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BENIGN PROSTATIC HYPERPLASIA;

CORRELATION OF PROSTATE GLAND VOLUME WITH AGE & ANTHROPOMETRIC PARAMETERS IN PATIENTS.

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ABSTRACT… Objectives: To study the effect of anthropometric measures on benign prostatic hyperplasia patients in a subset of Karachi population. **Study Design:** A cross-sectional study. **Setting:** Ziauddin University Hospital, Radiology Dept, Clifton. Karachi. **Method:** 103 benign prostatic hyperplasia patients was carried out. These patients were recruited from a urology clinic. The study subjects were divided on the basis of Age groups, body mass index groups and waist circumference groups. **Result:** Mean prostate volume of BPH patients was found to be was 62.7 ± 12.5 years. Mean BMI was found to 24kg/m^2. Mean waist circumference was found to be 73.8cms. Prostate volume was found to be doubled in waist circumference of greater than 90cm group. **Conclusion:** Prostate volume greatly enlarges with advancing age. Waist circumference is the only contributing factor among other anthropometric measures which causes growth of prostate volume.

Key words: Benign Prostatic Hyperplasia: BPH, Body mass index: BMI, waist circumference: WC, Prostate volume: PV.

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INTRODUCTION

The prostate is a pyramidal fibromuscular gland which lies in the lesser pelvis and surrounds the urethra from base of bladder to membranous urethra. The gland weighs about 8g in youth, but invariably enlarges with the development of BPH, it usually weighs 40g, but sometimes as much as 150g or even more, after the first five decades of life.[1]

The prostate gland harbors diseases like prostatitis, benign prostatic hyperplasia and carcinoma of the prostate. Benign prostatic hyperplasia is the most common prostatic pathology. Histologically, there is glandular and stromal hyperplasia of the gland along with involvement of periurethral zone.

Benign Prostatic Hyperplasia is a progressive disease and its greatest risk factor for progression is age.[2] Kok et al concluded in his study that during per year of follow up, total prostate volume increases to 2.2% and transition zone volume increases to 3.5%.[3]

Studies have proven that Prostate Volume of BPH patients varies not only with age[2] but also is affected by body mass index and waist circumference abnormal variations. These variables may need to be taken into account when evaluating patients for BPH.

The etiology of BPH is multifactorial. Obesity and other metabolic diseases have been linked with BPH.[4] While discussing, BPH with BMI. Kim et al. reported that BPH correlated positively with height and weight.[5]

The Baltimore Longitudinal Study of Aging found that waist circumference and height were associated with BPH.[6] Waist circumference which represents centrally obesity and these individual with central obesity have altered estrogen testosterone ratio of 2:1 which may influence prostate volume.[7] It has also been reported that central obesity increases the activity of the sympathetic nervous system worsening the urinary obstructive symptoms[8], as systemic noradrenaline, acting on adrenoreceptors,

promotes prostatic growth.[9]

H. A. Mosli et al. in their study proved racial differences in PV and stated that PV in Asian men is lower than that in white men.[10] It is reported in the literature that PV varies amongst different races.[11] Thus, the clinicians have to be aware of the possibility of prostate volume variation in different races in order to avoid diagnostic confusion. Therefore, to the best of our information this is the first demographic study reporting on the Prostate volume in a Karachi based BPH patients of different age groups.

BPH is the most common prostatic pathology. This study helps to determine the correlation of prostate volume with age, BMI, waist circumference. The results of this study will help in early detection of BPH in elderly (aged 40yrs and above) and obese men (increased BMI and WC).

This study may help to identify BPH patients at an early stage as the size of the gland is crucial in determining subsequent treatment and management to be offered to the patient.

MATERIAL AND METHODS

Setting

Study sample was completed in the Ziauddin University Hospital, Radiology Dept, Clifton. Karachi.

Target Population

BPH patients aged 40 years and above. 103 volunteers referred from Urology Clinic were included in this study.

Subjects were grouped into 4, age starting from 40yrs with a difference of 10 years. Subjects were grouped into 3 according to BMI: (>18 to 25) as normal weight, Overweight (>25 to 29), Obese (≥30) and into 2 groups according to their WC: waist circumference (<90 cm) is considered normal and (> 90 cm) is considered as central obesity. The classification of subgroups was based on WHO Criteria for Asians.[12]

Study Design

Cross-sectional study.

