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The Association between Estrogen Levels and Prostate Volume in Obese and Non-Obese Benign Prostatic Hyperplasia (BPH) Patients

Afsheen Khan, Naheed Khan, Syeda Bushra, Asma Aijaz, Iffat Raza, Shaheen Haider

ABSTRACT

Objective: To investigate the association between prostate volume and estrogen levels in obese and non-obese individuals suffering from Benign Prostatic Hyperplasia (BPH).

Study Design and Setting: Cross-sectional, analytical study

Methodology: The International Prostatic Symptom Score (IPSS) was used in the study to recognize sixty participants with BPH. The study examined patients' height, weight, waist circumference (WC), and body mass index (BMI). An IPSS score of less than 7 was seen as healthy. Using standardized BMI (25) and waist circumference (90cm), patients were split into two groups, with obese patients being placed in group A and non-obese patients being placed in group B. Using trans-rectal ultrasonography(TRUS), prostate gland's dimensions were measured, and blood samples were taken to determine serum estrogen levels.

Results: In comparison to the non-obesity group, which had a mean prostate volume (PV) of 31.21±6.771 ml, the obese group's PV was 36.13±3.673ml. It was statistically significant that there was a difference between the two groups (p=0.001). In the non-obese group, average level of estrogen was 309.72±73.62pmol/l, compared to 328.21±115.05pmol/l in the obese group (p=0.462). Correlation study (r=0.279,p=0.031) revealed a significantly ideal relationship between participants' blood estrogen levels and PV. Among patients who were obese, there was a significant positive correlation among blood estrogen levels and prostate size(r=0.638, p=0.0001).

Conclusion: When compared to the non-obese group, obesity significantly raises prostate volume in study participants, leading to benign prostatic hypertrophy. In addition, prostate volume and blood estrogen levels in obese males showed a significant positive association.

Keywords: Prostate, Estrogen, Body mass index, Obesity

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Afsheen Khan
Assistant Professor, Department of Anatomy
Shaheed Mohtarma Benazir Bhutto Medical College, Lyari
Email: drafsheenkhan2@gmail.com

Naheed Khan
Professor, Department of Anatomy
Dow University Of Health Sciences
Email: naheed.khan@duhs.edu.pk

Syeda Bushra Ahmed
Assistant Professor, Department of Anatomy
Shaheed Mohtarma Benazir Bhutto Medical College, Lyari
Email: sbushra.ahmed@hotmail.com

Asma Aijaz *(Corresponding Author)*
Assistant Professor, Department of Anatomy
Karachi Medical And Dental College
Email: asmafkh83@gmail.com

Iffat Raza
Associate Professor, Department of Anatomy
Karachi Institute of Medical Sciences
Email: razaiffat2@gmail.com

Shaheen Haider
Lecturer, Department of Anatomy
Dow International Medical College
Email: shaheen.haider@duhs.edu.pk

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INTRODUCTION:

The lower pelvis contains the prostate gland which is a tubule-alveolar, fibro-muscular, exocrine gland that is situated in the male lower pelvis, surrounding the neck of urinary bladder. Up to 30% of the entire male ejaculate is produced by prostatic fluid. The prostate gland weighs approximately 8gram throughout childhood but over the first 50 years of life, it can weigh up to 150gram. Benign prostatic hypertrophy (BPH) invariably causes it to become heavier after the first 50 years of life. Nocturia, urinary urgency, dribbling, and insufficient bladder emptying are typical signs of BPH. BPH risk factors include aging, family history, and metabolic problems. Urinary tract infections (UTIs), kidney and bladder damage are among the complications. The tests that are advised for diagnosis of BPH include post-void residual urine volume (PVR), digital rectal examination (DRE), and international prostate symptom score (IPSS).[1]

Prostatic enlargement and clinical symptoms are the result of a persistent, progressive, but discontinuous hyperplasia of both glandular epithelial and stromal components in BPH. Additionally, fibroblasts, blood vessels, nerve cells, and inflammatory cells are seen in the stromal components of

