



Determination of Prostate Gland Volume by Ultrasonography and Its Correlation with Anthropometric Measurements in a Subset of Karachi Population

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Authors' contributions

This work was carried out in collaboration between all authors. The concept, data collection and its analysis was done by authors IR and NH critically analyzed and gave the final approval. Author PG provided the clinical input. Author NZ helped in statistical analysis. All authors read and approved the final manuscript.

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ABSTRACT

Objectives: To establish the local reference range of prostate volume according to our subset of population. To correlate prostate volume (PV) with age, body mass index (BMI) and waist circumference (WC).

Methods: A cross-sectional study with 119 healthy adults aged 40-79 years without any prostatic pathology were recruited. The study population was categorized into 4 age groups (40 - <50 yrs,

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50 -<60 yrs, 60-<70 yrs, 70-<80 yrs), 3 BMI groups (healthy, obese and overweight) and 2 WC groups (<90 cm and >90 cm). A p-value of <0.05 was considered significant.

Results: The mean prostate volume was 21.7 ± 2.2 mls, mean body mass index was 28 ± 6 kg/m², whereas mean waist circumference was 95 cm. PV was found to be higher in obese and >90 cm waist circumference group. After applying multiple regression analysis, waist circumference correlated positively and significantly with prostate volume.

Conclusion: Mean prostate volume in our studied population was smaller than that of many western populations. Our study has proved that central obesity is the most important factor influencing prostate volume.

Keywords: Reference range; prostate volume; central obesity; anthropometric measurements.

1. INTRODUCTION

The prostate gland is the seat of many common diseases like prostatitis, benign prostatic hyperplasia and carcinoma of the prostate [1]. Recent years have shown that knowledge of PV has important clinical implications [2]. PV measurement is frequently used to diagnose abnormalities of the prostate [3].

PV varies widely throughout a man's lifetime, and also in the course of prostatic diseases [4]. It has been established that baseline prostate volume is an excellent predictor of future prostate enlargement and growth [5].

PV increases throughout life being approximately 250 mm³ (0.25 mls) at birth increasing to 10,000 mm³ (10 mls) at puberty [4]. After reaching adulthood, PV continues to increase from about 20 ml at age 40 to 40 ml at age 80 [6].

Measurement of PV is helpful in many clinical settings. For example, it is a predictor of clinical progression of prostate hyperplasia. It also helps in the selection of drug regimens. For example alpha blockers and 5-alpha reductase inhibitors, used in the treatment of prostate cancer are less effective if PV is less than 50 cm³ [4]. In addition PV helps in the surgery of benign prostatic hyperplasia and acute urinary retention. If PV exceeds 75 cm³, urologists opt for open surgery [7,8]. Other studies suggest that increased PV is a positive predictor for prostatectomy [9].

Prostate volume is also helpful in assessing prognosis of prostatic hyperplasia [10]. In the Olmsted County population based study, men who had prostate volume of less than 30 ml had median prostate growth of 1.7% per year whereas men who had PV of greater than 30 ml experienced median prostate growth of 2.2% per year [11].

Many studies have shown that PV in healthy adults varies not only with age [12] but also with body mass index(BMI), waist circumference(WC) and ethnicity [13-15].

A recent study from the United States on men who had undergone prostatectomy showed that BMI was positively correlated with prostate volume in those younger than 63 years of age [3]. A study published in UroToday International Journal revealed positive correlation of age with prostate volume [16]. Rohrmann et al. [17] in their study showed that an increase in BMI after age 25 was positively associated with lower urinary tract symptoms (LUTS).

The Massachusetts Male Aging Study found significant association between anthropometric measures and benign prostatic hyperplasia [18]. Tsukamoto et al. [3] conducted a study on 465 men, which showed that prostate volume correlated positively with central obesity as determined by measuring waist circumference but not with overall obesity as measured by BMI. Therefore, obesity may influence prostatic enlargement [19]. Centrally obese men have higher estrogen and lower testosterone levels which may influence prostate volume [15].

