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Assessment of Transrectal Ultrasound Quantitative Relationship between Prostate Size and Serum Level of Prostate-Specific Antigen in Onitsha North Metropolis, Anambra State, Nigeria

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Abstract **Case Studies**

Background: Prostate-specific antigen (PSA) testing is widely used in the evaluation of prostate disorders, but its diagnostic accuracy is limited by the influence of prostate size, as benign prostatic enlargement may produce PSA elevations similar to malignancy.

Aim: This study assessed the quantitative relationship between prostate size and serum PSA levels and evaluated the diagnostic value of PSA density (PSAD) in improving prostate disease differentiation.

Materials and methods: A prospective cross-sectional study was conducted among 185 male patients aged 40 years and above who presented with prostate-related conditions at Crescent Diagnostic Laboratory, Onitsha, Anambra State. Prostate dimensions and volume were measured using transrectal ultrasound, while serum total and free PSA levels were determined using chemiluminescent immunoassay. PSA density was calculated as the ratio of total PSA to prostate volume. Data were analyzed using SPSS version 24, employing descriptive statistics, Pearson correlation, multiple linear regression, and receiver operating characteristic (ROC) curve analysis.

Results: The mean age of the participants was 61.1 ± 10.7 years, and the mean prostate volume was 54.5 ± 53.5 cm^3. Total PSA showed a moderate positive correlation with prostate volume ($r = 0.403$, $p < 0.001$) and a weaker correlation with age ($r = 0.222$, $p = 0.002$). Regression analysis demonstrated that prostate volume was a significant independent predictor of PSA levels, whereas age was not significant after adjustment. PSA and PSAD values were highest in patients with prostate cancer. ROC analysis revealed that PSAD had superior diagnostic performance (AUC = 0.941) compared with total PSA (AUC = 0.899). An optimal PSAD cut-off value of ≥ 0.214 ng/mL/cm^3 achieved 100% sensitivity and 88.4% specificity, outperforming conventional PSA thresholds.

Conclusion: The prostate volume is a major determinant of serum PSA levels and that PSA density provides improved diagnostic accuracy. Incorporation of PSAD into routine prostate evaluation is recommended to reduce unnecessary biopsies and enhance evidence-based clinical decision-making.

Keywords: Benign, cancer, prostate, ultrasound.

INTRODUCTION

Prostate disorders represent a major health concern among aging males, with benign prostatic hyperplasia (BPH), prostatitis, and prostate cancer being the most prevalent conditions worldwide [1]. Prostate-specific antigen (PSA) is a glycoprotein enzyme secreted primarily by the epithelial cells of the prostate gland, which contributes greatly to the liquefaction of semen. Under normal physiological conditions, only small amounts of PSA enter the bloodstream; however, serum PSA levels may become elevated in various prostate-related conditions such as benign prostatic hyperplasia (BPH), prostatitis, and prostate cancer [2-4]. Owing to this, PSA testing has become one of the most widely utilized biomarkers for the early detection and monitoring of prostate disorders [2-4].

The size of the prostate gland generally increases with advancing age, primarily due to benign hyperplasia of both glandular and stromal tissue components. As the prostate enlarges, the total number of secretory epithelial cells increases, leading to higher serum PSA concentrations even in the absence of malignancy[5,6]. This physiological rise in PSA complicates the interpretation of test results, as elevated PSA levels cannot be attributed solely to prostate cancer. Consequently, differentiating between benign and malignant causes of PSA elevation based solely on PSA levels remains a major diagnostic challenge [7].

Understanding the quantitative relationship between prostate size and serum PSA levels is therefore critical to improving diagnostic accuracy. Studies conducted in various populations have consistently demonstrated a positive correlation between prostate size and PSA levels. For example, Aigbe *et al.[2]* reported a significant correlation between prostate volume and PSA among Nigerian men, suggesting that PSA may reflect gland size rather than malignancy alone. Similarly, Abotsi *et al*[8] in Ghana and Balagobi *et al*.[9] in Sri Lanka observed comparable trends, highlighting the universality of this relationship across different ethnic and geographic groups.

To address the limitations of total PSA measurement, researchers introduced the concept of PSA density (PSAD)**,** which is define as the ratio of serum PSA to prostate volume. PSAD provides a more refined diagnostic indicator by adjusting PSA levels according to gland size, allowing clinicians to differentiate benign from malignant conditions in patients with moderately elevated PSA values [10]. Numerous studies have confirmed that PSAD improves diagnostic specificity and reduces the rate of unnecessary prostate biopsies. For instance, Raza *et al[11]* demonstrated that a PSAD threshold of ≥ 0.15 ng/mL/cm³ enhanced diagnostic accuracy and minimized false-positive cancer diagnoses.

Recent investigations continue to refine this understanding. Salvi *et al*.[3] found that prostate volume was a stronger determinant of PSA elevation than age, emphasizing the need to interpret PSA in conjunction with gland size. Similarly**,** Neziri *et al*.[12] reported that PSA increases proportionally with both prostate size and age, supporting the integration of volume-adjusted PSA values in prostate cancer screening algorithms. A 2025 diagnostic model by Chou *et al*. [13] further demonstrated that combining PSA density with PSA kinetics significantly improved screening performance by reducing unnecessary biopsies and enhancing early cancer detection rates.

