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Research Paper

The Effects of Body Mass Index on Serum Prostatic Specific Antigen Level in Correlation to Age and Prostatic size

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ABSTRACT:

BACKGROUND:

Overweight and Obesity are major health problems characterized by excess adipose tissue. It is a growing global epidemic issue that is demonstrated to cause several mental physical disorders, including heart diseases, vascular disease, diabetes mellitus, and psychological disorders. Prostatic Specific Antigen (PSA) is considered the most dependent tumor marker of carcinoma of prostate. It is considering organ-specific tumor marker but not disease specific. It is the most prevalent screening tool for carcinoma of prostate and most proportion of prostatic carcinoma are diagnosed with prostatic biopsy when there is abnormally elevated level of serum PSA.

OBJECTIVE:

Our research study aimed to define the relationship of BMI (body mass index) as a marker of obesity with serum PSA level and their correlation to age and prostatic volume. This knowledge will help to avoid errors in the assessment of prostate disorders using PSA test for overweight and obese men.

PATIENTS AND METHODS:

Across sectional study was performed between the 3rd of May to the 28th of November 2022. Our study involved 115 cases with their age was more than 55 years. In 35 cases, their age was between 55 and 59 years, in 53 cases their age was between 60 to 69 years, and in 27 cases, the age was above 70 years. Their BMI categorized into 3 groups: group 1 include obese people (BMI > 27kg/m2) which includes 55 cases, group 2 overweights (BMI 23- 27 kg/m2) which include 37 cases, and group 3 includes normal weights (BMI 18.5 - 23kg/m2) which include 23 cases. Body mass index, total serum PSA and volume of prostate were measured for every case in this research and the results are analyzed statistically by using IBM-SPSS 26. A P-value ≤ 0.05 deemed significant for this study.

RESULTS:

Obese individuals exhibited significantly lower median serum PSA in comparison to overweight and normal BMI males 1.6, 2.2, 2.69 ng/ml, in group 1, group 2, and group 3 respectively. There is a considerable significantly negative correlation of PSA with BMI (Spearman's coefficient= -0396, p=0.001). Also, there was no statistically significant variation found between the groups regarding prostate size (p = 0.532). There was a positive correlation of serum PSA with the age (r= 203, p = 0.029). After adjusting for age, PSA was still negatively associated with BMI (p= 0.022). When the linear regression model was applied, again inverse relationship between PSA level and BMI is found (r = -0.335, P=0.0001), and serum PSA was level positively correlated to age (r = 0.207, p = 0.018).

KEYWORD: prostatic specific antigen, body mass index, prostatic volume, carcinoma of prostate, PSA, BMI, obesity.

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INTRODUCTION:

Obesity and overweight are defined by the World Health Organization (WHO) as "abnormal or excessive fat accumulation that presents a risk to health [(1)]. Obesity is marked by excess adiposity and is recently received great attention over the world. It is growing globally epidemic, with >50%

of adults over world classified to be overweight, and up to 30% classified to be obese (BMI) >27 Kg/m2] [2]. The propagation of obesity is greatly increasing than ever before [3]. With the increasing prevalence of obesity and importance of its detection, United States Centers for Disease Control and Prevention (CDC) define weight categorize (for adult), to overweight and obesity by assessing height and weight to compute a numerical value known as "body mass index" (BMI), it is serves as valuable tool to assess how body fat is determined. Its widespread adoption can be attributed to its convenience, safety, and affordability, despite it lacks ability to differentiate between lean body mass and fat mass [4].

Obesity is assessed and measured by various methods such as: waist circumference, body mass index (BMI), waist-hip ratio, skinfold, and the percent of body fat measurements [5]. According to WHO regarding BMI of Asian people, population were clarified to 3 categories: normal person (BMI 18.5 – 23 kg/m2), patient with overweight (BMI 23-27 Kg/m2), obese (BMI > 27 kg/m2) [6]. Various research studies have shown that obesity may causes both physical and mental health issues, included several types of cancer [7].