Sampling Technique

Samples were taken through non-probability convenience sampling.

Inclusion criteria

BPH patients aged 40 years and above.

Exclusion criteria

Use of medications affecting prostate volume such as 5-alpha reductase inhibitors and anti-androgens.
Acute or chronic urinary retention status.
Acute or chronic prostatitis.
Known case of prostatic carcinoma

Radiological Assessment

Subjects was scanned in supine position. Scanning was done with sonography equipment using 3.5MHz curvilinear probe, transducer was angled under symphysis pubis. Transverse sections were obtained at angulations of about 15° towards feet with full bladder. The length, anteroposterior and transverse diameters of prostate were measured on frozen images.[13]

Sanders et al. proposed that volumetric evaluation of prostate is based on the use of an ellipsoid model.

Prostate Volume by Prolate Ellipsoid Formula:

Anteroposterior Length x Transverse Length x Craniocaudal Length x 0.52.[14,15]

Statistical Analysis

Data was analysed on SPSS version 20. A sample size of 200 was calculated, keeping prevalence at 40%, confidence level of 95% and bound of error at 0.07%.

$$n = \frac{z^2 P(1-P)}{B^2}$$

n = no of samples.

z = standard error of mean = 1.96

P = 40%

B = absolute precision = 0.07

Frequencies and percentages were taken out for categorical variables. Mean and standard deviation was taken out of the numerical variables for the prostate gland volume. Quantitative variables were compared by using independent t test and ANOVA. Univariate analysis was applied for linear of relationship. Multiple linear regression was applied to determine the relationship between the prostate volume and anthropometric parameters. P-value < 0.05 was considered significant.

Anthropometric Parameters

Height and weight were measured by using normal standard anthropometric techniques.
Height was measured in meter (m).
Weight was measured in kilogram (kg).
BMI was calculated by weight/height^2 formula (kg/m^2).

Waist circumference measured in centimeters (cm) from mid-waist, between the lower rib margin and the iliac crest while the subjects were standing with their heels together, in quiet respiration.

RESULT

Characteristics of BPH Patients

The mean age of benign prostatic hyperplasia was 62.7 ± 12.5 years. The minimum and maximum age of BPH was 40 years and 89 years respectively. The mean prostate volume was found to be 42.5 ± 15.3 ml. General characteristics of subjects are shown in Table-I.

	Total Participants N= 103 Mean, Standard deviation.
Age (years)	62.7±12.5
Height(m)	1.70±.25
Weight(kg)	71.8±10.8
BMI	24.8±3.6
WC (cm)	73.8±15.3
PV (ml)	42.5±15.3

Table-I. General characteristics of BPH Patients.

Distribution of BPH patients according to Age

The patients in this study were divided into 5 age groups with a difference of 10 years, from 40 -92yrs respectively. Frequency distribution is shown in Figure-1.

Distribution of BPH patients according to Age groups.tt
Prostate Volume

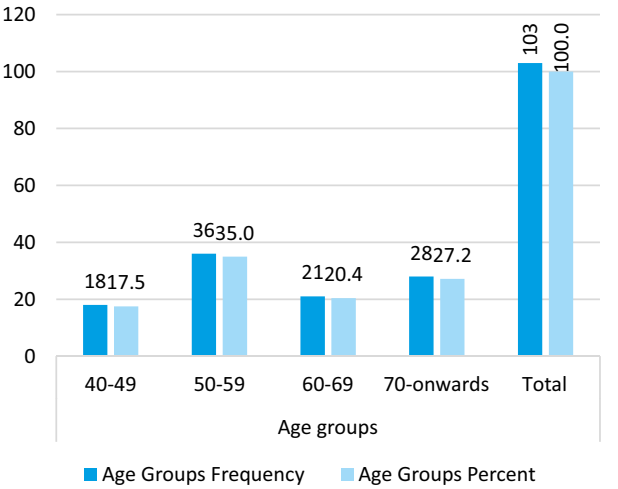

Figure-1. This diagram shows maximum number of BPH patients in age group 50-59 years.

