# CORRELATION STUDY BETWEEN SERUM PROSTATE SPECIFIC ANTIGEN AND BODY MASS INDEX

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**ABSTRACT**

**AIM**

To study the correlation between body mass index and Serum Prostate Specific Antigen (PSA) in a tertiary care hospital in Palakkad, Kerala.

**MATERIALS AND METHODS**

Men aged 30-85 years old were selected randomly with no history of prostate cancer. Data regarding age were taken along with measurements of weight and height using which BMI was calculated. PSA was measured at the central laboratory using Paramagnetic particle chemiluminescence immunoassay. Data were analysed using SPSS version 17.0 and reported as means±SD for continuous variables. Student's t-test and ANOVA were used to compare continuous variables and categorical variables respectively.

**RESULTS**

After screening for prostate cancer, 100 subjects were included in the study. Mean age was 56.7±18.7 (Range 30 to 85) years; mean BMI was 26.5±3.5 kg/m$^2$, and mean PSA was 2.45±1.23 ng/mL. Using BMI, participants were classified as 28% in the normal range, 55% as overweight, and 17% as obese. No significant difference in age was observed between BMI groups across age groups.

**CONCLUSIONS**

This study found an inverse relation between Prostate specific antigen and body mass index. Hence, care should be taken when interpreting the results of the same based on BMI of the patient concerned.

**KEYWORDS**

Correlation, PSA, Obesity, Body Mass Index, Prostate Cancer, Old Age.

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**INTRODUCTION:** According to the national cancer registries, incidence of some cancers are on a rise in India. For example, prostate, mouth and kidney among males; and uterus, breast, thyroid among females. Prostate is the second leading cause for cancer among males in cities like Delhi, Kolkata, Pune, Thiruvananthapuram. Worldwide, prostate cancer is the sixth leading cause for cancer deaths. Earlier it was found that the prevalence of prostate cancer in India was much lower than western countries but with acculturations and migrations, the percentages are almost catching up.[1] Obesity on the other hand is becoming a common household entity in India with World Health Organization (WHO) stating that it is one of most commonly neglected public health problem.[2]

According to the WHO World Health Statistics Report 2012, globally one in six adults is obese and nearly 2.8 million individuals die each year due to overweight or obesity.[3] Additionally, obesity is strongly associated with other metabolic disorders including diabetes, hypertension, dyslipidaemia, cardiovascular disease and even some cancers. The risk for these disorders appears to start from a body mass index (BMI) of about 21 kg/m$^2$.[4]

Overweight and obesity (High Body Mass Index) in India with 1.2 billion people is the second most populous country in the world and is currently experiencing rapid epidemiological transition. Undernutrition due to poverty which dominated in the past is being rapidly replaced by obesity associated with Industrialisation and urbanisation.[5]

Studies from different parts of India have provided evidence of the rising prevalence of obesity.[6] However, most reports have been region specific (mostly from urban areas). Further, different studies have used different methodologies, definitions and cut-off points for defining obesity, making comparisons difficult. To date, there has been no nationally representative study on the prevalence of obesity in India.

India is second most populous country in the world and the state of poverty is being converted soon to a state of obesity due to rapid industrialisation and easy availability of calorie rich foods. Despite several biological mechanisms

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that potentially link obesity to prostate cancer, the effects of obesity on serum PSA levels and prostate volume and the subsequent effects on the detection of prostate cancer are not consistent according to the available literature. There are several mechanisms which link obesity to prostate cancer, still the effect of obesity on serum PSA levels are not consistent. A recent study showed that a BMI >40 kg/m$^2$ was associated with a more than 50% increase in cancer mortality across a wide range of malignancies, including prostate cancer.[7] Hence, in this study, the correlation between body mass index with serum PSA levels will be studied.