Obesity also presents a technical challenge for the detection of carcinoma, as excess body fat may disrupt imaging and impede physical examination and other supplementary tests. Similarly, obesity may negatively affect the early diagnosis through the evaluation of soluble tumor marker levels in the blood [8].

Several studies have confirmed that men with obesity tend to have a larger prostate volume. Large cohort studies consistently shown that male who are obese have higher likelihood for developing (BPH) and (LUTS). Additionally, obese male was found to have a 3.5-fold greater risk for BPH and LUTS compared to non-obese male [9].

PSA is recognized as a most promising tumor markers in recent years. Notably, it is one of the limited tumor markers specific to an organ [10]. It serves as an important screening tool for carcinoma of prostate, with the majority of carcinoma of prostate cases being identified through a biopsy following a high PSA reading [9]. Several research studies investigated correlation between serum PSA in various populations with other factors including body max index as a marker of obesity, prostate volume and the age [11].

PSA define as a glycoprotein primarily secreted by cylindrical cells of prostate, greatly influenced by androgens. Despite being organ-specific, it is not exclusive to carcinoma. It functions as a serine protease which is a member of kallikrien gene family [12]. PSA present in both bound form (complexed, cPSA) and unbound form (free, fPSA) in the bloodstream. Among the proteins which found binding to PSA in the blood are ACT, α2-macroglobulin (A2M), and α1-protease inhibitor (API) [13]. Elevated levels of PSA in the bloodstream are likely a result of the disruption of cellular structure within the prostate gland [14]. The disruption of protective barrier provided by the basal layer and basement membranes within the normal prostate gland is the likely site for the release of PSA into the bloodstream. This phenomenon can occur in the context of prostate conditions (such as BPH, prostatitis, and carcinoma of prostate) as well as procedures cause manipulations of the prostate (e.g., prostate massage, prostate biopsy) [15]. As well, urinary retention and urinary catheterization and prostatic trauma, can also result in a transient surge in serum PSA level that persists for 4 or more weeks before returning to baseline values [16]. The normal serum PSA level in male is considered less than 4ng/ml [17].

There is positive correlation between serum PSA and age, so Age-adjusted PSA values can be employed to more accurate screening for carcinoma of prostate gland [10]. Presently in the United Kingdom, PSA value thresholds are utilized during the screening process for carcinoma of prostate, indicating the necessity for additional investigation via prostate biopsy. Guidelines from the National institute for health and care Excellence (NICE) recommend the use of age-specific cutoff PSA measurements as shown in the table below [18]).

Table 1: Age-specific cutoff PSA level [18].

Age(years)	Cut off-PSA level
50-59	≤3.0 ng/ml
60-69	≤4.0 ng/ml
70 and older	≤5.0 ng/ml

Because high serum PSA level is primarily an indication for prostatic biopsy and subsequent diagnosis of prostatic diseases, it is crucial to evaluate the impact of additional factor (coitus and digital rectal examination) on serum PSA level [19].

Regarding the correlation of PSA with body mass index, Obesity could potentially impact the detection of carcinoma of prostate during prostate cancer screening (20,21], specifically by affecting serum PSA levels.

Obese males tend to exhibit lower PSA levels compared to non-obese male [20,21], likely attributable to reduced peripheral testosterone concentrations [22], and/or plasma hemodilution, characterized by the dilution of tumor markers due to heightened volume of plasma, is one explanation. This phenomenon is underscored by the inverse association between body mass index and serum PSA level [23,24].

AIM OF THE STUDY:

Our research study aimed to define the relationship of body mass index (BMI) as a marker of obesity with serum PSA level. This knowledge will help to avoid errors in the assessment of prostate disorders using PSA test for overweight and obese men.

PATIENTS AND METHODS:

Across sectional study was proceed from 3rd of May to the 28th of November 2022. Our study involved 115 cases, with their age more than 55 years (35 patients aged 55-59 years, 53 patients involved were aged between 60 and 69 years and 27 patients involved aged 70 years and above). During the initial consultation, history and physical examination were conducted with measurement of weight and height [for calculation of BMI] and then cases sent for measurement of total serum PSA level and prostatic volume by trans rectal U/S. DRE also done for every case (after delivering of blood sample for PSA test).