There are a number of techniques that can be used to determine prostate volume such as Ultrasound, CT scan and MRI. In clinical practice, prostate volume is measured by ultrasonography which is of several types Transperineal (TPUS), Transabdominal (TAUS) and Transrectal (TRUS). However, according to American Institute of Ultrasound & Medicine guidelines transabdominal ultrasonography is preferred. It is simple, economical and a basic investigation. It is cost effective, can be performed quickly and non-invasively. It is widely used as a standard clinical tool for assessment of prostatic size.

Determination of local reference range is important as it is a predictor for clinical progression to BPH. Prior to this study international reference range was being used as our guidelines. This study will help one to determine correlation of prostate volume with BMI and WC in our population. This information will also serve as a screening tool for individuals with increased BMI and WC and help in correlating PV with ultrasonography.

2. MATERIALS AND METHODS

2.1 Subject Selection

This cross-sectional study was carried out over a period of 10 months. 119 healthy volunteers aged 40 and above participated in the study and underwent ultrasonographic examination at Ziauddin University Hospital, Clifton Campus, Karachi.

Patients who had a history of pelvic or prostatic surgery, recurrent urinary tract infection or bladder stones, acute or chronic urinary retention, acute or chronic prostatitis within previous 3 months and known cases of prostatic carcinoma, diabetes mellitus and hypertension were excluded from our study. Patients on antipsychotic and antiparkinson medications and on use of medications affecting prostate growth such as 5-alpha reductase inhibitors and anti-androgens were also excluded from the study.

Subjects were divided into 4 groups according to age starting from age 40 yrs with a difference of 10 years. Subjects were divided into 3 groups for BMI according to WHO classification, Healthy (>18 to 25 kg/m²), Overweight (>25 to 29 kg/m²), Obese (≥30 kg/m²) and into 2 groups according to their WC: normal waist circumference (<90 cm) and central obesity (> 90 cm). The classification of WC was based on WHO Criteria of Asia-Pacific obesity [20]. The study was conducted after approval from ethics review committee of Ziauddin University (Ref no: 0010115IRANA).

2.2 Measurements

Individuals aged 40 yrs and above were recruited. Informed consent was obtained from each participant. Subjects were recorded for height, weight, BMI and WC. Height and weight were measured by using normal standard anthropometric techniques.

BMI calculated by weight/height² formula and expressed in kg/m².

WC 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.

After taking clinical history, demographic data (age, height, weight and waist circumference), International Prostatic Symptom Score (IPSS) questionnaire was filled and calculated. Individuals with IPSS less than 8 were considered as healthy adults of this study. Transabdominal sonography of prostate volume was then carried out.

2.3 Transabdominal Sonography

Ultrasound machine Toshiba Xario version 0.09 with 3.5 Megahertz curvilinear transducer was used for measuring prostate volume. Subjects were examined in supine position. For better assessment transducer was angled inferiorly under symphysis pubis. Transverse sections were obtained at angulations of about 15° towards feet with a full bladder. The length, anteroposterior and transverse diameters of the prostate were measured on frozen images [21].

Sanders et al. [22,23] proposed that volumetric evaluation of PV is based on the use of an ellipsoid model. Accordingly anteroposterior (AP), craniocaudal (CC) and transverse (TW) length of each lobe were measured. The obtained result was then multiplied by a correction factor (0.52).

Prostate ellipsoid formula:

(Anteroposterior Length x Transverse Length x Craniocaudal Length x 0.52).

2.4 Statistical Analysis

Samples were taken through non-probability convenience sampling. Sample size 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

Data was analyzed on SPSS version 20. 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. Post hoc- LSD Fishers test was applied for pair wise comparison of between group means. Univariate analysis was applied to test the linearity of relationship among variables. Multiple linear regression was applied to determine the linear effect between the prostate volume and anthropometric parameters. P-value < 0.05 was considered significant.

3. RESULTS

3.1 Characteristics of Subjects

Mean age of subjects in this study was 52 ±9.17 years. The minimum and maximum age in our study was 40 and 79 years.

Table 1. Descriptive stats for total participants

	Total participants N= 119 mean, standard deviation
Age	52±9
Height (cm)	169±11
Weight (kg)	80±23
BMI (kg/m ²)	28±6
WC (cm)	95±10
PV (ml)	21.7±2.2

Age groups was categorized into group 1,2,3,4 i.e (40-<50), (50-<60), (60-<70), (70-<80) with 49, 37, 19 and 14 subjects respectively (Table 2).