BPH patients were divided on the basis of PV into 3 grades. Grade 1 had subjects with PV between 25-30ml, Grade 2 had subjects with PV between 31-50ml , Grade 3 had subjects with PV between 51-93ml. (Table-II)

grading of PV (ml)	**Frequency(n)**	**Percent %**
Grade 1 - 25-30	26	25.2
Grade 2 - 31-50	54	52.5
Grade 3 - 51-93	23	22.3
Total	103	100

Table-II. Distribution of BPH patients according to Grading of PV. 52% BPH patients had PV between 31-50 ml.

Prostate volume and age in BPH patients

Prostate volume increased significantly with age, with a mean age of 62.7 ±12.7 yrs (P-value 0.044). Highest volume was observed in age group 80-89 years. (Table-III) (Figure-2)

Scatter Plot between Prostate volume and Age in BPH patients.

R^2Linear=0.239

Age group (years)	1 (40-49)	2 (50-59)	3(60-69)	4(70 -onwards)	Total	P-value
	N=18	N= 36	N=21	N=28	N=103	
Prostate volume (ml)	Mean±SD 35± 5.7	Mean±SD 38.9 ± 8.3	Mean±SD 44.1 ± 11.2	Mean±SD 50.7 ±23	42.5±15.3	0.044*

Table-III. Association of Prostate Volume with Age in BPH patients. P<0.05*was considered significant.

Prostate volume and BMI in BPH patients

We divided BMI into 3 groups, normal, overweight and obese. There was no correlation found between prostate volume of BPH patients and BMI. (Table-IV)

Prostate volume and waist circumference in BPH patients

Mean prostate volume of BPH patients in waist circumference groups was found to be 42.5 ± 15 ml. A significant difference was found (p-value 0.03) between the two groups. PV was found to be higher in >90cm group. (Table-V) (Figure-3)

Scatter Plot between Prostate volume and WC in BPH patients.

Univariate analysis showed moderate correlation with age and strong correlation with waist circumference and IPSS and no correlation was found with BMI. (Table-VI)

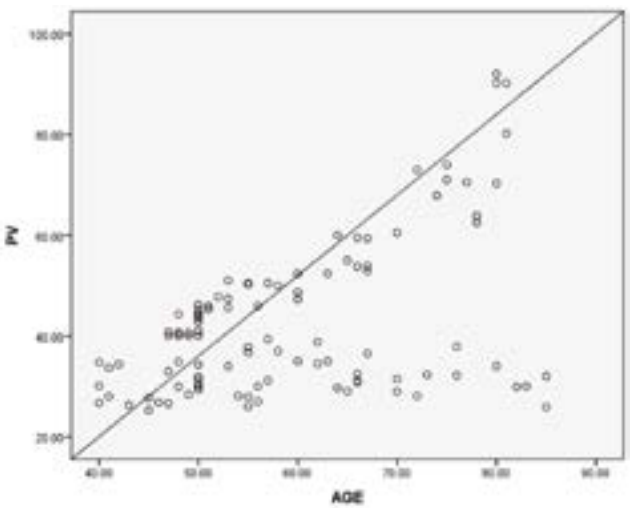

Figure-2. Graphically represents significant positive and moderate correlation between prostate volume of BPH patients and Age. (R =0.489, p=0.04)

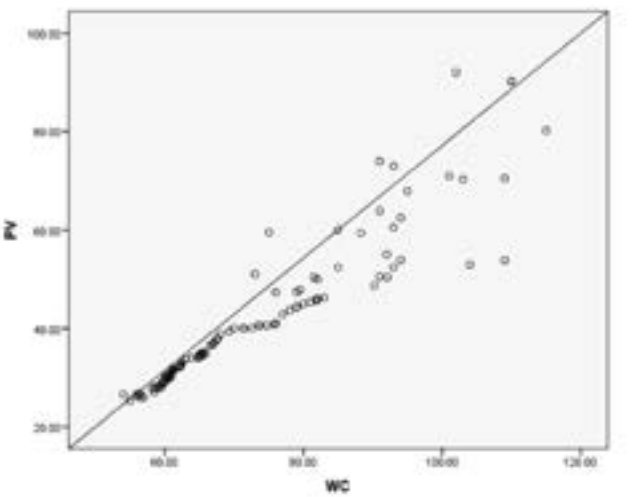

Figure-3. Graphically represents significant positive and moderate correlation between prostate volume of BPH patients and WC (R =0.931, p=0.03)