**MATERIAL AND METHODS: Subjects:** This cross sectional study was started after obtaining consent from institutional ethics committee. It was conducted over a one year period from April 2015 to April 2016. 100 subjects coming in for general health check-up were selected randomly. The subject details were taken which included age, prostate cancer history. Height and weight were taken. Screening was conducted to rule out prostate cancer by testing for serum PSA and a digital rectal examination. The men suspected to have prostate cancer by screening were excluded. BMI was calculated as weight in kilograms divided by squared height in meters (kg/m$^2$). The subjects were classified according to the WHO criteria for Asian populations, where patients with BMI <24.9 kg/m$^2$ were considered in the normal range, 25-29.9 kg/m$^2$ were considered overweight, and >30 kg/m$^2$ were considered obese.[8]

Serum PSA was estimated using Paramagnetic particle chemiluminescent immunoassay. One of the variations of the standard ELISA is Luminescent immunoassays, for example, fluorescent immunoassays. An enzyme converts a substrate to a reaction product that emits photons of light instead of developing a visible colour. Luminescence is described as the emission of light from a substance as it returns from an electronically excited state to ground state. The various forms of luminescence (Bioluminescence, Chemiluminescence, Photoluminescence) differ in the way the excited state is reached. The chemiluminescent substance is excited by the oxidation and catalysis forming intermediates. When the excited intermediates return back to their stable ground state, a photon is released, which is detected by the luminescent signal instrument.

**STATISTICAL ANALYSIS:** Data were analysed using SPSS version 17.0 and reported as means±SD for continuous variables. Student's t-test and ANOVA were used to compare continuous variables and categorical variables respectively. PSA levels (Mean ±SD) were calculated per BMI groups (Normal Range, Overweight, and Obese) and age groups (<40, 41-59, and >60 years).

Associations between BMI and PSA were examined by linear regression models and stratified by age. A P value of <0.05 was considered to be statistically significant.

**RESULTS:** After screening for prostate cancer, 100 subjects were included in the study. Table 1 shows the characteristics of study participants. Mean age was 56.7±18.7 years; mean BMI was 26.5±3.5 kg/m$^2$, and mean PSA was 2.45±1.23 ng/mL. Using BMI, participants were classified as 28% in the normal range, 55% as overweight, and 17% as obese.

| Sl. No. | Variable | Mean±SD |
|---|---|---|
| 1 | Age (years) | 56.7±18.7 |
| 2 | PSA (ng/mL) | 2.45± 1.23 |
| 3 | Body Mass Index (kg/m$^2$) | 26.5±3.5 |

***Table 1: Characteristics of Study Participants***

| Age Group | ≤ 40 | 41-59 | ≥60 | p |
|---|---|---|---|---|
| Normal weight | 1.64±1.01 | 1.75±1.11 | 2.40±2.1 | <0.01[a] |
| Overweight | 1.53±0.87 | 1.65±1.17 | 2.22±2.33 | <0.01[a] |
| Obese | 1.33±0.79 | 1.54±0.77 | 2.10±2.16 | <0.01[a] |
| P value | <0.01[b] | <0.01[b] | <0.01[b] | |

***Table 2: Distribution of Serum PSA over Age Groups and BMI Ranges***

a. Difference between age groups.
b. Difference between BMI groups.

**RESULTS:** Our study which included 100 participants were screened for absence of prostate cancer by digital rectal examination, prostate specific antigen. The baseline characteristics were as follows. The mean age was found to be 56.7±18.7 years. The mean PSA levels were found to be 2.45±1.23 ng/mL. And the body mass index was found to be 26.5±3.5 kg/m$^2$. The PSA levels were then categorised according to age and BMI and the following were the findings. It was found that as age increases the serum PSA levels increase and there is a significant difference between different age groups. Similarly, a negative trend was found as the BMI increases in all age groups. It was found that as BMI increases the serum PSA decreases. A significant difference was found between different age groups.

**DISCUSSION:** Protein Specific Antigen is a glycoprotein synthesised by cells in the prostate gland. It is also known as gamma-seminoprotein or kallikrein-3 (KLK3). It is encoded by KLK3 gene. It is a member of the kallikrein related peptidase family and is secreted by epithelial cells of the prostate gland. PSA is known to liquefy semen in the seminal coagulum and allows sperm to swim freely. PSA is being used as a screening parameter for prostatic cancer. A PSA level of <4 ng/mL is considered normal. A level more than this value qualifies for confirmation of the same using prostate biopsy. Prostatic cancer can be given a risk stratification as low, intermediate or high risk for developing metastatic disease or dying of cancer.

Prostate cancer is graded according to Gleason scoring. The scoring system is named after Donald Gleason, a pathologist at the Minneapolis Veterans Affairs Hospital, who developed it with colleagues at that facility in the 1960s.[9]

**Criteria for Each Risk Category are as Follows:**

- **Low Risk:** PSA < 10, Gleason score ≤ 6 and clinical stage ≤ T2a.
- **Intermediate Risk:** PSA 10-20, Gleason score 7, OR clinical stage T2b/c.
- **High Risk:** PSA > 20, Gleason score ≥ 8, or clinical stage ≥T3.