Post hoc comparison using the Fisher LSD test (Table 3) revealed significant mean difference of prostate volume within different age groups, but could not find significant difference of PV between individuals of 50-<60 years and 60-<70 years, 60-<70 and 70-<80 years age groups.

Table 2. Prostate volume in different age groups

Age group (years)	1 (40-<50)	2 (50-<60)	3(60-<70)	4(70-<80)	Total	P-value
	N=49	N=37	N=19	N=14	N=119	
Prostate volume (mls)	20.5±2.1	22±2.2	22.9±1.7	23.3±0.8	21.7± 2	0.032

p-value <0.05 considered significant

The BMI distribution of the subjects was as follows: 47, 38 and 34 in the healthy, overweight and obese groups respectively. Mean BMI in this study was 28.2± 6.2 kg/m² as shown in (Table 4).

The mean prostate volume of 119 individuals was 21.7 mls±2.2. The maximum and minimum values were 12 mls to 25.5 mls. PV was largest in the obese groups. There were significant differences in PV among various BMI groups (p = .046) Table 4.

On applying LSD Fishers test, it can be seen that all differences among mean prostate volume are found significant (Table 5).

The WC distribution was as follows: Subjects were 34 and 85 in <90 cm and >90 cm groups respectively. Mean WC in this study was 94 cm. PV was found highest in >90 cm groups. There was significant difference in PV among two groups (p = 0.03) as shown in Table 6.

3.2 Associations between PV, Age, BMI, WC

We examined the relationships between PV and Age, BMI, WC. By univariate analysis, PV correlated positively with obesity related parameters. PV correlated positively with age (p=0.032), positively with BMI groups (p=0.046) and positively with WC groups (p=0.003). The correlation coefficients were r = 0.471, r = 0.505, r = 0.604 respectively. However, when we applied multiple linear regressions, WC is the only significant factor in predicting PV as shown in (Table 8).

4. DISCUSSION

In this study 40-79 year old Pakistani men from a generally healthy population with no known prostatic pathology were recruited in order to determine the local reference range of PV. Many countries are now determining reference range of prostate gland volume [9] since it is influenced by a number of factors such as age, body mass index (BMI), waist circumference (WC) and ethnicity.

