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The Relationship Between Prostatic Volume And Serum Estrogen In Obese Versus Non Obese Males With Benign Prostatic Hyperplasia

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Abstract: Background: Old age, obesity and androgens are more vulnerable to prostatic disorders. Benign Prostatic Hyperplasia (BPH) is a common problem for adults. **Objectives:** To determine the morphological changes of prostate gland and effects of Estrogen levels in obese versus non-obese males with BPH. **Methods:** A cross sectional study was conducted on sixty patients in an emergency clinic of Dr. Ruth Pfau, Dow university of Health Sciences, Karachi from 17th May 2019 to 15th February 2020(IRB-1182/DUHS/approval/2019). All selected patients have BPH and assessed by Global prostate side effect score >7. Patients with BPH were divided into two groups obese and non-obese, as indicated by Body Mass Index (BMI) and waist circumference (WC). Group A (obese) had BMI ≥ 25; WC ≥ 90cm and group B (non-obese) had BMI < 25; WC < 90cm. Trans rectal ultrasound and estimation of serum Estrogen was performed to analyzed the length, width, diameter and volume of prostate. **Results:** The mean prostate volume was higher in the obese group 36.13±3.673ml while in non-obese group it was 31.21±6.771 ml, which was found to be statistically significant (p = 0.001). The mean Estrogen levels in obese group were 328.21±115.05pmol/l, while in non-obese group it was 309.72±73.62pmol/l (p=0.462). Significant positive correlation was observed (r = 0.279, p-=0.031) between prostate volume and serum Estrogen levels in study participants. **Conclusion:** Obesity and serum Estrogen levels had significant effect on the prostate volume as compared to non-obese participants within same age group which showed significant moderate positive correlation with prostate volume in obesity.

Keywords: Benign Prostatic Hyperplasia, Obesity, Trans-rectal ultrasonography, Body mass index, Waist circumference, Serum Estrogen

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Introduction

Benign prostatic hyperplasia, prostatitis and carcinoma of prostate are the frequently occurring diseases in males due to prostate gland [1] . The changes in prostatic volume (PV) are common throughout in the man's life [2]. Recently, in a longitudinal study the total volume of prostate is observed to be increased 3.5% per year in transition zone. Prostate volume (PV) measurement has great importance for the assessment of future enlargement in many clinical settings [2]. It has been observed that men had less than 30ml of prostatic volume, showed 1.7% growth in median

prostate per year; nevertheless, those have more than 30ml of PV presented median prostate growth of 2.2% per year [2]. A majority of voiding problems in the elderly men are due to BPH [3]. It is a non-malignant growth of the prostate. It has been considered the fourth most common sickness in men matured over 50 years [4]. Its frequency is about 40% in men aged 50-years or above and about 90% in men aged 80-years or above [5]. Individuals suffering from BPH do not require any type of treatment unless they become symptomatic. Long term complications of BPH include urinary tract infections (UTI), inflammation of bladder (cystitis), and rarely renal failure [6]. The patients who have familial BPH have a risk of developing the disease earlier [7].

Recent research suggest that systemic metabolic disturbances especially obesity may contribute significantly in the pathogenesis of BPH [8]. Further, genetic, metabolic, neuroendocrine, psychological, and environmental factors contribute in the development of obesity [9].

PV has a strong direct association with age as well [10]. Estrogen levels in men with central obesity have higher tendency to effect on prostate volume. It is essential for modulating libido, erectile function and spermatogenesis. Latest advances has revealed that extreme estrogenization during prostatic growth may cause the high frequency of BPH in the maturing male populace [13]. The goal of the current study is to find out the role of obesity on prostatic volume compared to non-obese men of same age group and to find out the effects of Estrogen on prostatic enlargement.

Material and Methods

A cross sectional study was conducted in an emergency clinic of Sindh territory, Dr. Ruth Pfau, and Dow university of health sciences (DUHS), Karachi during 17th May 2019 to 15th February 2020 after approval from Institutional review board of DUHS (IRB-1182/DUHS/approval/2019). All experiments were conducted according to the ethical standards for human experimentation established in the Declaration of Helsinki **Considering the statistics of 5% margin of error and 95% confidence interval sample size was estimated by Open Epi** (www.openepi.com)**, version 3 online calculator [by taking mean values for non-obese and obese 35.59 ± 2.94 and 49.23 ± 3.18 (S.D) 95% CI].** Formula: n = [DEFF*Np (1-p)]/ [($d^2/Z^2_{1-\alpha/2}$*(N-1) +p*(1-p)]. Total 60 patients were enrolled and consented to take part in current study. All selected patients had BPH, which was assessed by global prostate side effect score (IPSS) more than 7, matured between 50 to 80 years were included for the study. The patients with known prostatic malignancy or recently diagnosed for any pelvic pathologies, prostatic medical procedure, kidney or bladder abnormalities and relationship of any mental problems were excluded from the study.

