negative relationship with age (0.002) and BMI (-0.068) respectively. Both age (P=.98) and BMI (P=.36) however was not significantly associated with PSA levels and did not affect or determine PSA measurements (Table 4).

Table 4. Linear regression model examining the effect of BMI and age on PSA levels

Model 1	Beta coefficient (SE)	P-value
Age	.002 (8.87)	.98
BMI	-.068(19.03)	.36

BMI=Body Mass Index

4. DISCUSSION

We sought to determine the impact of BMI and age on serum PSA levels. Our study demonstrates that in a population of predominantly African origin, there is a correlation between PSA levels with age and BMI. However these associations were of no significance in the determination of PSA levels in men when adjusted to determine effect using linear

regression models. Therefore age and BMI are independent of PSA and have no effect on measurements of the tumor marker.

We found a negative but insignificant correlation between PSA and BMI. This was confirmed in the regression analysis, which was done to determine the independent effect of BMI on PSA levels. This is line with other studies, which sought to establish a relationship between BMI and PSA levels in men of African descent. One of such studies conducted in Jamaica on the relationship of BMI and PSA found a negative correlation between the two but also lost its significance when adjusted for age [16]. Other studies have also reported absolutely no effect of BMI on PSA levels [8,9].

Contrary to our finding, others have demonstrated a significant effect of BMI on PSA levels. However, most of these studies were amongst men of other origins, ranging from Hispanics to Koreans [6,17]. Although there might not be evidence that race affects relationships such as these, only studies conducted in men of African origin have demonstrated a similar trend as found in our study [18]. Our findings therefore suggest that the effect of BMI on PSA levels may not be as strong as that in men of other ethnic origin.

Obesity is also known to increase prostate volume, another condition under which PSA levels may differ [8]. Like in a similar study we failed to measure prostate volumes to determine its effect on BMI [16]. It is however worthy to note that in studies where this was done increasing BMI did not show a concurrent increase in prostate volume [19].

With reference to our findings in this study, there have been proposed explanations to this inverse but insignificant relationship between BMI and PSA levels. These have been called the hormone hypothesis and the dilution hypothesis. In the former, peripheral aromatization of testosterone to oestrogens in adipose tissue is believed to result in lower testosterone, higher oestrogen concentrations, and lower sex- hormone binding globulin. These together, result in diminished production of PSA [6].

The latter hypothesis suggests that BMI is associated with a higher plasma volume, which results in a lower PSA concentration, creating a haemo-dilution effect [6]. Other studies have measured plasma volumes in relation to PSA levels as well as other tumor markers and confirmed this hypothesis [20,21].

Our findings imply that the use of PSA in early detection of prostate cancer may be negatively impacted, such that lower levels in these men may lead to a delayed diagnosis and unfavorable prognosis. However, BMI does not determine or have an effect on PSA measurements. Specific reference ranges with respect to different ranges of BMI has been suggested [22]. We however suggest interpretation of PSA levels with clinical findings and other diagnostic methods such as histopathology, digital rectal examination (DRE) and imaging studies.

Our study also demonstrated a positive correlation between age and PSA levels. This however did not show any significant effect on the determination of PSA levels (P=0.976). The CHAMP study, the largest cohorts so far to have studied the effect of age on PSA levels, especially in older men, revealed a similar finding. They reported a concurrent increase in serum PSA levels with increasing age [11].

Although age-specific references have been established for PSA levels, most of these studies are those conducted on older aged men only, whiles others have used very small

sample sizes [11]. Furthermore, PSA levels have been shown to differ amongst various ethnic groups of men of the same age group, another indicator that age may not have an effect on PSA levels, as there may be other cofounders.

This could be a contributing factor to the contrary finding in our study that age has no effect on PSA levels but only correlates with it. Studies have shown that the probability of developing prostate cancer increases from 0.005% in men younger than 39 years to 2.2% in men between 40 and 59 years and 13.7% in men between 60 and 79 years, another evidence to support the age correlation theory [23]. Moreover age-specific reference ranges have been established on the basis of correlation found between age and PSA levels and not the effect of age on PSA levels. Thus the use of age-specific reference ranges may not be warranted in this population. Rather results of PSA analysis must not be used in isolation but in context of clinical details and other diagnostic procedures done on patient-specific basis. It is also an indication that risk increases with age and as such proper health preventive measures be taken with increasing age.

5. CONCLUSION

Our study confirms previously reported inverse relationship between PSA value and BMI and the direct relation between PSA and age. However, these did not demonstrate an independent effect on PSA levels. The significance of our finding and its impact on PSA and its uses does not indicate a rationale to change the accepted abnormal value in obese and older patients. We suggest that PSA values should be used in the context of the clinical scenario and other PSA altering factors.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this cross sectional study and accompanying images.

ETHICAL APPROVAL

This study was approved by the Institutional Review Board of the University of Cape Coast (IRB/UCC), the committee of research ethics of the KBTH, and the authorities of MDS–Lancet laboratories, Ghana.

ACKNOWLEDGEMENTS

The authors are grateful to the staff and patients of the Departments of pathology and surgery, KBTH and the management of MDS-Lancet Laboratories for their immense contribution in making this work a success.

COMPETING INTERESTS

The authors declare that there is no conflict of interest regarding the publication of this article.

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