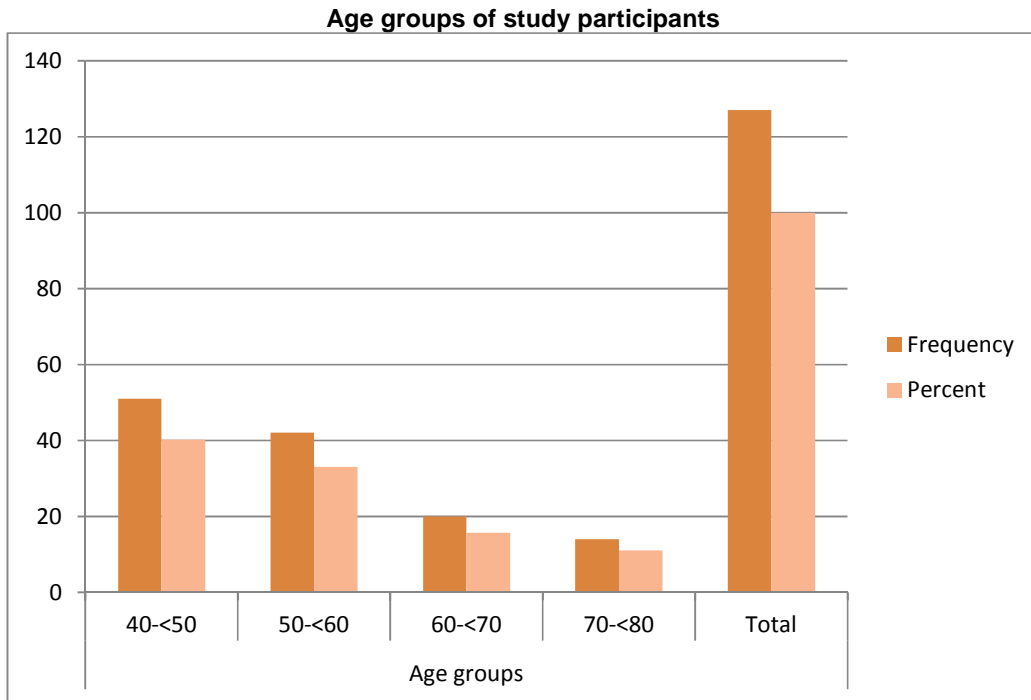


Fig. 1. Depicts frequency of study participants in age groups

Table 3. Correlation of prostate volume within different age groups

Multiple comparisons						
Dependent variable: Prostate volume LSD (Fishers Post Hoc)						
(I) agegp	(J) agegp	Mean difference (I-J)	Std. error	Sig.	95% Confidence interval	
					Lower bound	Upper bound
40-<50	50-<60	-1.54067*	.42726	.000	-2.3864	-.6949
	60-<70	-2.54686*	.54099	.000	-3.6177	-1.4760
	70-<80	-2.82829*	.61868	.000	-4.0529	-1.6037
	Total					
50-<60	40-<50	1.54067*	.42726	.000	.6949	2.3864
	60-<70	-1.00619	.55707	.073	-2.1089	.0965
	70-<80	-1.28762*	.63279	.044	-2.5402	-.0350
60-<70	40-<50	2.54686*	.54099	.000	1.4760	3.6177
	50-<60	1.00619	.55707	.073	-.0965	2.1089
	70-<80	-.28143	.71452	.694	-1.6958	1.1329
70-<80	40-<50	2.82829*	.61868	.000	1.6037	4.0529
	50-<60	1.28762*	.63279	.044	.0350	2.5402
	60-<70	.28143	.71452	.694	-1.1329	1.6958

*. The mean difference is significant at the 0.05 level

Table 4. Prostate volume in BMI groups

BMI groups	Normal weight	Over weight	Obese	Total	P-value
Total	N=47	N=38	N=34	N=119	
Prostate volume (mls)	20.4±2	22.1±1	23±1.7	21.7±2	0.046

P-value <0.05 considered significant

Table 5. Correlation of prostate volume within different BMI groups

Multiple comparisons						
Dependent variable: Prostate volume LSD (Fisher's Post Hoc)						
(I) BMIgp	(J) BMIgp	Mean difference (I-J)	Std. error	Sig.	95% Confidence interval	
					Lower bound	Upper bound
Healthy	overwt	-1.72739 [*]	.42790	.000	-2.5743	-.8805
	Obese	-2.80134 [*]	.42477	.000	-3.6421	-1.9606
Overwt	healthy	1.72739 [*]	.42790	.000	.8805	2.5743
	Obese	-1.07395 [*]	.45321	.019	-1.9710	-.1769
Obese	healthy	2.80134 [*]	.42477	.000	1.9606	3.6421
	overwt	1.07395 [*]	.45321	.019	.1769	1.9710

*. The mean difference is significant at the 0.05 level

Table 6. Prostate volume in WC groups

WC groups	<90 cm	>90 cm	Total	P-value
Total	N=34	N=85	N=119	
Prostate volume (mls)	19.6±2	22.5±1	21.7±2	0.03

