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PJBS

ISSN 1028-8880

**Pakistan
Journal of Biological Sciences**

ANSI*net*

Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan



Research Article

Impact of Prostate Specific Antigen and Testosterone Hormone Levels in Patients of Benign Prostatic Hyperplasia in Khartoum State-Sudan

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Abstract

Background and Objective: Lower Urinary Tract Symptoms (LUTS) and Benign Prostatic Hyperplasia (BPH) are progressive ailments resulting from androgenic imbalances and aging that can lead to serious long term complications. Objective of this study was to determine the relationship between prostate-specific antigens and testosterone hormone levels in patients with BPH before transurethral surgery. **Materials and Methods:** This case control study was done on 112 serum samples collected from two secondary care centres in Khartoum, Sudan. Collected serum samples were analyzed by ELISA and fluorescence enzymes immunoassay to measure testosterone, total PSA level and free PSA levels, respectively. **Results:** Out of 112 patients, 56 BPH diagnosed patients were included in the study with mean age 67.10 ± 7.90 years. Total PSA (T. PSA) levels were higher in patients (14.1 ± 10.6 ng mL⁻¹) than the control group (2.21 ± 1.01 ng mL⁻¹). Total 52% of patients had total PSA level in the gray zone ($4-10$ ng mL⁻¹) and 33% had total PSA more than 10 ng mL⁻¹. Testosterone levels were low in patients 3.97 ± 2.84 ng mL⁻¹ when compared to the control group 4.95 ± 0.59 ng mL⁻¹. **Conclusion:** The present study revealed that, there was a strong association between T. PSA level and testosterone hormone in BPH patients, which suggested that monitoring of testosterone level is useful in patients with prostate enlargement.

Key words: Prostate-specific antigen, benign prostatic hyperplasia, testosterone, hypogonadism, transurethral surgery

Citation: Ayman A.M. Alameen, Thawiba A.M. Osman, Shawgi A. Elissidig and Muhammad Atif, 2020. Impact of prostate specific antigen and testosterone hormone levels in patients of benign prostatic hyperplasia in Khartoum State-Sudan. Pak. J. Biol. Sci., 23: 1431-1435.

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Benign Prostatic Hyperplasia (BPH) is a common disease, with progressive increase in its incidence¹. It affects men above the age of 50 years with incidence as high as 80% in men between 70-80 years having BPH-associated Lower Urinary Tract Symptoms (LUTS)². LUTS is a clinical demonstration of BPH comprising of irritative (frequency, urgency and nocturia) and obstructive sign and symptoms (difficulty in passing urination, weak and interrupted urinary stream and incomplete bladder emptying sensation)³.

In healthy male individuals, Prostate Specific Antigen (PSA) is confined to the prostate gland and very little amount is present in the bloodstream. Higher levels of PSA have been found in patients with prostatic diseases and thus, PSA is done to screen, diagnose and monitor patients suffering from prostatic disorders⁴. Estimation of serum PSA is commonly done in the early diagnosis of prostate cancer. However, there is one limitation of PSA testing, which is its low specificity in diagnostic gray zone (4.0-10.0 ng mL⁻¹) in which prostate cancer is present in just 25% of patients. Early-stage prostatic cancer patients have PSA level lower than 10.0 ng mL⁻¹, whereas, patients with advanced disease have PSA levels more than 10.0 ng mL⁻¹. By using these low PSA cutoff values for screening of prostatic cancer have resulted in many unnecessary biopsies⁵. Moreover, concerns pertaining to the influence of testosterone on the prostate gland, especially, any potential role in development of prostate cancer have encouraged further investigations in this regard⁶.

Many researches have demonstrated the relationship between PSA levels and obesity and univariate logistic analysis showed Body Mass Index (BMI) as a predictor of obesity plays a vital role on serum PSA levels. Antichymotrypsin bound PSA is eliminated through the liver. Hence, liver ailments can change serum PSA level⁷.

Androgens perform a key role in the onset and development of both BPH and prostate cancer. Testosterone is the most important androgen found in the blood of men, whereas dihydrotestosterone (DHT), which is its active metabolite, predominantly found in the prostate gland⁷. The BPH related LUTS and hypogonadism are common ailments in old men⁸.