BPH. There can be possibility that each of these stromal and epithelial elements will contribute to the development of BPH. The term histological BPH refers to tissue remodeling including fibromuscular matrix and epithelial tissue, as well as proliferation of stromal and epithelial cells in prostate transition zone. Additionally, the gland displays periurethral zone involvement in addition to glandular and stromal hyperplasia. Due to progressive nature of BPH, the greatest risk factor for its occurrence is age. In addition to age, studies have revealed that a number of obesity-related factors also have an impact on prostate volume (PV) of BPH patients. Obesity and metabolic diseases have been associated to BPH.[2, 3]

The literature claims that prostate volume differs amongst various racial groupings. Male Asians have lesser PV than male whites. [4] PV measurements are crucial for discussing possible growth in several medical contexts. The median yearly prostate growth in men with PV=30 ml was 1.7%, whereas the median annual prostate growth for men with PV above 30 ml was 2.2%.[5]

Both digital rectal examination and prostate ultrasonography can measure prostate size. Since it evaluates all three dimensions of volume, trans-rectal ultrasonography (TRUS) is a useful method for assessing PV. The peripheral zone (PZ), central zone (CZ), and transitional zone (TZ) constitute roughly 75%, 20%, and 5% of the gland volume, respectively, in adolescents, though these ratios vary with age.

Benign prostatic hypertrophy begins in TZ and eventually may spread throughout the gland completely.[6] In older men, BPH is mainly responsible for voiding issues.[7] This prostatic hypertrophy is benign. It is ranked as the fourth most prevalent disease in males over 50. It affects 90% of men over 80 and about 40% of men over 50 on a regular basis. [8] Patients with familial BPH are more likely to experience the onset of condition earlier.[9]

BPH is caused by a variety of risk factors, including androgenic hormones, genetic predisposition, and changes in the detrusor muscle with aging. According to a new study, systemic inflammation and oxidative stress have been linked to an elevated risk of BPH by serum adipokines, extremely active hormones released by excess adipose tissues. The pathogenesis of BPH may be significantly influenced by systemic metabolic disorders, notably obesity. According to recent investigations genetic, metabolic, neuroendocrine, psychological, and environmental factors all have a role in obesity. [3, 10]

The investigation's findings will aid in the early detection of BPH in elderly individuals (50 years of age and older). This study might help in early identification of BPH patients because the size of the gland has a significant role in deciding patient's future medical treatment and therapy.

METHODOLOGY:

In this cross-sectional, analytical investigation, 60 BPH patients from Dow University of Health Sciences and Dr. Ruth Pfau's emergency hospital were included. After receiving institutional review board approval (IRB-1182/DUHS/Approval), the study was carried out. To find participants, a non-probability consecutive sampling strategy was used. The sample size was determined with the open Epi calculator. The sample size was calculated using a 95% confidence interval and an 80% test power. The computed sample size was 2 (1 for each group, group A-Obese and group B-Non-obese)). To fulfil statistical requirement, 30 samples were taken in each group making a total of 60 (obese 30, non-obese 30).

The study included all BPH patients between the ages of 50 and 80 who had an IPSS score greater than 7 with the condition. The Asian cutoff values of Body Mass Index (BMI) > 25 and Waist Circumference (WC) > 90 cm were used to determine obese men.

Non-obese participants were included on the basis of BMI ranging from (= 25) and (WC < 90cm). Exclusion Criteria included the patients with known prostate cancer, previous prostate surgery and previous pelvic surgery of any type and patients with history of kidney and bladder disorders such as renal stones, bladder stone.

All patients had trans-rectal ultrasonography (TRUS) using an ultrasound machine (Type Doppler machine and Toshiba firm model Nemio XG) to measure the volume and size of the prostate. To determine their oestrogen levels, blood samples from each subject were taken. 5 ml of blood were collected to estimate the amount of estrogenic hormones. The prostate typically has a capacity of 30 ml, and the normal range of oestrogen concentrations is 99.4 to 192 pmol/l. [11]

The baseline characteristics of obese and non-obesity participants were calculated using descriptive statistics, such as mean, standard deviations, frequency, and proportions. The Shapiro-Wilk test was used to determine normality because the distribution of the data wasn't expected to be uniform. The mean differences between age groups were examined using the Mann-Whitney test and the Kruskal Wallis test. Statistical significance was defined as a P-value of 0.05 or less. The data were examined using SPSS, version 21 of the statistical package for the social sciences.