An examination proforma was generated based on segment qualities, clinical, past, family history and way of life issues. Anthropometric estimations especially BMI and gauge routine examinations were recorded. The research helped to indicate the changes in the morphological structure of Prostate gland, measured by trans-rectal ultrasonography (TRUS) using Ultrasound machine named (Type Doppler machine and Toshiba company model Nemio XG) for measuring the size and volume of prostate. The width was estimated between the internal piece of the container, the range from the bladder neck to the unmistakable sub-par limit and the length from the internal of the case to the reasonable furthest reaches of the change zone at the verumontanum [14]. The temporary zone was examined in cross over and sagittal planes with the subject in the left sidelong decubitus position by ellipsoid formula (height × length × width $\pi/6$) [15]. All participants had undergone blood tests for investigating Estrogen levels in Dow University of Health Sciences laboratory, Sadder area, Karachi according to laboratory protocols. Normal levels of Estrogen ranges: 99.40-196 pmole/l. For Estrogen estimation five ml of blood was drawn from antecubital vein by applying antiseptic measures into EDTA containing vacutainer tubes (BD.UK). Serum separated by centrifugation of blood at 3000 rpm for 10 minutes within one hour after collection and stored in Eppendorf tubes. Each tube was labeled with patient's identification number and was immediately stored at -86^{o}C until further analysis.

Statistical Analysis:

Data was analyzed using (SPSS) adaptation 21.0. The mean, standard deviations, frequency and proportions were calculated for baseline characteristics of participants. Normality was assessed using Shapiro-Wilk test, data was not assumed as normally distributed. Kruskal Wallis and Mann-Whitney test were used to associate the means differences between these groups. To assess the associations between all exposure variables with obesity, the Chi-square test was performed. Furthermore, Pearson Correlation analysis was completed to know the relationship between prostate volume and. The p-value less than 0.05 were considered significant. All results were presented in tables, diagrams and disperse plot.

Results

In our study population, 60 patients were involved in the study. The mean age range 65 ± 9.98 years (range 50-80 years.). Members were enlisted on the basis of International Prostate Side effect Score (IPSS) score > 7 with BPH. The study population was distributed into two groups, obese and non-obese, each comprising of 30 individuals. Age was classified into groups 1, 2, 3 i.e. (50-60), (61-70) and (71-80) years. The age distribution of study participants is shown in Figure **1**, majority of 23 participants (38.3%) were ranged between 71-80 years, while 18 (30%) participants were between 61-70 years and 19 (31.7%) participants were between 50-60 years.