BMI or body mass index is the term which defines the classification of people into normal weight, overweight obese. The classification is given by the World Health Organization (WHO) and is such that <18.5 is underweight, 18.5-24.9 normal weight, 25.0-29.9 overweight and >30 is obese. The various classes of obesity are defined as follows. 30.0-34.9 is taken as class I obesity, 35.0-39.9 class II obesity, 40.0–49.9 class III obesity, 50.0–59.9 class IV obesity, > 60.0 class V obesity.[8]

According to Giovanni De Pergola et al, the data published in the last 25 years show that obesity is a cause of about 20% deaths from cancer in women and 14% in men.[10] They also state that these data may be underestimated as the average weight has risen worldwide over the same time. In an article by Jaggers et al, it was found that there was a positive multivariable adjusted association between cancer mortality and abdominal obesity and that the cancer mortality increases by 24%.[11] It has been stated that the mechanism with which obesity causes cancer can either be direct due to changes in the metabolic milieu which leads to generalised tumours or in specific sites due to effect of obesity like gallbladder stones, etc.[10]

In article by Splindler SR, it is stated that calorie excess leads to increased cancer incidence as positive energy balance promotes cancer cell proliferation and tumour progression. So in the same effect it was found that limited longterm calorie intake led to a decrease in cancer incidence and extended longevity in rodents. Rapid and reversible induction of the longevity, anticancer and genomic effects of caloric restriction.[12] One of the hypothesis explaining the association between obesity and cancer is that of insulin resistance. It is known that excess body weight is directly correlated with insulin resistance which results in hyperinsulinaemia. This hyperinsulinaemia acts as a growth factor for tumour progression.

In a study done by Albanes D et al, it was proposed to study the mitogenic and growth-stimulatory effects of insulin-like growth factors on the causation of prostate cancer as the studies for the same gave an unclear picture. A direct association noted between levels of serum insulin and higher risk of prostate cancer.[13] According to Freedland et al, it was stated that obesity cannot be associated with an overall incidence of prostate cancer, but presence of obesity definitely makes prostate cancer more fatal and aggressive. Obese men also have higher rates of death from prostate cancer.[14]

These studies highlight the point that cancer detection schemes need to be more aggressive in people with high BMI. In this study, it was found that as age increases there was an increase in Serum PSA levels. And there was a significant reduction in its levels with increase in BMI. Previous studies have shown a similar inverse relationship with BMI. In a study done by Baillargeon J et al where association of body mass index was studied, it was found that high BMI was associated with lower PSA level after controlling for age and race after controlling for age and race.[15] Chia et al and Kim et al in their studies also found a negative correlation between serum PSA and BMI.[16,17]

The mechanisms behind the inverse association of BMI and PSA are unclear. Obesity as such is associated with multiple metabolic derangements. It is hypothesised that it may influence PSA levels in several ways. Kuboto et al in their article have stated that one reason for reduction in PSA value in obesity could be haemodilution wherein because of increase in plasma volume there is an apparent reduction in PSA value in plasma.[18] PSA is being taken as a function of plasma volume.[19] One more hypothesis given for the same is steroid hormone metabolism hypothesis which states that metabolic derangements caused by obesity affect multiple hormones and growth factors like leptin, oestrogen, insulin and insulin like growth factors. These hormones might be causing an increase in serum PSA levels.[20]

Studies done in the west also showed a similar picture wherein there was a negative correlation between BMI and PSA levels.[21,22]

**CONCLUSION:** Our study concluded that BMI is inversely associated with PSA levels and directly associated with age. The fact that obesity itself is a cause for various cancers and that PSA levels are significantly lower in obese individuals raises a cause of concern over diagnostic potential of using PSA in patients with high BMI. There have been studies in the past which have shown aggressive prostate cancer in obese men.[23] Major concern is that haemodilution related reduction in PSA in obesity will lead to a later diagnosis of prostate cancer in these individuals. Therefore, some groups have suggested using PSA which is adjusted for BMI, to bring into reality is a big task as what we are talking about is a statistically significant difference and not a distinct clinical difference.[24] Hence, this particular point is open for further research and experimentation as to how PSA screening can be utilised effectively over various age groups and BMI.

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