RESULTS:

A study with 60 participants, on the basis of prostate volume (PV). Specifically, 47 participants have a prostate volume greater than or equal to 30 ml (78.3%), and 13 participants have a prostate volume less than 30 ml (21.7%). Only 8 individuals (13.3%) and 52 participants (86.7%) had serum estrogen levels below 192 pmol/l.

The overall mean prostate volume (of 60 participants) obtained in our study was 33.67± 5.944ml.

The average estrogen concentration was 318.96±96.21pmol/l.

The range of the normal serum estrogen level is 99.400–192 pmol/l. The mean prostate volume in the obese group was 36.13±3.673 ml compared to 31.21±6.771 ml in the non-obese group, with a statistically significant difference (p=0.001) (Table 1).The mean estrogen levels between the obese group and the non-obese group were not different significantly (p=0.462; 328.21±115.05pmol/l vs. 309.72±73.62 pmol/l, respectively). When research participants of different ages were divided into obese and non-obesity groups, the 61-70 age groups had the highest difference. This finding was statistically significant (p-value=0.044).

When individuals with differed PV (30 ml and 30 ml) were divided into the obese group and the non-obese group (Figure 1), the group with PV 30 ml showed the greatest difference, and the result was statistically significant (p-value=0.005) (Table 2). When participants with differed estrogen levels were separated into the obese group and the non-obesity group, a difference was observed in the group with estrogen level 192, but it was not statistically significant (p-value=0.353).

The correlation research revealed a weak correlation (r=0.279, p-value=0.031) between prostate volume and serum estrogen levels .

Further classification based on obesity status revealed a significant positive association between prostate volume and blood estrogen levels in obese individuals (r=0.638, p-value=0.001) (Figure 2). However, among non-obese patients, there is no relationship between prostate volume and serum estrogen levels (r = 0.160, p-value = 0.931) (Figure 3)

Table 1: Obesity and non-obesity differences in mean prostate volume and mean estrogen levels

	Non-obese mean±SD	Obese mean±SD	p-value
Prostate volume (ml)	31.21±6.771	36.13±3.673	0.001*
Serum estrogen levels (pmol/l)	309.72 ±73.62	328.21±115.05	0.462

*p-value = 0.05 statistically signifcant , Test applied: Mann Whitney test

Table 2: Study participants' characteristics grouped based by obesity

Features	Obesity		p-value*
	Non-obese	Obese	
	n (%)	n (%)	
Prostate Volume			
< 30 ml	11(37.5)	2(15.4)	0.005*
= 30 ml	19(40.4)	28(59.6)	
Estrogen levels			
< 192pmol/l	3(37.5)	5(62.5)	0.353
=192pmol/l	27(51.9)	25(25)	

*p-value = 0.05 statistically significant, Test applied: Chi-square analysis

Figure 1: Trans-rectal ultrasonographic illustration of prostate gland > 30ml volume in A Obese man B Non-obese man

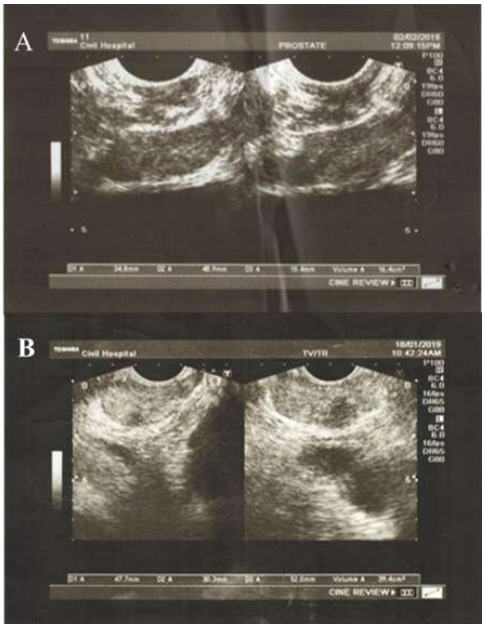


Figure 2: Correlation between prostate volume and estrogen levels in obese patients