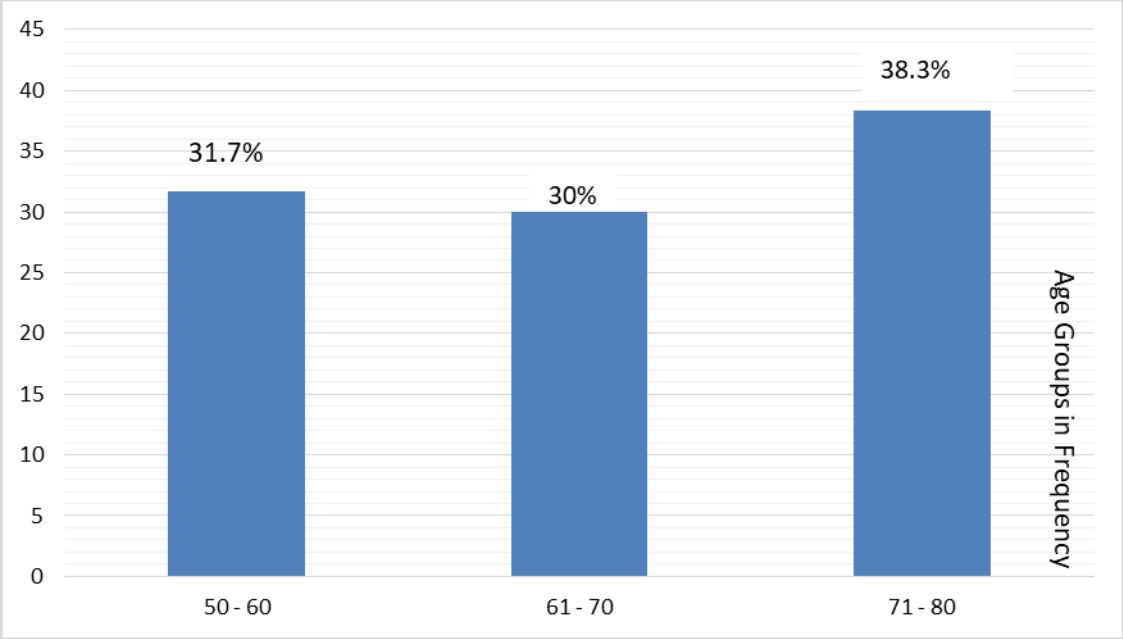

Figure 1: Age distribution of study participants (n=60)

The mean prostate volume found in obese group was 36.13±3.673 ml, while in non-obese group was 31.21±6.771 ml (p = 0.001) shown in Figure 2. While the mean Estrogen levels found in obese group was 328.21±115.05pmol/l while in non-obese group was 309.72±73.62pmol/l, showing an insignificant difference (p = 0.462) mentioned in Table **1**

The descriptive characteristics of 60 study participants on the basis of PV and Estrogen levels are shown in Table 2. Out of 60, 47 participants were classified as having PV ≥ 30 ml with a high percentage of 78.3%, while 13 men were classified as PV < 30ml with a percentage of 21.7. Serum Estrogen levels were found to be ≥ 192 in 52 participants (86.7%) while 8 participants (13.3%) had < 192. The characteristics of study participants stratified according to Obesity are shown in Table **2**. When obese group was compared with non- obese group in different age group

study participants, the maximum difference was obtained in 61-70-year-old age group, and the finding was statistically significant (p-value=0.044). Similarly, when obese group was compared with non- obese group in participants with different PV **(**< 30 ml and ≥ 30 ml), the maximum difference was obtained in group with PV≥ 30 ml and the finding was statistically significant (p-value=0.005). Similarly, when obese group was compared with non- obese group in participants with different Estrogen levels, the difference was obtained in group with Estrogen level ≥ 192, but it was insignificant (p-value=0.353).

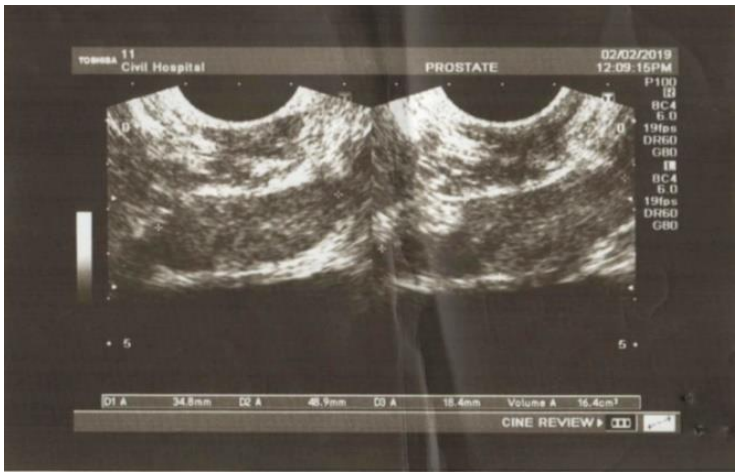

Figure 2: Trans rectal ultrasonographic illustration of prostate gland ≥30ml volume in non-obese man.

Table 1: Study participants according to mean prostate volume and mean estrogen levels in obese versus non-obese

		Non obese	**Obese**	**p-value**	
Prostate Volume	mean ± SD	31.21 ± 6.771	36.13±3.673	0.001	Significant
Serum Estrogen Levels	mean ± SD	309.72 ±73.62	328.21±115.05	0.462	

p-value calculated by Mann-Whitney test and <0.05 was considered statistically significant.