Exclusion criteria include patient with history of prostatic cancer, previous prostatic surgery, prostatitis, hormonal therapy (like 5-alpha reductase inhibitors), DRE with 7 days before the screening, cystoscopy or prostatic needle biopsy within one month before the screening and urine retention relieved by urethral catheterization in past few days.

Body mass index, total serum PSA and measurements of volume of prostate were done for every case in this research study. The body mass index (BMI) was computed using the weight in kilograms and height of the individuals in meter, Patients were categorized based on the WHO body mass index (BMI) criteria for Asians in to three groups: G1 obese (BMI > 27kg/m2) which includes 55 cases, G2 overweight (BMI 23-27 kg/m2) which includes 37 cases, and G3 normal (BMI 18.5- 23 kg/m2) with their number is 23 cases [4].

Total serum PSA was analyzed by (monoclonal antibody technique and enzyme linked immunoflourescent assay), using MINI VIDAS set.

Statistical analysis:

The statistical analysis was carried out using IBM-SPSS 26. The normality of the data was assessed via the Shapiro-Wilk test, leading to the selection of nonparametric tests. Medians, ranges, and quartiles were calculated for the analysis. Kruskal-wallis test used to calculate the difference between the three groups and the Mann-Whitney test to find the difference between two groups in the measurable data.

A p-value of ≤ 0.05 was deemed significant for the study. The Age adjustment formula for PSA was used to remove the impact of age on PSA level across BMI groups.

The Spearman's correlation coefficient was used to investigate the relationship between serum PSA level and BMI, "r" is correlation coefficient. A strong correlation between two variables is

indicated by values close to 1, whereas values close to 0 suggest a weak or poor correlation. The positive sign of "r" indicates direct relation while the negative sign indicates inverse relation. Linear regression value was also calculated.

RESULTS:

Table (2) shows the differences of age, PSA, BMI, and Prostatic Volume (PV) among study groups and reveals that differences of age and PV among study groups are statistically non-significant. Medians and (25, 75) quartiles of PSA are 1.6 (0.93, 1.94) ng/ml, 2.2 (1.45, 2.9) ng/ml, and 2.69 (1.53, 3.2) ng/ml in the group1, 2, and 3 respectively with statistically significance among. The real difference just presents between group1 with group 2 and between group 1 and group3. The difference of BMI medians among the study groups is statistically significant.

Table 2: The differences of age, PSA, BMI, and PV among study groups.

Parameters	G1 Obese men (BMI>27) n=55	G2 Overweight men (BMI 23-27) n=37	G3 Normal men (BMI<23) n=23	p-value*	p- value**
	Median (25,75) quartile	Median (25,75) quartile	Median (25,75) quartile		
Age (years)	65.0 (59.0,70.0)	65.0 (60.0,72.0)	64.0 (59.0,72.0)	0.738	-------
PSA (ng/ml)	1.6 (0.93,1.94)	2.2 (1.45,2.9)	2.69 (1.53,3.2)	0.001	1-2 0.002 1-3 0.001
					1-2 0.009
BMI (kg/m^2)	29.4 (28.3,31.2)	25.3 (24.6,26.2)	21.7 (20.7,22.5)	0.003	2-3 0.000
					1-3 0.003
PV (ml^3)	49.5 (41.5,58.0)	47.0 (36.0,56.0)	42.0 (31.5,55.0)	0.532	-------

* Kruskal-wallis test ** Mann-Whitney test

Figure (1) demonstrates the distribution of PSA medians with BMI of the study sample in respective to age groups and portrays PSA medians are the higher at BMI (23-27kg/m2) than that at BMI(<23kg/m2) apart from the age group (≥70) years within which the median of PSA is the highest at BMI (<23kg/m2). Lowest PSA medians are at BMI (>27kg/m2), within all age groups.

