Original Article

Correlation Between Prostate Volume and Prostate-Specific Antigen in Nigerian Men with Symptomatic Histologically-Diagnosed Benign Prostatic Hyperplasia

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Abstract

Background: Prostate-specific antigen (PSA) is elevated in the serum of most men with prostatic diseases. Benign prostatic hyperplasia (BPH) is the commonest of these diseases. The degree of enlargement of the prostate may determine the amount of PSA elaborated. Several reports in some parts of the world have shown a significant correlation between prostate volume (PV) and PSA. However, only a few reports have been documented in Nigeria, especially in the South-South region. **Aim:** This research aimed to ascertain if there is any correlation between prostate volume (PV), total PSA (tPSA), and free PSA (fPSA) in men with histologically diagnosed BPH. This knowledge may help in the estimation of PV from a given PSA. **Patients and Methods:** This prospective hospital-based study was carried out in a southern Nigerian tertiary hospital between November 2017 and October 2018. Eighty (80) eligible and consenting patients participated in the study and were enrolled at first contact in the urology clinic. Each patient's blood was taken for PSA estimation. The prostate volume was estimated by transrectal ultrasound scan (TRUS). Those who had tPSA values greater than 4 ng/mL whose biopsy report showed prostate malignancy were excluded from the study. A proforma was used to collect patients' sociodemographic and clinical information. Data were entered and analyzed with Statistical Package for Social Sciences version 22 (SPSS Inc., Chicago, IL, United States). For all statistical tests, $P < 0.05$ was regarded as significant. **Results:** The mean age of the patients for this study was 68.03 years. The mean prostate volume was 87.9 mL with a range of 34 to 234 mL. The mean tPSA was 5.5 ng/mL with ranges of 1.1 to 21.1 ng/mL. There was a significant correlation between PV and tPSA with a P value of 0.0001. This correlation was also shown between PV and fPSA with a P value of 0.0001. **Conclusion:** There is a statistically significant correlation between PV and PSA (both free and total) in men with symptomatic histologically diagnosed BPH. This finding showed that larger benign prostate glands elaborated greater amounts of PSA. It may, therefore, be appropriate to say that it is not in all cases of elevated serum tPSA that the possibilities of malignancy or inflammation should be entertained.

Keywords: *Benign prostatic hyperplasia, prostate specific antigen, prostate volume*

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Introduction

Benign prostatic hyperplasia (BPH) is a regional nodular growth affecting the transition zone of the prostate gland. It is a common benign neoplastic

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condition affecting men and accounted for 83% of cases of prostate tumors in a study done in Benin City, Nigeria.[1] Several studies have reported that BPH was the most common prostate lesion accounting for 63% to 83% of prostate diseases.[1-3] A study done by Boyle and Napalko showed evidence of prostatic hyperplasia in over 80% of autopsies conducted in men over 70 years of age. In the same study, 40% of men aged 50--64 years had symptoms compatible with the disease.[4]

Benign prostatic hyperplasia produces symptoms in affected men and these symptoms are referred to as lower urinary tract symptoms (LUTS). BPH results clinically in LUTS and the cumulative risk for the development of acute urine retention increases with age.[5] These LUTS are classified as voiding and storage symptoms. Not all men with an enlarged prostate have these symptoms; only one in ten males over 50 years present with LUTS due to BPH.[6]

Clinical diagnosis is based on the presence of LUTS and enlarged prostate on digital rectal examination. Ultrasonography of the prostate and measurement of prostate-specific antigen (PSA) are widely used as screening tools for ruling out prostate adenocarcinoma.[6] The normal total serum level of PSA is between 0 and 4 ng/mL in cases of BPH. The mean tPSA level range in Nigerian men with BPH is 35.5 ± 44.9 ng/mL compared to control of 2.22 ± 2.90 ng/mL.[7] Symptomatic men with tPSA <4 ng/mL may be safely managed as benign prostatic enlargement in the absence of suspicious DRE and USS findings.[8]