Table 2: Characteristics of study participants stratified according to obesity (n=60)

Characteristics	**Percentage Distribution of Participants**	**Obesity**		**p-value***	
		Non-obese	**Obese**		
Age in groups		**n (%)**	**n (%)**		
50 – 60 years		14(73.7)	5(26.3)		
61 – 70 years		7(38.9)	11(61.1)	0.044	Significant
71 – 80 years		9(39.1)	14(60.9)		
Prostate Volume					
< 30 ml	13 (21.7%)	11(37.5)	2(15.4)		
≥ 30 ml	47 (78.3%)	19(40.4)	28(59.6)	0.005	Significant
Estrogen levels					
< 192 pmole/l	8 (13.3%)	3(37.5)	5(62.5)		
≥192 pmole/l	52 (86.7%)	27(51.9)	25(25)	0.353	

Table 2: *p-value calculated using Chi-square analysis

Discussion

Age is a very important contributory factor in prostatic volume, for every one year, there is 4% increase in prostate size. The prostate gland grows at different rates in different age groups. The underlying morphological changes in prostate gland as a result of advancing age and the developmental rate was determined to be 0.81 % per year relating to 0.2 ml/year.

The age categorization of study participants in current study (figure 1) is from 50 to 80 years. The maximum number of study participants being observed in their seventh decade (38.3%). It is well established that there is a specific link of prostatic growth with advanced age [16]. Advanced age causes urological problems, which can affect the quality of life significantly[16].

Study participants were recruited on the basis of IPSS scores greater than 7, so a volume greater than 30 is vulnerable according to their enlargement. The highest prostate volume observed in our study is 42ml. In contrast, a research conducted in Pakistan by Raza et al. [17] on 103 BPH cases, out of which 80 participants had PV lower than 50ml while 23 participants had PV greater than 50ml. Approximately 90ml was the maximum PV in their study [1]. Furthermore, another review noticed 65.6% of the patients had a PV between 25 to 50ml and 35% of participants had PV more than 50ml and by Babian et al. 18 close by. Accumulative evidences revealed the PV between 20 to 50ml in large number of patients [19] Similarly, in an Indian research 79% of patients had PV between 25 to 50ml [20].

In the current study the mean PV of obese participants is 36.13ml while in non-obese group is 31.21ml (table1). Contradictory to our findings a research conducted on Korean population demonstrated that the mean PV were 18.8ml and 21.8ml in non- obese and obese participants respectively on 146 men over the age of 40 years [21]. Another study stated the similar effects regarding high levels of prostate volume in obese than non-obese which are according to our finding [14]

A research observed the relationship of 103 obese participants with PV. Hence, reported that mean PV was 36ml in non-obese and 54ml in obese males [1]. Positive association between obesity and PV was also observed by other study showing the linear relationship between the two variables [22, 23]. Our results are in consistent with the study mentioned. It could be due to the fat deposition which causes the adipose tissue to accelerate the aromatization of circulating Testosterone into Estrogen which influence the PV [24].

Current study Table **2** compared obese with non-obese participants on the basis of age, PV and estrogen levels and observed significant findings in age group 61-70 years and PV ≥ 30ml and low significant difference in serum Estrogen levels (≥192pmole/l). The most probable cause of significance in obese participants was lack of exercise, sedentary life styles, improper diet and smoking, which contributed a lot to prostate enlargement ≥ 30ml, in age group 51 – 60 years and estrogen level ≥ 192 pmole/l as per our findings. In contrast to current research the previous studies have reported prostatic enlargement at higher age groups of 80 years or more in 44.0% participants with significant difference among obese and non-obese groups [25]. Similarly the higher PV had been observed in obese participants in more advanced age groups [26, 27]. Our findings of serum Estrogen levels are in agreement with latest study conducted in 2022 which reported that the adipose tissue of both male and female obese individuals is characterized by higher estrogen receptors as compared to non-obese subjects [28]

Previous studies reported that the risk factors contributed in the pathogenesis of the prostate gland are advanced age, obesity and androgen levels [29, 30]. In the present study Table **2.** Estrogen levels were high in obese persons with advance age. Similar to our findings, Estrogen estimation in obese males with advancing age were also observed with increased Estrogen levels in men aged 70 years and above [31]. An interesting research performed on candidates matured 20-29 years had expressively more noteworthy estradiol levels contrasted and more established members [32]. An inverse correlation between age and the estradiol levels were observed [33].