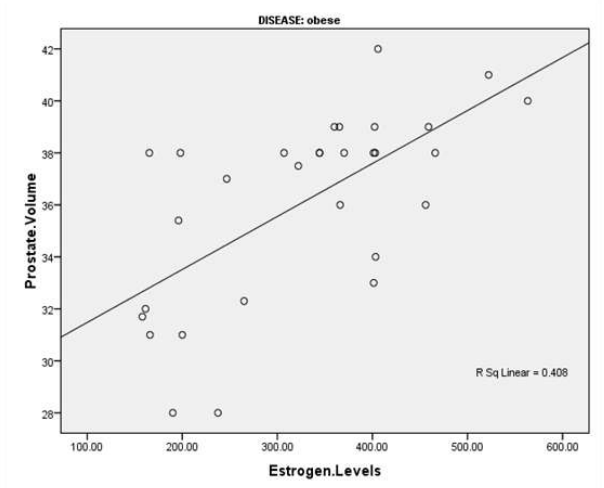
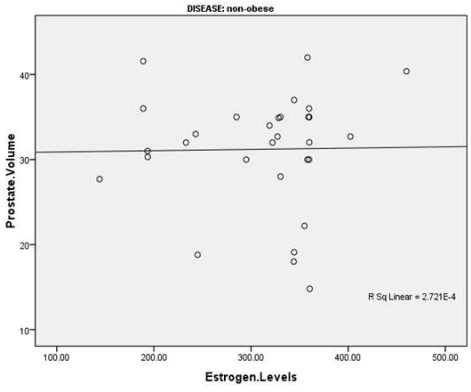


Figure 3: Correlation between non-obese patients' blood estrogen levels and prostate volume



DISCUSSION

It is well established that several factors, including aging, ethnicity, obesity, genetics, sex steroid hormones, modifiable lifestyle factors, and inflammation, can induce morphological volumetric changes in the prostate gland. The prostate gland can vary for a variety of causes, such as advanced age, obesity, and androgen hormones in men**.**

People are more likely to experience prostate problems as they get older. Benign prostatic hypertrophy (BPH), or unhealthy prostatic enlargement, is a prevalent issue for elderly men. Lower urinary tract issues are linked to it, can adversely affect quality of life. Age, ethnicity, obesity, genetics, sex hormones, modifiable life factors, and inflammation are generally accepted as known stimulators of morphological volumetric changes and enlargement of the prostate gland. Throughout a man's life, his prostate gland develops and undergo several morphological changes. Future growth and development are strongly correlated with prostatic volume (PV).[12]

The current study, which was conducted on a sample of Karachi residents who were attending a tertiary care hospital, is the first population-based study to demonstrate a positive correlation between PV and estrogen levels in obese participants.

The largest prostate volume in our investigation was found to be 42 ml. In contrast, 103 patients were exposed to benign prostatic hypertrophy in a Pakistani study by Raza et al., of whom 80 had PV smaller than 50 ml and 23 had bigger than 50 ml. [13] In their research, a prostate sample's greatest volume was 90ml. In addition, a 2005 study by Ochiai et al. discovered that 35% of individuals had a prostate volume greater than 50 ml, while 65.6% of patients had one between 25 and 50 ml. [14]

The analysis by volume assessment among people with prostate enlargement has significance in many manners. It is able to detect both the disease's progress and its complications. Numerous studies found that in healthy persons, obesity influences the prostatic volume . The mean prostate volume of obese patients in the current study was 36.13ml, compared to 31.21ml for the non-obese group. The findings are in coherence with the results of Zaza et al who reported higher PV in obese patients compared to normal weight, and underweighted patients, however; contradicts from the study on the Korean population in which 146 men over the age of 40 had mean prostate volume of 18.8 ml in non-obese individuals and 21.8 ml in obese participants. [15]