BMI groups	Normal weight	Over weight	Obese	Total	P-value
Total	N=60	N=27	N=16	N=103	
Prostate volume (ml)	36.7± 12.5	48.7 ± 15.3	54 ± 14.9	42.5 ± 15.3	0.258

Table-IV. Association of Prostate volume with BMI in BPH patients. p<0.05 is considered significant.

WC groups	<90 cm	>90 cm	Total	P-value
N	N= 84	N= 19	N=103	
Prostate volume (ml)	36.9 ± 8	67.6 ± 13	42.5 ± 15	0.03*

Table-V. Association of Prostate Volume with waist circumference in BPH patients. P<0.05 was considered significant.

Variables	R	P-value
Age	0.489	0.044*
BMI	0.442	0.258
WC	0.931	0.030*
IPSS	0.621	0.035*

Table-VI. Univariate Analysis of BPH patients with Age, anthropometric parameters and IPSS R was determined by Pearson's correlation coefficient, P was determined using ANOVA.

DISCUSSION

The patients with BPH in our study were between 40-89 years of age with a mean age of 62.7±12.5 years (Table-I).The maximum number of patients were in their fifth decade (35%). This is comparable to a study done by Roehrborn CG et al on American patients with a mean age of 63.7 years.[16] Another study done on white Europeans focusing on symptomatic BPH patients with age ranging between 40-80 years and a mean age of 63.5 years were comparable to mean age of BPH patients in our study.[17]

The mean PV of benign prostatic hyperplasia patients in our study was found to be 42.5ml. This was in accordance with that of Nepalese population.[18] However mean PV in Turks[19], Europeans17, Americans[20] and Africans[21] was higher than that of our population. There are number of causes such as aging, genetics, steroid hormones, smoking, alcohol and metabolic syndrome such as obesity, dyslipidemias and cardiovascular diseases have long been associated with BPH. Our study has been affected by which one of these causes could not be looked into, but these may have account for high PV of BPH patients of the above four studies. However, PV is reported to be lower in Indians[22] and Chinese[2] as compared to our study population. One reason could be that Indians and Chinese males are generally of a small physical stature compared to Pakistani males. We found a linear relationship between prostate volume and body weight. Body weight of a person reflects the level of human growth and development under the influence of a person's genotype and environment .Genotype and environment reflect mostly on the person's ethnicity.[23]

In our study of 103 BPH patients, 80 patients had prostate volume lower than 50ml followed by 23 patients with prostate volume more than 50ml. The lowest prostate volume for BPH patients in our study was 25.60ml and the maximum prostate volume in our study was 90ml (Table-II).

A study by Babian et al showed 65.6% of the patients had a prostate volume between 25 to 50ml and 35% of the patients had prostate volume more than 50ml.[24] Another study by Collins et al on the pattern of prostate enlargement in BPH also showed the maximum number of patients having a prostate volume ranging between 20 to 50ml.[25] An Indian study reported 79% of patients with prostate volume between 25 to 50ml.[26] Our results are comparable to those of above 3 studies.

The grading of prostomegaly varies in different studies. According to Micheal Vary classification of prostate volume on Transabdominal Ultrasound.[27]
<50 ml – Grade 1
50 to 80ml – Grade 2
>80 ml – Grade 3

According to Aguirre et al, classification of prostate volume
Grade 1- less than 30ml
Grade 2- 30 to 50ml
Grade 3- 50 to 80ml[28]

Our grading was similar to Aguirre et al. considering the multiple factors (body weight, aging, androgens) influencing PV. The similarity of results of PV of our study with those of Mc vary and Aguirre could be due to coincidence of factors which influence PV among the study population of these studies. The size of prostate is important because it helps Urologist in decision making whether the patient requires TURP or open prostatectomy. Usually patients with PV of 70ml or more require suprapubic prostatectomy.