Prostate-specific antigen (PSA) is a serine protease that is produced almost exclusively by the epithelial cells of the prostate gland. Serum tPSA value increase by 4% per milliliter rise of PV[9] and it is the part bound to alpha-1-anti-chymotrpsin (ACT) that is detectable by current immune assays.[10] A similar rate of increase obtains for the fPSA (unbound) component.[11]

A correlation between total prostate-specific antigen (tPSA) level and prostate volume has been found in Korean men with histologically-proven BPH, although the correlation between fPSA and PV was stronger.[12] In another work done in Saudi Arabia in men with a mean age of 64.2 years, PV of 35.2 mL and tPSA of 2.2 ng/mL, the PV was significantly correlated with PSA.[13] Udeh and colleagues in Jos, Nigeria studied 120 men with histologically-proven BPH. They found a mean age of 65 years, PV of 72.79 mL and PSA of 12.44 ng/mL with a correlation between PV and tPSA, and a *P* value of 0.05.[14]

Large prostate glands may elaborate more PSA levels and as such can be managed as a benign disease.[8,14] A correlation of PV and PSA may be useful in counseling patients and thereby allaying their fears especially when a high PSA level is obtained.

This study therefore aimed to ascertain the correlation between prostate volume and total/free prostate-specific antigen (PSA) in men with BPH.

Patients and Methods

This was a prospective observational study carried out in the urology surgical outpatient clinic of our hospital from October 2017 to September 2018.

The study population included all patients seen in the urology outpatient clinic with LUTS and DRE findings of BPH with tPSA of <4 ng/mL, or DRE findings of BPH with tPSA >4 ng/mL and histological confirmation of BPH.

The sample size was determined using the Yamane formula[15]

$n = N/(1 + Ne^2)$, where

n = sample size

N = sample population which is an average of the total number of new patients seen in urology outpatient clinic over a 3-year period.

e = confidence interval (0.05)

$n = 100/(1 + 100 \times 0.05^2)$

$n = 80$

Patients with suspicious DRE findings, patients on luteinizing hormone-releasing hormone analogue, patients on finasteride, alpha-adrenoceptor blocker at first assessment, patients who have acute prostatitis, patients with histologically-diagnosed cancer of the prostate, prostatic intra-epithelia neoplasm or atypical small acinar proliferation, those who have had any form of prostate surgery, and patients that opted out were excluded from this study. Patients who fulfilled the selection criteria were enrolled into the study after the aims and objectives were explained to them and informed consent was obtained.

A comprehensive clinical history and detailed examinations were done for each patient enrolled, with emphasis on digital rectal examination findings. For each patient, 5.0 mL of blood was collected under the aseptic condition from a peripheral vein into a plain bottle. This was immediately sent to the chemical pathology laboratory for PSA analysis using DRG ELISA. A value of 4 ng/mL was used as a cut-off to determine those that will be subjected to TRUS biopsy. Other tests which included urine microscopy, culture and sensitivity, full

blood count, serum electrolyte, urea and creatinine were also requested as part of routine investigations.

TRUS was done for all the patients for prostate volume estimation in the radiology department. Additionally, prostate biopsy was done in the same setting for those who had PSA levels >4 ng/mL. The patients were told to empty their bowel at home before coming to the hospital and their bladder just before the procedure. They were all requested to commence oral antibiotics (ciprofloxacin 500 mg and metronidazole 400 mg) in the morning of the procedure before leaving their homes and continued for three days as par unit protocol. The left lateral decubitus position was used for both prostate volume estimation and biopsy. A tube of xylocaine gel was gently emptied into the rectum and DRE was repeated. The end firing rectal probe was covered with a latex condom after first filling the condom with acoustic gel. A needle guide was improvised with rubber tubing and held with a rubber band to the probe. The probe was gently introduced into the rectum and focused on the prostate gland. The prostate gland was scanned measuring the length, width and anterior posterior diameter after setting the ultrasound machine in prostate mode. Prostate volume was calculated using the prolate ellipsoid formula (transverse diameter x longitudinal diameter x anteroposterior diameter x $\pi/6$).