p-value <0.05 considered significant

Table 7. Univariate analysis of prostate volume with anthropometric measurements

Age	R	0.471	p-value	0.032
BMI	R	0.505	p-value	0.046
WC	R	0.604	p-value	0.003

r : Correlation coefficient ,p-value < 0.05 is significant

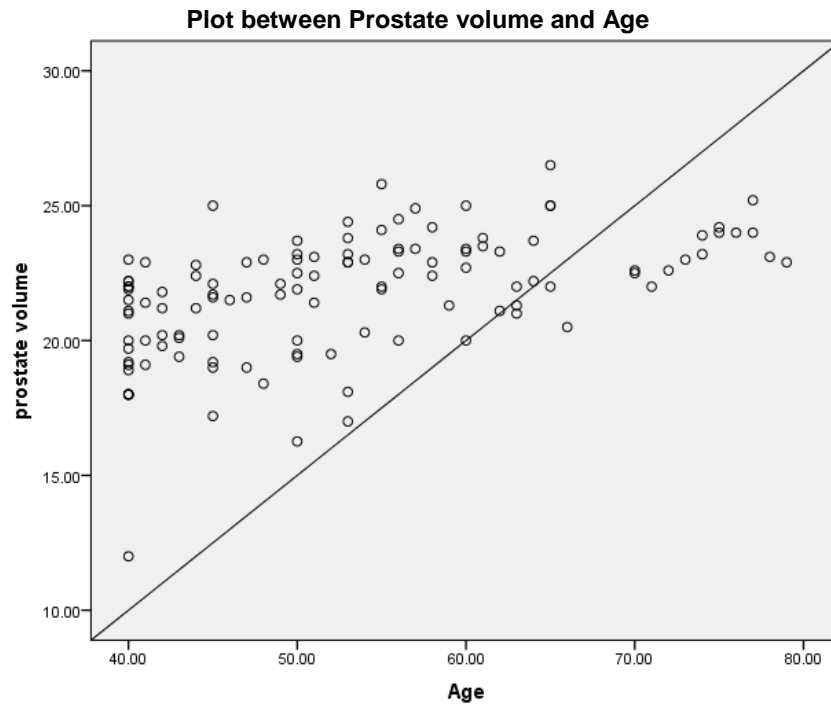


Fig. 2. Graphically represents the significant positive correlation between age and prostate volume

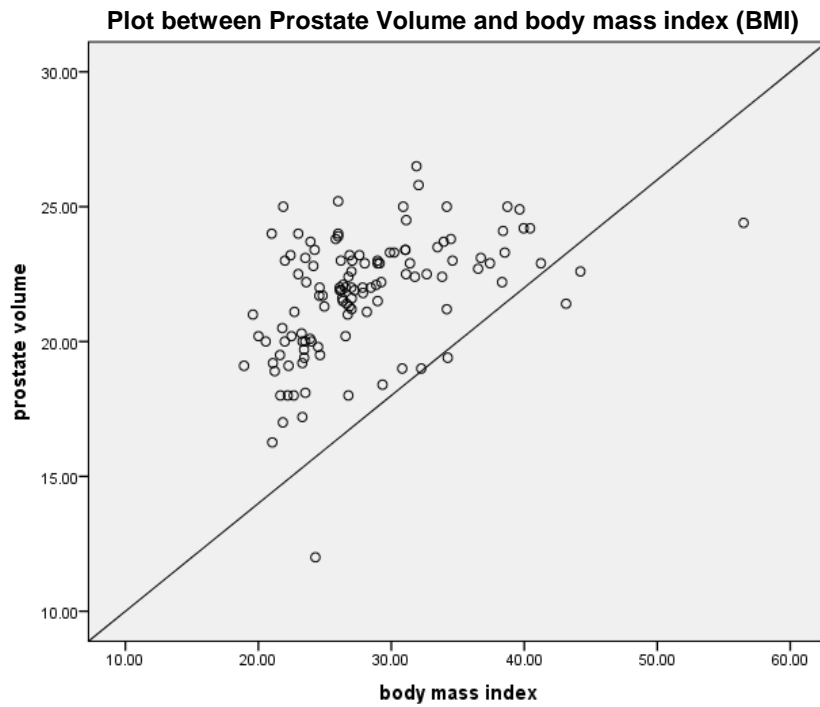


Fig. 3. Graphically represents significant positive correlation between prostate volume and body mass index (BMI)