Mean PV in BPH patients was found to be 35ml,38.9ml,44ml and 50.77ml in age groups 1,2,3,4 respectively (Table-III) and highest PV(50.77ml) was in age group 4 (70 years

onwards). The results of the current study is in accordance with the result of the study published in UroToday 2012 in which positive correlation of age with prostate volume was reported.[26] One of the possible aetiology for highest PV in age group 4 could be that as men age prostate volume continues to increase. J.T Issac proposed a hypothesis regarding BPH development 1) Dihydrotestosterone theory explains that androgen metabolism is altered and there is a shift and increase formation of DHT as 5 alpha reductase enzyme is increased which cause hyperplastic growth of gland. 2) embryological reawakening theory explains that there is increase in stromal and epithelial cells interaction 3) Stem cell hypothesis suggests that there is increase in clonal stem cells resulting in hyperplasia of gland.

We could not find positive association of BMI in benign prostatic hyperplasia patients (Table-IV). DeFronzo et al looked at modifiable risk factors for LUTS specifically in black men and found no greater risk with increasing BMI.[29] Laven et al found out that low birth weight and abdominal obesity but not BMI, were associated with an increased risk of BPH.[30] There are studies which report positive relationship between BMI and PV, but the effect of BMI on PV depends on ethnicity. A Malaysian study which compared three ethnic populations of Malaysia found out that the ratio between BMI to PV was highest in Chinese men than that of Indians and Malays.[11] Therefore, the different ethnicities of patients in our study could be the reason why we could not find a positive association of BMI and PV in BPH patients.

While correlating WC with BPH patients as shown in Table-V, we found strongest correlation between them as compared to BMI groups. These results were similar to the study done on 25,892 Health Professionals males, those men with waist circumference of 109 cm or more had (38%) BPH surgery and majority (100%) of them ended up with LUTS as compared with waist circumference of less than 89cm which had no LUTS.[31] In a Norwegian study increased waist circumference was associated with LUTS.[32] Studies have revealed that waist circumference have been positively associated with BPH.

Another Korean study have revealed that waist circumference is an independent risk factor of benign prostatic hyperplasia. A study of NHANES III concluded that obese men with increased waist circumference is more associated with LUTS and BPH surgeries.[13] Rohrmann et al concluded that men with larger waist circumference (>102 cm) were more likely to have LUTS.[13]

This is the first demographic study done on Karachi population that showed evidence that WC or central obesity is strongly correlated with PV of BPH patients. In our study its shown that men with greater than 90cm have increased prostate volumes as compared to men with lesser than 90cm waist circumference. Physical inactivity, alcohol and central obesity are associated with increased prostate volumes in a number of research studies.

The reasons behind that central obesity or adiposity contributes to BPH is still unclear but one of the pathogenesis could be that increased conversion of testosterone into estrogen hormone could lead to BPH.

Other studies suggest that insulin, IGFs, IGF- 3 protein promotes prostatic growth, as insulin has similar structure as IGF[33], IGF-3 protein receptor is located on prostate gland.[34] Therefore, patients with metabolic syndrome such as diabetes, obesity or hyperinsulinemia have increase predisposition of higher prostate volume .In BLSA cohort study men with diabetes have 2 fold likelihood of falling prey to BPH and men with increased fasting glucose are 3 fold more likely to have BPH and BPH surgeries.[34]

CONCLUSION

Prostate gland volume of BPH patients increased significantly with increasing age. Waist Circumference >90cm is an independent risk factor for prostatic growth. Central obesity is the most important factor influencing prostate gland volume in BPH patients.

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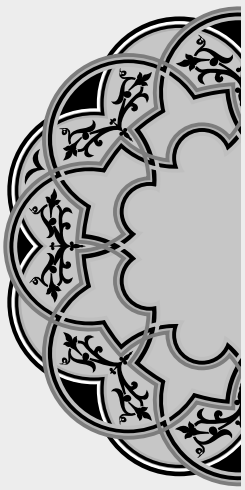

"Smooth seas do not make skillful sailors."

African Proverb

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Iffat Raza	Statistical analysis, designed the study, write up manusctipt	
2	Dr. Sahrish Mukhtar	Managed in literature research	
3	Dr. Mahrukh Kamran	Critical analysis	