Relationship between PSA levels and testosterone is crucial, especially in patients receiving Testosterone Replacement Therapy (TRT) in addition to those patients who are at increased risk of prostate cancer. Previous studies have established contrary associations between testosterone and PSA showing no association or a positive association⁹. This

difference may be observed because of the reason that association between PSA and testosterone were performed on patients receiving TRT.

This study intended to examine the relationship between free and total prostate specific antigens and testosterone hormone levels in elderly men with benign prostatic enlargement who never been treat by TRT. This relationship can be useful in diagnosis and monitoring the progression of the disease.

MATERIALS AND METHODS

Study area: The study was carried out at Department of Chemical Pathology, Faculty of Medical Laboratory Sciences, University of Khartoum, Sudan from February, 2018-April, 2018.

Ethics statement: Study approval was obtained from Institution Review Board (IRB) of health ethical committee of Department of Chemical Pathology, University of Khartoum. The purpose of the study was clearly explained to volunteers participating in this study by taking informed written consent and they were given the rite to withdraw at any time.

Sample size: This randomized case control study was carried out on 112 old men, out of which 56 subjects were controls and 56 were patients. Sample size was calculated by a standard formula which results in 28 individuals and we took (2n = 56 sample). Samples were collected by simple random selection from Ibn Sina Hospital and Asia Hospital, Khartoum, Sudan, before performing transurethral resection procedure (TURP) for the patient group.

Inclusion and exclusion criteria: All participants who had gone through rectal examination were excluded from this study. A strict selection criterion was used to select patients suffering from LUTS or Acute Urine Retention (AUR) with cauterization. These patients were having no history of liver disease, no malignant prostate enlargement, no TRT, no recent digital rectal examination, with no ketoconazole or diuretic use and abnormal urine analysis. Age matched control subjects were included in the study with no LUTS or AUR.

Blood samples were collected in a plain container, centrifuged and separated serum were stored at -20°C until used for determination of testosterone, total and free PSA.

Analytical techniques: Enzyme-linked immunosorbent assay (ELISA) kits were purchased from Fortress Diagnostics Limited

(United Kingdom). Semi-automatic analyzer BTS 350 plus (Spain) was used for testosterone and total PSA measurements. Free PSA levels were measured with TOSHO AIA-360 fluorescence enzymes immune analyzer. Procedure for all measurements was controlled by control material provided by kits manufacture.

Patients were split into three different groups corresponding to total PSA levels: PSA lower than 4.0 ng mL⁻¹ (group 1), PSA 4.0-10.0 ng mL⁻¹ (group 2) and PSA level higher than 10.0 ng mL⁻¹ (group 3).

Statistical analysis: The SPSS ver.17 was used for statistical analysis. Pearson correlation for the three different groups was done to assess the correlation between total PSA and testosterone levels in addition to age and body mass index. Data was expressed as average and standard deviation between different groups.

RESULTS

Serum samples from patients and controls were analyzed for testosterone, total and free PSA levels by using immunoassay.

Body Mass Index (BMI): A slight increase in BMI was observed in patient's group as compared to the control group with mean BMI level of 25.14±8.03 in patients as compared to the control group (23.35±1.09). Mean age of the patients was 67.10±7.90 and mean age of the control group was 68.05±7.32 (Table 1).

PSA and testosterone: Total PSA was markedly increased with mean value of 14.07±10.59 ng mL⁻¹ in the patient group compared with 2.21±1.01 ng mL⁻¹ in control group. Testosterone levels were low in patients (3.97±2.84 ng mL⁻¹) in comparison with the control group (4.95±0.59 ng mL⁻¹) (Fig. 1). In this study, BPH patients were classified into 3 groups; 8 patients (13%) with total PSA less than 4 ng mL⁻¹, 31 patients (52%) in the diagnostics gray zone of total PSA (4-10 ng mL⁻¹) and 20 patients (33%) with total PSA more than 10 ng mL⁻¹. This study found is a slight increase in mean testosterone level in group with T. PSA between 4-10 ng mL⁻¹ with no significant difference among the 3 groups (Table 2).