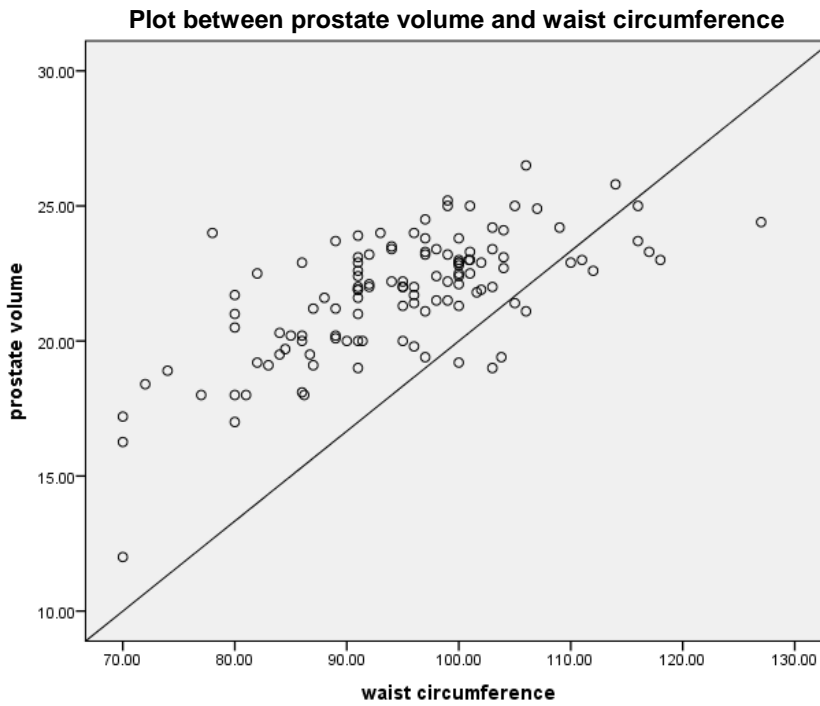


Fig. 4. Graphically represent significant positive correlation between prostate volume and waist circumference

Table 8. Multiple linear regression applied to determine independent predictors of PV

Variables coefficient	Coefficient	p-value	VIF
Age	0.346	0.0001	1.055
BMI	0.247	0.001	1.32
WC	0.404	0.0001	1.366

PV: prostate volume, BMI: body mass index, WC: waist circumference, VIF: Variation inflation factor

A review of the literature shows that mean PV is highest in the US [24], lower in Australia [25] and even more lower in China [12]. In Bangladesh [21] it is lowest. The mean prostate gland volume of Pakistani men in our study are lower than those found in the above four countries.

The available data in the literature suggests several possible reasons for the low PV in our study population. Laven et al. [26] in a study of Swedish men found that low birth weight was associated with increased risk of high PV, and our study could not document the birth weight of our subjects because of lack of demographic data. It is pertinent to add that no study exists in our country which documents PV in the different ethnic populations of Pakistan. Therefore, our study might have been affected by selection bias due to our heterogenous study population. The literature also reports that migration [27] affects PV and our study population included migrants.

Our study has demonstrated that PV increases with age. Mean PV found in our study were 20.5 mls, 22 mls, 22.9 mls, 23.3 mls in age groups 1, 2, 3, 4 respectively (Table 2). The difference in PV among age groups was significant ($p < 0.05$). Sung Jin Yim et al. [28] also found positive correlation with age. A study done by H.A. Mosli et al. [29] in 2010 also showed positive correlation of PV with age. However, C.S Agarwal et al. [30] in 2010 found no correlation of prostate volume with age. The largest mean PV reported in this study is in age group 4 (70-79) yrs (23.3±9 ml). The reason for highest PV in this age group is because it is proven that as men age, prostate volume continues to increase. Dmochowski et al. [31] while reviewing bladder neck obstruction found out that despite decreasing levels of testosterone, there are increasing levels of dihydrotestosterone (DHT) with age, (DHT) a metabolite of testosterone, converted through 5 α -reductase and androgen receptors remain high. Type 2 5 α -reductase is a critical mediator of hyperplastic prostatic growth in later age. Besides this enzyme growth factors like Insulin like growth factor TGF- β also play important role in proliferation of prostatic stroma.

Despite, high prevalence of BPH in aged men, pathogenesis of benign prostate hyperplasia is not well understood. Aging, androgens, estrogens, growth factors, inflammation and some modifiable risk factors including obesity have been reported to play an important role in the etiology of BPH. Which of these factors were affecting our study population could not be ascertained and may account for finding insignificant mean difference of prostate volume between age groups 50-<60 yrs and 60-<70 yrs, 60-<70 yrs and 70-<80 yrs (Table 3). In our study, we used the ellipsoid method of ultrasound instead of more accurate planimetric method. Therefore, variations of PV in the men of our study could be due to observer error.

