Prostate diseases
Original article

Comparison of the pre-treatment testosterone levels in benign prostatic hyperplasia and prostate cancer patients

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Abstract

Objectives: To compare serum testosterone and prostate specific antigen (PSA) levels of patients diagnosed of prostate cancer to those with benign prostatic hyperplasia (BPH).

Subjects and methods: One hundred and thirteen male patients with or without LUTS who had indication(s) for prostate biopsies were recruited. Blood samples were analysed for serum testosterone and serum PSA. Prostate sizes were measured and PSA densities calculated before trans-rectal prostate biopsies were performed.

Results: On histology of prostate biopsy specimens, 54 patients (47.8%) had prostate adenocarcinoma while 59 patients (52.2%) had BPH. Serum testosterone levels were lower in the prostate cancer group (23.09 ± 2.31 nmol/L *versus* 24.37 ± 1.94 nmol/L in the BPH group) but this difference was not statistically significant ($p = 0.671$). Serum testosterone also did not differ significantly with Gleason grade and Gleason score in patients with prostate cancer.

Serum PSA and PSA density (PSAD) values were significantly higher in men with prostate cancer, and also in prostate cancer patients with high grade disease.

Conclusion: Serum testosterone levels of patients with prostate cancer did not significantly differ from those of patients with BPH and were not related to grade in prostate cancer patients.

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Introduction

Prostate cancer is the second most frequently diagnosed cancer of men and the incidence varies by race/ethnicity, with African-Americans at highest risk in America [1]. In the African subregion, prostate cancer presents approximately a decade earlier than it does in western countries, however, the patients still present with advanced disease in over 70% of cases [2,3]. In these patients, the disease also tends to progress more rapidly and Gleason score tends to be higher [3]. Though the Nigerian nationwide incidence is yet to be directly evaluated [2], Nigerian men seem to be at also at high risk of prostate cancer like the African-Americans judging from data gleaned from the population-based and hospital based cancer registries which indicate that prostate cancer is the commonest malignant tumour among Nigerian men [4].

Though the search for novel (and more prostate cancer specific) tumour markers continues, serum PSA estimation remains an important tool for Prostate cancer detection [5]. Tissue and serum level of androgens in those with or without prostate cancer have over the years been part of the focus of the search for better tumour markers for prostate cancer. Serum testosterone and other androgens are considered important in the growth and development of the prostate as well as in the pathogenesis of prostate cancer [6]. However, over the years, reports have been conflicting with no clear consensus and the importance of its determination for patient management in terms of diagnosis, prognosis and staging has been poorly understood [6,7]. Researchers have at different times reported low serum testosterone levels [8–10] and high serum testosterone levels [11,12] in patients with prostate cancer when compared to those without prostate cancer. Some found no significant differences in serum testosterone levels on comparison [13–16]. A review of 25 studies comparing testosterone levels in a total of 2767 controls and 1481 patients with prostate cancer reported that the mean testosterone levels at diagnosis were the same in both groups in 15 studies (60%), higher in prostate cancer patients in four (16%) and lower six (24%) [6].

After an online PUBMED search, a study conducted in our institution by Osegbe and Ogunlewe [17] (published in 1988) was the only similar study found. They measured and compared serum testosterone levels in prostate cancer, benign prostatic hyperplasia (BPH) and normal patients and found that serum testosterone was significantly lower in those with prostate cancer.

There is a paucity of studies of such research in the predominantly black sub-Saharan Africa, therefore, we also sought to compare pre-treatment serum testosterone levels in benign prostatic hyperplasia (BPH) and prostate cancer patients presenting in our centre in Nigeria.

Subjects and methods

This study was a prospective comparative study conducted at our institution over 16 months (March 2013–June 2014). Approval was obtained from the Research and Ethics Committee of the Lagos University Teaching Hospital before commencement of the study. Male patients above 40 years with or without symptoms of prostatic disease who had indications for prostate biopsy were enrolled into the study from the Urology Outpatient Clinics and wards after informed consent had been obtained. The indications for prostate biopsy were features suggestive of prostatic malignancy on digital rectal examination and/or serum PSA elevated above the level expected for age. The age-specific levels used were 0–2.5 ng/ml for men aged 40–49 years, 0–3.5 ng/ml for those aged 50–59 years, 0–4.5 ng/ml for those aged 60–69 years and 0–6.5 ng/ml for those aged 70–79 years. Patients excluded from the study were those on 5-α reductase inhibitors, those that already had radiotherapy as treatment before presentation, those already on androgen deprivation therapy and men on androgen supplementation for hypogonadism.