For those who had indications for prostate biopsy (tPSA >4 ng/mL), a trucut biopsy needle was introduced via the rubber tubing and six (6) core biopsies were obtained at the para-sagittal plane for each lateral lobe taking a biopsy from the apex, mid-portion and the base, respectively. Biopsied tissues were immediately put inside a container with 10% buffered formalin and sent to the histopathology laboratory for analysis.

Data collection was done using a structured proforma. All vital information including biodata, clinical, radiological and laboratory findings were recorded in the proforma and then transferred into a spreadsheet for analysis. The statistical analysis was carried out using the Statistical Programming for Social Sciences version 22 (SPSS Inc., Chicago, IL, United States). Mean and standard deviation were calculated for age, PV, fPSA, and tPSA. Pearson's correlation coefficient was used to test the strength of the relationship between fPSA, tPSA and PV. Simple linear regression was used to quantify the linear relationship between fPSA, tPSA, and PV. The *P* value was set at 0.05.

Results

Eighty-eight (88) patients were recruited for this study. Eight patients (8) who had a prostate biopsy on account of tPSA >4 ng/mL were excluded because of the finding of prostate cancer in six (6) patients and prostatic intraepithelial neoplasia in two (2) patients. A total of 80 men with BPH were therefore studied.

The greatest proportions (67.5%) of the patients were between 60 to 79 years. The age range for the population studied was between 51 to 104 years, with a mean of 68 years ± 9SD [Table 1].

The values for tPSA ranged from 1.1 ng/mL to 21.8 ng/mL with a mean of 5.5 ng/mL ± 4.0SD. The fPSA values ranged from 0.32 ng/mL to 9.3 ng/mL with a mean of 2.1 ng/mL ± 1.5SD. The PV values ranged from 34.0 g to 234.0 g with a mean of 87.9 g ± 40.4SD [Table 1].

There was statistically significant correlation between PV and tPSA (p = 0.0001), PV and fPSA (p = 0.0001), prostatic volume and tPSA ≤10 ng/mL (p = 0.0001) and PV and total PSA >10 ng/mL (p = 0.038) [Table 2].

The strength of the relationship between PV and tPSA was moderately correlated (r = 0.442), between PV and tPSA >10 ng/mL was r = 0.600 (strong correlation), PV and tPSA ≤10 ng/mL was moderately correlated (r = 0.495) PV and fPSA moderately correlated (r = 0.457) [Table 2].

A linear regression was performed to predict the total value of PSA from prostatic volume. The equation for

Table 1: Demographic and prostatic indices of participants

Variables	Frequency	Percent (%)
Age Group (years)		
50--59	16	20.0
60--69	33	41.3
70--79	21	26.2
>80	10	12.5
Prostate Volume (PV)		
30--100 mL	59	73.8
>100--235 mL	21	26.2
Total Prostate Specific Antigen (tPSA)		
0--4 ng/mL	43	53.8
>4 ng/mL	37	46.2

Table 2: Correlation between fPSA, tPSA, and PV

Variables	rho (p)	*P*	Regression Model
Prostatic Volume vs Total PSA	0.442	0.0001	y=0.0472x+1.3519
Prostatic Volume vs Free PSA	0.457	0.0001	y=0.014x+0.8119
Prostatic Volume vs Total PSA (>10 ng/ml)	0.600	0.038	y=0.0398x+10.991
Prostatic Volume vs Total PSA (≤ 10 ng/ml)	0.495	0.0001	y=0.0305x+1.657