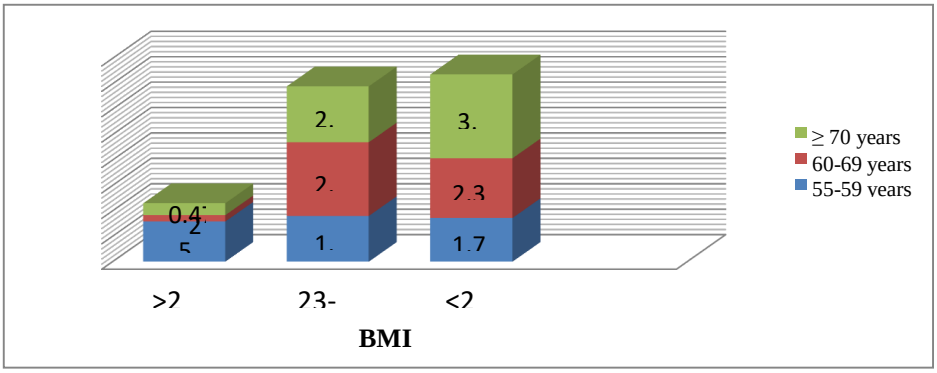

Figure 1: Distribution of medians of PSA with BMI of the study sample in respective to age groups.

Table (3) shows the differences of Age adjusted PSA among study groups and reveals a significant difference especially between group1 (Median=1.43) and group3 (Median=2.17).

Table 3: The differences of Age adjusted PSA among BMI groups.

Parameters	G1 Obese men (BMI>27) n=55	G2 Overweight men (BMI 23-27) n=37	G3 Normal men (BMI<23) n=23	p-value*	p- value**
	Median (25,75) quartile	Median (25,75) quartile	Median (25,75) quartile		
Age adjusted PSA	1.43 (0.93, 2.27)	1.72 (1.10, 3.06)	2.17 (1.53, 2.70)	0.022	1-3 0.011

* Kruskal-wallis test ** Mann-Whitney test

Table (4) shows correlations of PSA with age and BMI depicts direct and statistically significant correlation of PSA with age while the correlation with BMI is statistically significant inversely correlated.

Table 4: Correlations of PSA with age and BMI.

Parameters	Spearman's rho Correlations (r)	p-value
Age	0.203	0.029
BMI	-0.396	0.001

Table (5) demonstrates the linear regression of PSA with BMI and age and portrays that the PSA is regress in statistically significant inverse way with BMI at (p=0.001) as shown in Figure (4) and in positive significant way with age in Figure (5).

Table 5: Linear regression of PSA with Age and BMI.

Model[a]	Unstandardized Coefficients		Standardized Coefficients	p-value	95.0% Confidence Interval for B	
	Beta	Std.Error	Beta		Lower Bound	Upper Bound
(Constant)	2.295	0.885		0.011	0.542	4.049
BMI	-0.074	0.019	-0.335	0.001	-0.112	-0.036
Age	0.025	0.010	0.207	0.018	0.004	0.044

a. Dependent Variable: PSA

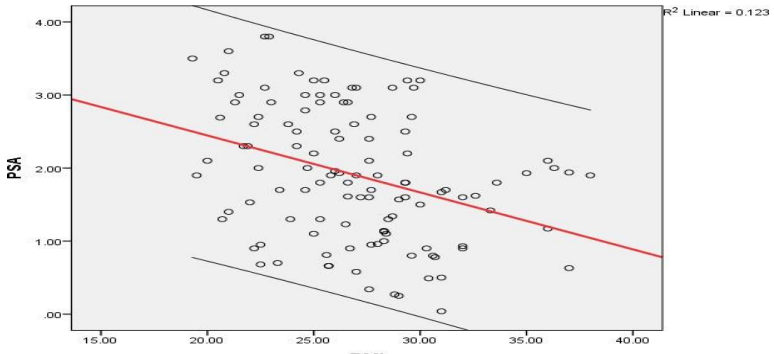

Figure 2: Regression line between PSA level and BMI with 95% confidence interval.