To investigate the relation among age, T. PSA and testosterone hormone, Pearson's correlation was performed. This study found a positive correlation between testosterone hormone level and age of patients (Fig. 2). Regarding, correlation of F/T. PSA ratio with age, this study found a strong

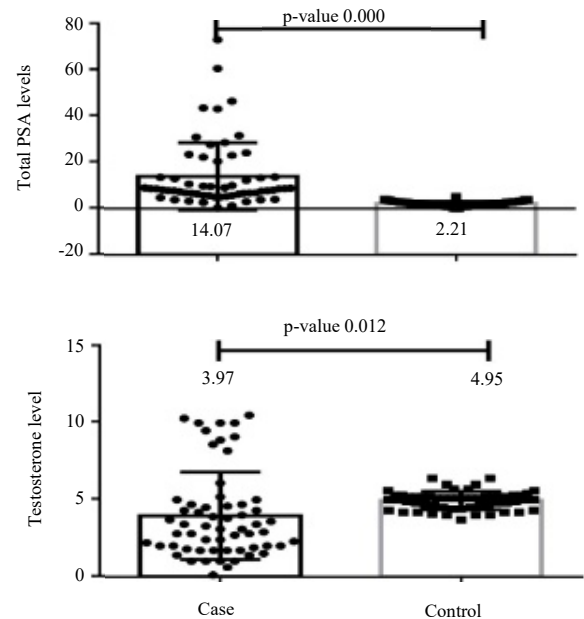


Fig. 1: Comparison of total PSA and testosterone levels between case and control groups

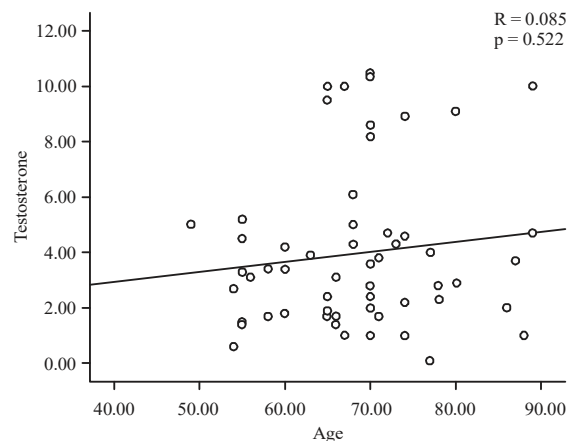


Fig. 2: Correlation between testosterone and age in BPH patients

Table 1: Mean age and BMI of the study groups

Variables	Case (Mean±SD)	Control (Mean±SD)	p-value
Age	67.10±7.90	68.05±7.32	0.504
BMI	25.14±8.03	23.35±1.09	0.095

Table 2: Mean testosterone levels across total PSA subclass

PSA class	Number	Percentage	Mean±SD	p-value
<4 ng mL ⁻¹	8	13	3.80±2.58	0.941
4-10 ng mL ⁻¹	31	52	4.06±3.03	0.821
>10 ng mL ⁻¹	20	33	3.88±2.78	0.951