This study has introduced new concepts in evaluation of prostatic volume with respect to anthropometric parameters namely body mass index and waist circumference. The implications of its results can be applied in clinical evaluation of patients. Total prostate gland volume significantly and positively correlates with age, BMI and WC.

Many studies have suggested that BMI is one of the strongest determinants for prostate gland volume. Our study found positive association of PV with BMI ($r = 0.505$). The results of our study are in accordance with those of Monawara M et al. [21] in 2012 who found significant relationship of prostate volume with BMI. Mean PV in this study found to be highest in obese groups (23.1±1.7 mls). However, Jin Ho Park et al. [32] in 2009 also concluded that as BMI increases prostate volume also increases and PV in obese groups was found out to be the greatest. Lee et al. and Xie et al. [15,19] reported that prostatic volume was greater in obese than normal subjects. This study confirmed positive correlation with BMI & WC. However, when we applied multiple linear regression WC was the only factor related to prostatic hyperplasia.

Thus, the strongest correlation found in our study was between prostate gland volume and waist circumference as shown in Table 8. Our results are in accordance with a study done in Korea

conducted by Lee et al. [13] in 2012 which showed positive correlation of PV with BMI & WC and found out that WC was an independent risk factor of BPH. The Baltimore Longitudinal Study of Aging revealed those with a greater WC had an increased likelihood of BPH [33]. Studies have shown that men with larger WC tend to have more BPH surgeries and LUTS than men with normal WC [34]. Rohrmann et al. [35] found out men with larger waist circumference (>102 cm) were more likely to have LUTS. This is the first demographic study done in Pakistan to provide evidence that WC or central obesity correlated significantly with PV. It also showed that men with waist circumference of >90 cm have higher prostate volume than men with waist circumference of <90 cm (Table 6). Our results are in concordance with those of a study, conducted on 602 patients (>40 yrs) by Lee et al. [36] found out that men with waist circumference of >90 cm experienced increasing storage symptoms. Central obesity and lack of physical exercise were placed among the top risk factors for the development of BPH [37].

Several pathophysiologies could explain increase in PV due to central obesity. Abdominal obesity is known to be associated with a number of cardiovascular [38] and hormonal responses including an increase in renal venous pressure as well as increased renin and aldosterone levels.

Cohen hypothesized that chronic venous congestion in obese men, exposes the prostate to increased testosterone levels and also increased oxidative stress both of which causes increased cellular activity of stromal and epithelial cells of the prostate [39].

Another suggested pathophysiology which explains the health risks of increased WC is hyperinsulinemia [40-42] caused by tissue insulin resistance in obesity which stimulates autonomic nervous system, particularly the sympathetic nervous system [43]. Increased sympathetic activity [44] causes bladder outlet obstruction (LUTS) and changes in prostate vascularity, as alpha receptors are present in bladder neck, blood vessels and prostatic capsule [45]. Also due to overactivity of the sympathetic nervous system, systemic adrenaline acting via α_1 -adrenoreceptors promotes stromal prostatic growth exacerbating the dynamic outflow resistance in the lower urinary tract. It is also possible that hyperinsulinemia acts directly on the prostate. Insulin has similar structure to

IGF-1 and thus binds to the IGF receptor in the prostate resulting in stimulatory effect on prostate growth [45].

Other reason could be that as abdominal fat accumulates, this adipose tissue acts as an endocrine organ which secretes a number of hormones such as resistin and leptin whose effects on PV requires further research. Central fat depot having increased adipose tissue also accelerates aromatization of circulating testosterone into estrogens, increasing E:T ratio [46] and thus may influence PV.

5. CONCLUSION

Mean prostate gland volume in our studied population was smaller than developed and underdeveloped countries. It is concluded that PV has a strong linear relationship with age. There is also a significant correlation with BMI and WC, when the effects of obesity related metabolic diseases were excluded.

It is concluded that WC >90 cm is an independent risk factor for prostatic growth. Central obesity is the most important factor influencing prostate gland volume. Anthropometric data like age, BMI and WC can therefore be used to predict PV prior to ultrasonography.

ETHICAL APPROVAL

Ethical approval was from Ethical Review Committee of Ziauddin University, Karachi, Pakistan.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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