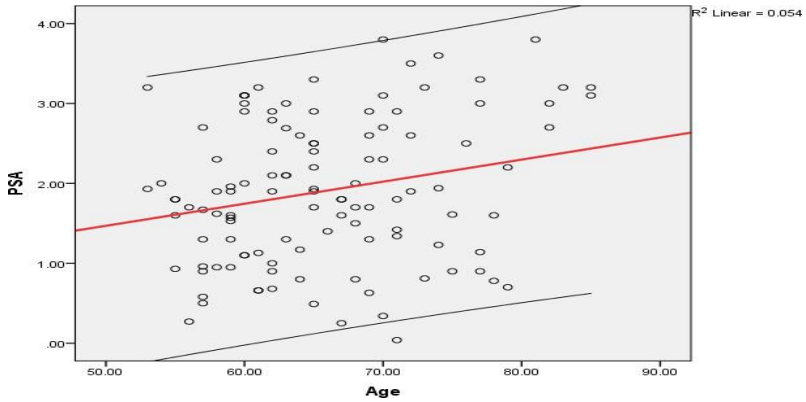

Figure 3: Regression line between PSA level and Age with 95% confidence interval.

DISCUSSION:

Regarding PSA level across BMI groups significant differences were observed in PSA levels across the 3 BMI groups in our study with lowest PSA medians in obese patients (p value = 0.001), which similar to study done by Farhan SD [25] ($p < 0.001$) and study done by Helal NN [10] ($p < 0.001$).

For prostatic volume in our study, there was no statistically significant variance in the size of prostate gland across the BMI groups (p value= 0.532), that suppose there was minimal or no effect of prostatic volume on PSA level across BMI groups in this study. This is similar to the study Helal NN [10], (P=0.48). While in study done by Farhan SD [25], PSA density was calculated for adjustment of PSA for prostatic volume which is not measured in our research study.

This research study revealed that overweight males exhibited reduced PSA levels compared to those of average weight (p=0.001). After adjusting PSA for age, it was still negatively correlated with BMI (p=0.022). According to Spearman's correlation, there was a negative correlation between PSA and BMI (coefficient -0.396, p=0.001) and correlated with age positively (coefficient 0.203, p= 0.029). Results were similar to study done by Chiu PK. et al [6].

Using a linear regression model with PSA as the dependent variable, a strong inverse relationship was observed with a significant linear trend between PSA level and BMI (r=-0.335, p=0.001), and positively related to age (r= 0.207, p=0.018). These results were similar to studies done by Farhan SD [25] and Liu M. et al [26].

The finding of this study which indicated an inverse relationship between PSA level and BMI was similar with results reported in other research studies like Pater LE et al [27], Chiu PK et al [6] and Yue L et al [28]. A study done by Arab, D. et al [12] concluded a positive correlation between serum PSA level and age (r=0.3, P=0.001), but no

relationship between BMI and serum PSA level (r=0.006, P= 0.89)

The reason of a negative association found between PSA and BMI has been explained by these two hypotheses:

1. Endocrine disruptions linked with obesity resulting in increased conversion of testosterone to estrogen inside fatty tissue could be associated with reduced PSA production [29].
2. The volume dilution theory proposes that lower PSA level in obese male is primarily result of the dilution effect of larger blood plasma volume [30].

CONCLUSION:

In our study we concluded that serum PSA level was observed to decrease with an increase in BMI and increases with age. This suggests that the interpretation of PSA levels may quire adjustment based on the obesity status of the case. Our finding revealed that obese male exhibit lower serum PSA level compared to non-obese male within the same age group, consequently, it could potentially take a longer duration for their PSA level to escalate to a point necessitating prostatic biopsy. So, there should be a low threshold for prostatic biopsy in obese men. Use of tests like PSA density (correlation of PSA to prostate volume) or PSA velocity (annual arising of serum PSA) may lead more accurate assessment of PSA level to adjust the effect of other parameters on PSA level.

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