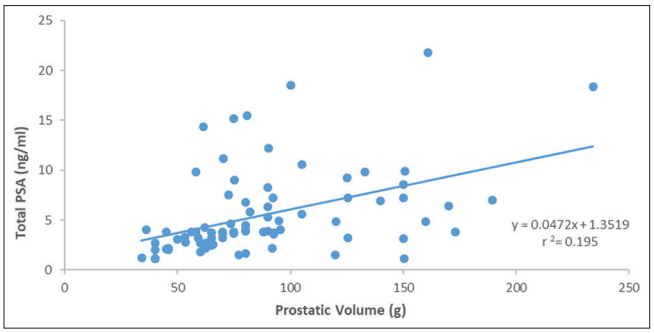

Figure 1: Relationship between PV and tPSA

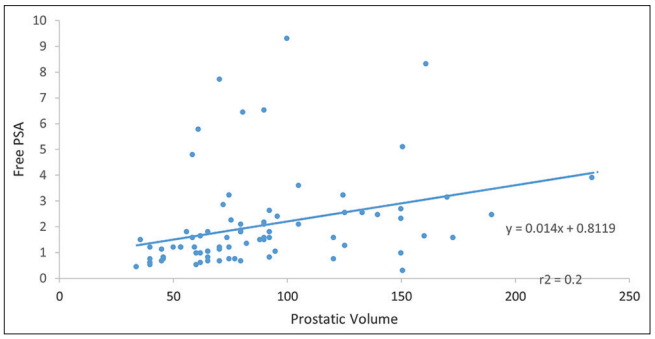

Figure 2: Relationship between PV and fPSA

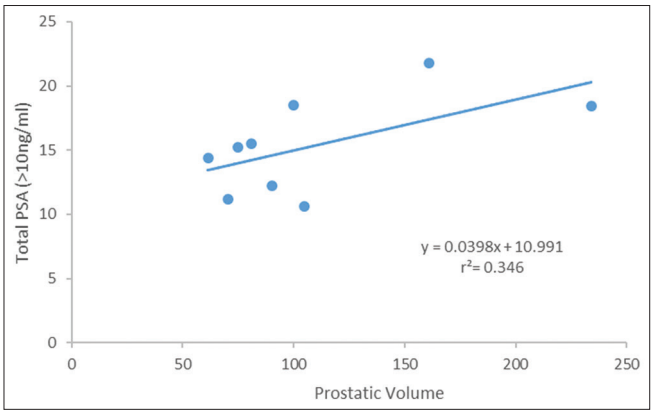

Figure 3: Relationship between PV and tPSA (>10 ng/mL)

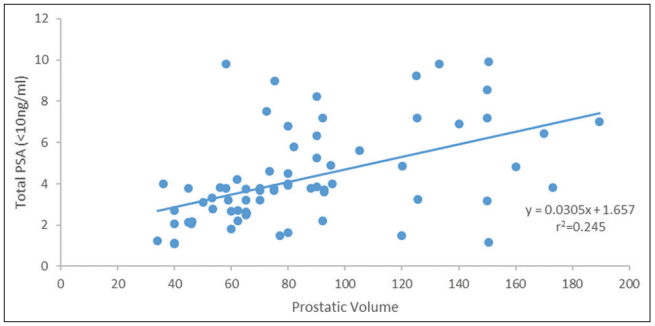

Figure 4: Relationship between PV and tPSA (≤10 ng/mL)

the model was $y = 0.0472x + 1.3519$. For a unit change in PV, tPSA changes by 0.0472. Prostatic volume explains 19.5% of the variation in tPSA [Figure 1].

A linear regression was performed to predict fPSA from PV. The equation for the model was $y = 0.014x + 0.8119$. For a unit change in PV, fPSA changes by 0.014. Prostatic volume explains 20.9% of the variation in fPSA [Figure 2].

A linear regression was performed to predict total PSA >10 ng/mL from PV. The equation for the model was $y = 0.0398x + 10.991$. For a unit change in PV, tPSA changes by 0.0398. Prostate volume explains 34.6% of the variation in total PSA >10 ng/mL [Figure 3].