According to our results, a different study found that obese individuals had larger prostate volume levels than non-obese individuals. [11] The significant association between obesity and prostate volume discovered by other researchers supports the linear relationship between the two variables in investigations. [16]

Due to its impact on prostate development and enlargement, androgen status and obesity is a universal health concern, especially in developing nations, and significance should be given to diagnosis and correction at the community level. It might be because of the fat deposition, which accelerates the adipose tissue's metabolism of estrogen-inducing circulating testosterone into estrogens. [17]

There were no obvious differences between the two groups (obese and non-obese) according to numerous studies that presented their findings about the relationship between estrogen levels, prostate volume, and obesity.[18]

Our study's obese group had mean estrogen levels that were greater (328.21 pmole/l) than the non-obesity group (309.72 pmole/l), which is consistent with previous investigations conducted worldwide.[19] Few studies have found a statistically significant connection between estradiol levels and obesity-related variables including BMI and waist circumference. [20] However, a small number of recent researches did not find any link between estrogen and obesity. [21, 22]

It is important to determine the prostate volume in BPH using the serum oestrogen levels. This may be because the prostate gland needs androgenic hormones to maintain the tissues' normal level of metabolism. According to the current study's findings estrogen levels and prostate volume have a strong positive link. In China, a research with 949 people found no link between estrogen and prostate volume.[20] On Contrary, other researchers found a strong correlation between prostate volume and serum estrogen levels. [23]

The most remarkable finding in the current study's examination of obese males was the elevation of prostate volume with rising serum estrogen levels, which demonstrated a positive association. Due to excess fat, which starts aromatase activity and raises estrogen levels, there may be an increase in prostate volume when oestrogen levels are high. [20] Furthermore, oestrogen can also indirectly affect adipogenesis by controlling important stages in the manufacture of other steroid hormones. This is in reference to estrogen capacity to increase the activity of 11-hydroxysteroid dehydrogenase type 1 , a crucial enzyme for the upregulation of adipogenesis in human adipocytes which in turn can lead to a rise in prostate volume.

The majority of the participants were obese with estrogen levels >192pmol/l in the age groups 50–60 years, but no significant differences were seen in the age groups 61–70 years and 71–80 years where the majority of the participants were obese. Previous research has shown that advance age, obesity, and different levels of androgen are risk factors for the pathogenesis of the prostate gland. [20, 22, 23] In the current investigation, men who were obese and older had high estrogen levels. In a study with elevated estrogen levels in men aged 70 and beyond, estrogen changes in obesity and advanced age were also noted, and these results are consistent with our findings. [24] however, Age and estradiol levels have

been found in one investigation to be inversely correlated.[25]

The prostate-related parameters identified at a single moment in time, the limited sample size, the lack of testosterone-related data, and the research was restricted by the lack of a comparison between prostate volume calculated by TRUS and actual findings.

The study has several limitations. It was conducted at a single facility with a limited sample size. We suggest for future studies to compare prostate volume with real specimens such as cadavers and to confirm the influence of estrogen on prostate volume with advancing age, further studies with large sample size are recommended. It is also recommended that clinicians should make a strategy for assessment of prostate gland by correlating International prostatic symptom score with prostate volume measurements by trans-rectal ultrasonography and serum estrogen levels to ensure early detection of disease and prevent adverse outcomes of benign prostatic hypertrophy.

CONCLUSION:

The study highlighted a significant association between obesity and prostate volume and subsequent development of benign prostatic hypertrophy as compared to non-obese. There is also a significant positive association of estrogen levels with prostate volume that need to be evaluated in obese males for early detection and prevention of adverse outcomes of benign prostatic hypertrophy.

Authors Contributions:
Afsheen Khan: Study Design and Setting, Drafting of work
Naheed Khan: Drafting of work
Syeda Bushra Ahmed: Data Collection
Asma Aijaz: Data Collection
Iffat Raza: Analysis of Data
Shaheen Haider: Analysis of Data

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