Other clinical data collected included the bio-data (age, sex, occupation, marital status), presenting complaints, duration of illness/problems, history presenting complaints including lower urinary tract symptoms and haematuria, any history suggestive of expected complications (like acute urinary retention, renal failure), history suggestive of prostatic malignancy (and metastases) and history of co-morbid conditions (e.g. diabetes mellitus, hepatic diseases, hypertension). Physical examination findings were also noted.

Fasting blood samples were collected between 7 am and 10 am. Serum was stored at $-80\,^{\circ}$C and were subsequently analysed by quantitative determination for serum prostate specific antigen and testosterone using enzyme immunoassay kits made by Rapid labs (UK). Analytical sensitivity for the total PSA assay kit was 0.3 ng/ml while that of the total testosterone kit was 0.2 nmol/l. The analysis of the serum samples were done by 2 chemical pathologists working together who were blinded to the histology results or clinical status of the patients.

The sizes of the prostates were measured using a 3.5 MHz trans-abdominal ultrasound probe and the volumes were expressed in cm^3. Subsequently, trans-rectal prostate biopsies (minimum of 10 cores − sextant + 4 extended cores) were done for all patients with histology of the prostate biopsy specimens which formed the basis for categorising the patients into 2 groups – prostate cancer group and benign prostatic hyperplasia (BPH) group. The Gleason grades and scores were also recorded for the prostate adenocarcinoma specimens on histology. The histology of the specimens was done by a pathologist specialised in prostatic diseases who was blinded to the results of the serum PSA and testosterone.

The data were analysed using the Statistical Package of Social Sciences (SPSS) version 16.0. The Student's t-test was used for test of significance with confidence interval of 95%. A p-value of <0.05 was considered statistically significant.

Results

A total of 113 patients were recruited and on histology of the prostate biopsy specimens, 54 men (47.8%) had prostate cancer (prostate cancer group) while 59 men (52.2%) had benign prostatic hyperplasia (BPH group). The overall mean age was 67.9 ± 7.8 years (range 47–85 years) while the mean ages were 68.9 ± 7.9 years and 66.9 ± 7.6 years in the prostate cancer and BPH groups respectively. Patients in their seventh and eighth decades of life cumulatively accounted for 75.1% of all patients.

Overall, the mean serum PSA was 30.23 ± 26.41 ng/ml (range 0.02–88.36 ng/ml) while the overall mean serum testosterone was 23.8 ± 15.9 nmol/L (range 1.25–95.05 nmol/L). Within the individual groups, 46 (75.93%) of patients in BPH group had serum PSA

Table 1 Serum testosterone, PSA levels and PSA density in the 2 groups.

Variables	Prostate cancer group ($n = 54$)	BPH group ($n = 59$)	p-Value
Age (years, mean ± SD)	68.9 ± 7.9	66.9 ± 7.6	0.170
Serum testosterone (nmol/L, mean ± SD)	23.1 ± 16.9	24.4 ± 14.9	0.671
Serum PSA level (ng/ml, mean ± SD)	45.8 ± 24.3	16.0 ± 19.4	<0.001
PSA density (ng/ml per ml, mean ± SD)	1.02 ± 2.4	0.2 ± 0.2	0.016

levels <20 ng/ml while 41 (77.96%) of prostate cancer patients had serum PSA levels ≥20 ng/ml.

Mean serum PSA levels were 45.8 ± 24.3 ng/ml and 16 ± 19.4 ng/ml in the prostate cancer group and BPH group respectively with statistically significant difference on comparison (p-value = <0.001) while the serum testosterone levels were 23.1 ± 16.9 nmol/L and 24.4 ± 14.9 nmol/L in the prostate cancer and BPH groups respectively with no statistically significant difference on comparison (p-value = 0.671) as shown in Table 1. The PSA density showed statistically significant difference on comparison with mean values being 1.02 ± 2.4 ng/ml/ml in the prostate cancer group and 0.2 ± 0.2 ng/ml/ml in the BPH group.

On further analysis of the prostate cancer group, Gleason grade 4 was the primary grade in 23 (42.6%) of the patients in the group while Gleason grade 3 was the primary pattern in 18 (33.3%). In the group, 24 (44.4%) had Gleason scores of ≥8 while patients with Gleason scores 6 and 7 cumulatively accounted for 24 (44.4%) more of the patients. The mean serum testosterone levels were 20.2 ± 14.1 nmol/L and 27.3 ± 20.1 nmol/L in those with primary Gleason's grades ≥4 and those with primary Gleason's grades <4 respectively with no statistically significant difference on comparison (Table 2).

Mean serum testosterone results levels of those with Gleason's scores <8 was 24.1 ± 18.1 nmol/L compared to 21.8 ± 15.7 nmol/L in those with Gleason scores ≥8 as also shown in Table 2 (p-value = 0.631). The serum PSA levels were significantly higher in those with primary Gleason grade ≥4 and in those with Gleason scores ≥8 as shown by the p-values of 0.017 and 0.027 respectively (Table 2).