There are many mechanisms that have been postulated by which obesity exacerbates BPH. A recent study contradict our findings conducted in Charlotte Maxeke Johannesburg academic hospital (CMJAH) showed there is no correlation between body mass index and prostatic volume [34].

Conclusions

Obesity had significant effect on PV in BPH as compared to the non-obese group within the same age range and serum levels of Estrogen, which showed significant moderate positive correlation with prostate volume in obesity. The connections between proportions of BPH and endocrine varieties in maturing men merit further assessment in a longitudinal report.

Limitations

We were unable to contrast PV estimated by TRUS. Factors were noticed only at a single time point. The best way to observe its growth, a longitudinal study would be performed in order to obtain exact growth rate. The small sample size and absence of testosterone related data are also the limitation of study

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No animals were used in this study. The study on humans was conducted in accordance with the ethical rules of the Helsinki Declaration and Good Clinical Practice.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

None.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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REFERENCES

1. Williams NS, Bulstrode CJ, O'connell PR. Bailey & Love's short practice of surgery: Crc Press; 2008
2. Raza I, Hassan N, Gul P, Jafri A, Zehra N, Younas N. Determination of prostate gland volume by ultrasonography and its correlation with anthropometric measurements in a subset of karachi population. J. adv. med. 2016: 1-12.
3. Chute C, Panser L, Girman C, Oesterling J, Guess H, Jacobsen S, et al. The prevalence of prostatism: a population-based survey of urinary symptoms. J Urol 1993; 150(1): 85-9.
4. Issa MM, Regan TS. Medical therapy for benign prostatic hyperplasia--present and future impact. AJMC 2007; 13: S4-9.

5. Lee G, Shin J, Choi H, Jo A, Pan S, Bae D, et al. Cynanchum wilfordii ameliorates testosterone-induced benign prostatic hyperplasia by regulating 5α-reductase and androgen receptor activities in a rat model. Nutrients 2017; 9(10): 1070.
6. Roehrborn CG, McConnell JD, Lieber M, Kaplan S, Geller J, Malek GH, et al. Serum prostate-specific antigen concentration is a powerful predictor of acute urinary retention and need for surgery in men with clinical benign prostatic hyperplasia. Eur Urol 1999; 53(3): 473-80.
7. Lee C-L, Kuo H-C. Pathophysiology of benign prostate enlargement and lower urinary tract symptoms: Current concepts. Tzu Chi Med. J 2017; 29(2): 79.
8. Xie L-P, Bai Y, Zhang X-Z, Zheng X-Y, Yao K-S, Xu L, et al. Obesity and benign prostatic enlargement: a large observational study in China. Eur Urol 2007; 69(4): 680-4.
9. Fujita K, Hayashi T, Matsushita M, Uemura M, Nonomura N. Obesity, inflammation, and prostate cancer. J Clin Med Res 2019; 8(2): 201.
10. Gómez-Ambrosi J, Silva C, Galofré J, Escalada J, Santos S, Millán D, et al. Body mass index classification misses subjects with increased cardiometabolic risk factors related to elevated adiposity. Int J Obes 2012; 36(2): 286-94.
11. Kim GW, Doo SW, Yang WJ, Song YS. Effects of obesity on prostate volume and lower urinary tract symptoms in Korean men. KJ Urol 2010; 51(5): 344-7.
12. Lee S, Min HG, Choi SH, Kim YJ, Oh SW, Kim YJ, et al. Central obesity as a risk factor for prostatic hyperplasia. Int J Obes 2006; 14(1): 172-9.
13. Ajayi A, Abraham K. Understanding the role of estrogen in the development of benign prostatic hyperplasia. Afr J Urol 2018; 24(2): 93-7.
14 Milonas D, Matjošaitis A, Jievaltas M. Transition zone volume measurement–is it useful before surgery for benign prostatic hyperplasia? Rev Inst Med 2007; 43(10): 792.
15 Tirabassi G, Cignarelli A, Perrini S, Furlani G, Gallo M, Pallotti F, et al. Influence of CAG repeat polymorphism on the targets of testosterone action. Int. J. Endocrinol 2015; 2015.
16 Jakobsen H, Torp-Pedersen S, Juul N. Ultrasonic evaluation of age-related human prostatic growth and development of benign prostatic hyperplasia. Scand J Urol Nephrol 1988; 107: 26-31.
17 Raza I, Hassan N, Gul P, Jafri A, Zehra N, Younas N. Determination of Prostate Gland Volume by Ultrasonography and Its Correlation with Anthropometric Measurements in a Subset of Karachi Population. J. adv. med 2016: 1-12.
18 Ochiai A, Fritsche HA, Babaian RJ. Influence of anthropometric measurements, age, and prostate volume on prostate-specific antigen levels in men with a low risk of prostate cancer. Eur Urol 2005; 66(4): 819-23.
19 Collins G, Lee R, McKelvie G, Rogers A, Hehir M. Relationship between prostate specific antigen, prostate volume and age in the benign prostate. Br J Urol 1993; 71(4): 445-50.
20 Fowke J, Motley S, Cookson M, Concepcion R, Chang S, Wills M, et al. The association between body size, prostate volume and prostate-specific antigen. Prostate Cancer Prostatic Dis 2007; 10(2): 137-42.
21 Lee RK, Chung D, Chughtai B, Te AE, Kaplan SA. Central obesity as measured by waist circumference is predictive of severity of lower urinary tract symptoms. BJU Int 2012; 110(4): 540-5.
22 Park J-H, Cho B-L, Kwon H-T, Lee C-M, Han H-J. Effect of body mass index and waist circumference on prostate specific antigen and prostate volume in a generally healthy Korean population. J Urol 2009; 182(1): 106-11.
23 Wallner LP, Morgenstern H, McGree ME, Jacobson DJ, Sauver JLS, Jacobsen SJ, et al. The effects of body mass index on changes in prostate-specific antigen levels and prostate volume over 15 years of follow-up: implications for prostate cancer detection. CEBP 2011; 20(3): 501-8.
24 Wu A, Shi Z, Martin S, Vincent A, Heilbronn L, Wittert G. Age-related changes in estradiol and longitudinal associations with fat mass in men. PloS one 2018; 13(8).