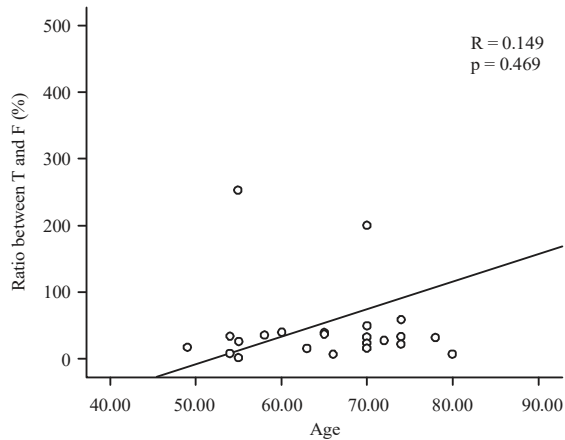


Fig. 3: Correlations between free to total PSA ratio and age among BPH patients

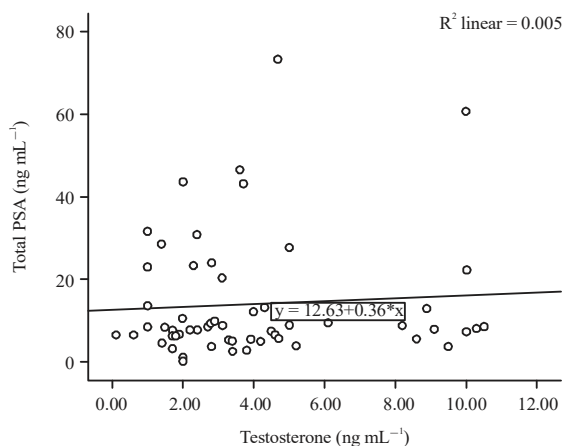


Fig. 4: Correlations between total PSA and testosterone among BPH patients

positive correlation between them, that means the PSA level increase with an increase in age (Fig. 3). This study also found a positive correlation between the total PSA and testosterone level (Fig. 4). Total PSA and F/T. PSA ratio and free PSA and testosterone levels had shown no correlation with BMI.

DISCUSSION

This study has investigated whether testosterone hormone level plays a role in mandating adjustment of total PSA level in patients with BPH. Study conducted by Elzanaty *et al.*⁹ showed a statistically significant positive correlation between PSA and testosterone levels by employing adjusted multivariate analysis⁹ which agreed with our findings.

Jacques *et al.*¹⁰ presented that both age and BMI showed a strong linear correlation with PSA level. The possible reason for this association is the low androgen levels and higher estrogen levels in obese men which can affect PSA production due to the presence of androgen response element located in the PSA promoter region¹⁰. This result is consistent with the current research.

Orakwe *et al.*¹¹ proposed that for each 1 kg m⁻² rise in BMI, prostate volume expanded by 0.41 cc. So, as compared to the men with normal BMI, overweight and obese men had increased chances of prostate enlargement, this risk was particularly high for very obese men¹¹.

Heracek *et al.*¹² performed a study in BPH and prostate cancer patients when compared with serum androgen level they depict no significant difference. Previous researches which compare serum testosterone level between BPH and prostate cancer patients also showed no significant difference. The level of testosterone hormone slightly reduced in prostate cancer patients, but there was no difference of statistical significance in testosterone level in BPH patients¹². This study outcomes are similar to previous research results.

Usoro *et al.*¹³ study observed a statistically significant positive correlation between age and PSA levels in control group and also in patients with BPH, whereas, it was not statistically significant in prostate cancer group. They found significant negative associations between serum testosterone level and age of patients in the control group and patients with prostate cancer¹³.

Tanwar *et al.*¹⁴ observed a positive correlation between age and PSA level which is in agreement with this study. They found a negative correlation between age and testosterone hormone level and a weak negative, but statistically significant correlation between testosterone and PSA levels in BPH patients which is in disagreement with the current study¹⁴. This study findings are in disagreement with the findings of favilla *et al.*¹⁵ and corona *et al.*¹⁶, who reported that no significant correlation between PSA and testosterone hormone level.

The BPH is a very common problem in old age men which results in serious complications. More studies should be designed in future to see the correlation of testosterone hormone level with PSA levels in different populations of the world and also the role of obesity should be determined in detail on the development and progression of BPH.

CONCLUSION

This study found a positive correlation between testosterone and PSA levels in BPH patients so, the adjustment

of testosterone hormone, in this case, would adjust the level of total PSA as a result of this study. This study recommends to periodic testing of testosterone hormone level whenever to check PSA level as a routine checkup. In the diagnostic and prognostic workup for the prostate disorder, associating testosterone and PSA levels may increase the predictive accuracy of prostate disease tests.

SIGNIFICANCE STATEMENT

This study discovers the possible correlation between obesity, testosterone hormone level and PSA in BPH that can be beneficial for the proper diagnosis and prevention of the disease. This study will help the researchers to uncover the pathology of BPH and prevent unnecessary biopsies because of raised PSA levels in the diagnostic grey zone that many researchers were not able to explore. Thus, a new direction can be taken in the diagnosis of BPH by considering the measurement of BMI and testosterone hormone levels along with PSA levels in BPH patients.

ACKNOWLEDGMENT

Persons who contributed to the work are all included in the authors list.

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