A linear regression was performed to predict tPSA ≤10 ng/mL from PV. The equation for the model was $y = 0.0305x + 1.657$. For a unit change in PV, tPSA, changes by 0.0305. Prostatic volume explains 24.5% of the variation in tPSA ≤10 ng/mL [Figure 4].

Discussions

The mean PV of 87.9 mL found in this study is higher than what was found in the Caucasians (43.7 mL)[16] and Asians (36.9 mL)[17] but compares favorably with some reports from other parts of Nigeria and Africa.[18] Badmus *et al.*,[18] in a work done in Ile-Ife between 2003 and 2009 found a mean prostate volume of 83.8 mL among patients with BPH. The higher prostate volumes seen in blacks may be attributed to their increased sexual activities from polygamy.[19,20] This could also be due to the late presentation of patients to the clinic and racial predisposition. Our patients here have poor health awareness and often seek medical help when there are complications. Also, there are reports of molecular differences in the prostate gland of black men and that of other races.[21]

Compared to the prostate volume documented by Badmus *et al.*,[18] this study found a relatively higher mean prostate volume in men with BPH. The difference in prostate volume could be due to differences in the age groups used in his study and also because trans-abdominal prostate volume estimation was done for all the patients. A study done by Ibinaye showed a very low prostate volume which could have been a result of the population that was used for the study.[22] Udeh *et al.*[14] reported a mean prostate volume of 72.79 mL which is lower than what was found in this study probably because the age range they studied was different from that of the population used in this study. They also used trans-abdominal ultrasonography for prostate volume estimation. Prostate volume estimation by transabdominal method may also not compare adequately with TRUS estimation.

The mean tPSA value of 5.5 ng/mL found in this study was higher than that of Asians.[23] This is expected as

Africans have large prostate volumes as was found in this study and would be expected to elaborate more PSA. The cut-off PSA value of 4.0 ng/mL generally used for the management of BPH may have to be adjusted in our setting. This is because some patients who had values well above this level had histology of BPH after subjecting them to TRUS biopsy. The mean tPSA in this study was lower when compared with values from Udeh *et al*.[14] This could be attributed to the fact that digitally guided trans-rectal prostate biopsy was done for the patients in their study. Digitally guided biopsies are associated with high levels of false negatives.

Their study also found a statistically significant correlation between prostate volume and tPSA in men with histological proven BPH. Udeh *et al*.[14] and Hochberg *et al*.[24] reported similar findings and pointed out that in patients with BPH proven by TRUS biopsy, prostate volume and PSA had a statistically significant correlation. A significant positive correlation was also seen between prostate volume and fPSA although with a weaker correlation, *P* value of 0.0001.

Conclusion

This study showed a positive correlation between prostate volume and prostate-specific antigen (total and free) in men diagnosed with BPH. This study showed that larger benign prostate glands elaborated greater amounts of PSA.

Limitations of this study

1. A larger sample size would have made the result better.
2. Patients who had tPSA <4 ng/mL were not subjected to prostate biopsy.
3. Those with hard, nodular prostate were all excluded from the study.

What is already know on this topic

1. Prostate-specific antigen (PSA) is elevated in the serum of most men with prostatic diseases.
2. The degree of enlargement of the prostate may determine the amount of PSA elaborated.

What this study adds

1. The volume of the prostate gland should be put into consideration when interpreting PSA.
2. The use of tPSA estimation may be adequate for evaluating men with suspected BPH. Recourse to other forms of PSA like fPSA may be useful when further evidence is needed to exclude cancer.

Authors' contributions

EA, and EI conceive the study and drafted the protocol. EA, FEO and UIA collected the data. EA, FEO, UIA and EI did the statistical analysis, interpreted the results, and drafted the initial version of the manuscript. All authors read and approved the manuscript

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Ethical approval number

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Conflicts of interest

There are no conflicts of interest.

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