25 Alanazi AB, Alshalan AM, Alanazi OA, Alanazi MS, Alanazi AI, Alanazi AH, et al. Epidemiology of senile prostatic enlargement among elderly men in Arar, Kingdom of Saudi Arabia. Electronic physician 2017; 9(9): 5349.
26 Ng TP, Jin A, Chow KY, Feng L, Nyunt MSZ, Yap KB. Age-dependent relationships between body mass index and mortality: Singapore longitudinal ageing study. PLoS One 2017; 12(7).
27 Canning KL, Brown RE, Jamnik VK, Kuk JL. Relationship between obesity and obesity-related morbidities weakens with aging. J. Gerontol. A Biol 2014; 69(1): 87-92.
28 Koźniewski K, Wąsowski M, Jonas MI, Lisik W, Jonas M, Binda A, Jaworski P, Tarnowski W, Noszczyk B, Puzianowska-Kuźnicka M, Kuryłowicz A. Epigenetic Regulation of Estrogen Receptor Genes' Expressions in Adipose Tissue in the Course of Obesity. International Journal of Molecular Sciences 2022 May 26; 23(11): 5989.
29 Zeng Q-S, Xu C-L, Liu Z-Y, Wang H-Q, Yang B, Xu W-D, et al. Relationship between serum sex hormones levels and degree of benign prostate hyperplasia in Chinese aging men. Asian J. Androl 2012; 14(5): 773.
30 Chin K-Y, Soelaiman I-N, Mohamed IN, Ahmad F, Ramli ESM, Aminuddin A, et al. Sex hormones in Malay and Chinese men in Malaysia: are there age and race differences? Clin 2013; 68(2): 159-66.
31 Bjornerem A. Endogenous sex hormones in relation to age, sex, lifestyle factors, and chronic diseases in a general population: the Tromso Study. J Clin Endocrinol Metab 2004; 89: 6039-47.
32 Khvostova E, Otpuschennikov A, Pustylnyak V, Gulyaeva L. Gene expression of androgen metabolising enzymes in benign and malignant prostatic tissues. Horm. Metab. Res 2015; 47(02): 119-24.
33 Orwoll E, Lambert LC, Marshall LM, Phipps K, Blank J, Barrett-Connor E, et al. Testosterone and estradiol among older men.. J Clin Endocrinol Metab 2006; 91(4): 1336-44.
34. Mampa E, Haffejee M, Fru P. The correlation between obesity and prostate volume in patients with benign prostatic hyperplasia at Charlotte Maxeke Johannesburg Academic Hospital. African Journal of Urology 2021 Dec; 27: 1-6.