Discussion

Patients in their seventh and eighth decades of life cumulatively accounted for 75.1% of the overall number studied and most patients with prostate cancer had high risk disease as evidenced by percentage with serum PSA >20 ng/ml and Gleason grade ≥4 or Gleason score ≥8. These findings are similar to previously published data and confirm that prostatic diseases are significant problems of men in our region and that the black Nigerian male usually presents with high grade poorly differentiated tumours [2,18].

From the results of our study, the serum PSA (and calculated PSA density) showed significant difference in values on comparison and was higher in patients with prostate cancer when compared to those with BPH (p = <0.001 for serum PSA and p = 0.16 for PSA density). In their study using suprapubic prostatectomy specimens, Hill et al. [16] also demonstrated that the serum PSA was the best discriminator between those with and those without prostate cancer after they found that the serum PSA was significantly higher in those with prostate cancer (p < 0.00001, Mann–Whitney test).

In the prostate cancer group, the serum total PSA was also found to be significantly higher in those with primary Gleason grades ≥4 and Gleason scores ≥8 when compared to those with lower grades or scores. Schatzl et al. [19] also found that patients with high grade prostate cancer (Gleason score ≥8) had significantly higher serum PSA values.

In our study, the serum testosterone levels found to be slightly lower in patients with prostate cancer but there was no statistically significant difference from the serum levels in BPH patients (p-value = 0.671). Heracek et al. [7] also compared serum androgen levels in patients with BPH and prostate cancer and found no significant difference in levels. Samples used for histologic diagnosis in the study by Heracek et al. [7] were simple and radical prostatectomy specimens unlike the prostate biopsy specimens used in our study but the results were still similar. Other similar studies comparing BPH and prostate cancer patients also demonstrated no significant difference in serum testosterone [11,16,20]. Our findings however were different from that of Osegbe and Ogunlewe [17] (conducted in our institution and published in 1988) which showed that in Nigerian patients with advanced prostatic cancer, the serum testosterone concentrations were significantly lower than those of Nigerians with normal prostate and BPH. The patients with prostate cancer in our study included both patients with advanced (and/or metastatic) disease and those with organ confined disease. Osegbe and Ogunlewe [17] also studied androgen metabolites and the androgen concentration in the prostatic glands of their patients. Lower serum testosterone levels in patients with prostate cancer were also reported by authors in other centres [8–10].

There were no significant differences in the serum testosterone values when those with primary Gleason grades ≥4 and Gleason scores ≥8 were compared to those with lower grades or scores,

Table 2 Serum testosterone and PSA levels of patients in different primary Gleason grade and Gleason score categories.

Variables	Primary Gleason grade			Gleason score		
	≥4 ($n = 32$)	<4 ($n = 22$)	p-Value	≥8 ($n = 24$)	<8 ($n = 30$)	p-Value
Serum testosterone (nmol/L, mean ± SD)	20.2 ± 14.1	27.3 ± 20.1	0.135	21.8 ± 15.7	24.1 ± 18.1	0.631
Serum PSA level (ng/ml, mean ± SD)	52.2 ± 21.4	36.4 ± 25.6	0.017	53.9 ± 22.1	39.3 ± 24.3	0.027

respectively. Similar findings were demonstrated by Massengill et al. [21] in their study though the specimens used for histology were radical prostatectomy specimens. This is a major limitation in our study since grading between prostate biopsy specimens and the more representative radical prostatectomy specimen may be discordant due to sampling errors with the needle biopsy and higher grade adenocarcinoma may be missed [22]. Also, adenocarcinoma may be entirely missed on needle biopsy due to same sampling error [23]. However, grade on biopsy material has also been shown to correlate fairly well with that of the subsequent prostatectomy specimen especially with extended biopsy protocols rather than sextant biopsy protocol [22,23]. On the other hand, studies by Schatzl et al. [19] and Ide et al. [20] found that patients with high grade prostate cancer had significantly lower serum testosterone values.

Conclusion

Serum testosterone levels in prostate cancer patients (though lower) were not significantly different statistically from the levels in BPH patients. Serum testosterone levels did not also significantly differ with pathological grade in prostate cancer patients.

Prostate specific antigen (PSA) and PSA density on the other hand were significantly higher in the prostate cancer group of patients. The serum PSA level was also higher in those with high grade prostate cancer when compared to those with lower grades. Thus, serum PSA (with or without DRE) assay currently still remains an important investigation for detecting prostate cancer in men.

Ethical committee approval

This study obtained the approval from the Lagos University Teaching Hospital Health Research Ethics Committee (LUTHHREC).

Conflict of interest

None declared.

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