Despite these advancements, variability in the quantitative relationship between PSA and prostate size persists across populations, influenced by factors such as age, ethnicity, hormonal status, lifestyle, and measurement techniques. As a result, there is a growing need for population-specific studies to establish reliable reference ranges and diagnostic cutoffs tailored to local clinical settings. Assessing the quantitative relationship between prostate size and serum PSA levels is thus essential for refining diagnostic thresholds, reducing false-positive results, and improving prostate cancer screening accuracy. Such research contributes to more individualized patient care, better resource utilization, and improved outcomes in urological practice.

MATERIALS AND METHODS:

1. Study Design

A cross-sectional prospective study was conducted to assess the relationship between serum PSA values and prostate size. With this study design, data were collected from each patient at single point in time during the study.

2 Study Locations and Area

This study was carried out in Crescent Diagnostics Laboratory, Onitsha, Anambra State, Nigeria. It is privately own medical diagnostic centre, licensed and registered by the Anambra State Ministry of Health with registration number: MH/AWK/M: 47/7881/2016. The centre has a team of qualified specialists, including radiologist, sonologists, radiographers, cardiologist and medical laboratory scientists. The diagnostic centre receives an average of 356 patients annually, specifically those with prostate-related conditions.

Onitsha North LGA is situated in the northern part of Anambra, with its headquarters in GRA Niger Drive. The LGA shares boundaries with Onitsha South, Idemili North, and Ogbaru Local Government Area to the east. The population of Onitsha North LGA is approximately 261,075 people, as of the 2006 census.

3.3 Target Population

The target population comprises all males aged 40 years and over living in Onitsha North and Onitsha South Local Government Areas of Anambra State.

3.4 Sample Size

The sample size was determined using Cochran's formula 1975 (cited in Singh and Masuku, [14].Cochran's initial sample size (n_0) was calculated as:

$$n_o = \frac{Z^2 Pq}{e^2}$$

n_0 = required sample size

Z = confidence level at 95% (standard value of 1.96)

p = estimated population proportion (use 0.5 if unknown),

e = margin of error at 5% (standard value of 0.05).

q =1-p

$$n_o = \frac{1.96^2 X\ 0.5X0.5}{0.05^2} = 384.16 \approx 384$$

However, because the accessible populations of eligible patients attending the Crescent diagnostics laboratory are within average 356 per annual, which is less than 10,000, the finite population correction (FPC) was applied:

Considering the finite accessible population of N = 356 eligible patients, the sample size was adjusted using the finite population correction formula:

$$n_o = \frac{n_o}{1 + \frac{n_o - 1}{N}}$$

$$n_o = \frac{384}{1 + \frac{384-1}{356}} = \frac{384}{1 + \frac{383}{356}} = \frac{384}{1 + \frac{383}{356}} = \frac{384}{2.07584} = 184.9$$

$$n_o \approx 185$$

Therefore, the final minimum required sample size for this study was 185 participants**,** which was used for data collection and analysis.

3.5 Sampling Method

A consecutive sampling technique was adopted for this study. All eligible male patients who presented at Crescent Diagnostic Laboratory during the study period and consented to participate were recruited. The study procedure was clearly explained to each prospective participant, and only those who voluntarily agreed to undergo prostate ultrasound assessment and PSA testing were included. Participants who met the inclusion criteria were selected in the order in which they presented to the facility until the required sample size was attained. This method was considered appropriate because patients naturally reported to the diagnostic center for routine or symptom-driven prostate evaluation, and it allowed for the systematic inclusion of all consenting individuals without bias.

3.6 Inclusion criteria

i. All adults males above 40years of age without a lower urinary tract infection were included into the study, having given their consent to participate in the research.

ii. Patients with no pretreatment were included.

iii. Patients with no history of prostate cancer were included.

3.7 Exclusion criteria

i. All patients with contraindications to transrectal ultrasound, such as haemorrhoids and peri-anal infections were excluded.

ii. Patients with urinary catheters were excluded.

iii. Any patient who has had a recent digital a rectal examination, urethral instrumentation, or perineal trauma, or sexual intercourse within the previous of two weeks was excluded (Excluding patients who've had these activities within two weeks helps ensure more accurate PSA test result).

iv. Patients who declined to give consent were exclude

3.8 Ethical Consideration

Approval for the research design and protocol was obtained from the Research Ethics Committee of the Anambra State Ministry of Health (Ref:MH/PRS/1244/VOL.172). Additionally, both verbal and written consent were obtained from each patient before being enlisted for the study.

3.9 Instruments for data collection

Ultrasound scans of the participants' prostate glands and blood samples for PSA laboratory testing were obtained.

Transrectal Ultrasound (TRUS) System: A high-resolution Medison SONOACE X8 Ultrasound machine (MODEL; MNT-17 X8, MADE; Korean and YEAR: 2016) with a 7MHz endocavitary transrectal probe was used to visualize and measure the prostate gland. Prostate dimensions captured included: Length (cm) – measured in the sagittal plane, Height (cm) – measured in the sagittal plane, Width (cm) – measured in the axial plane

Prostate volume (PV) was calculated using the ellipsoid formula:

PV=0.52×L×H×W

PSA testing equipment: Venous blood samples were analyzed using a chemiluminescent immunoassay analyzer (CLIA)**.** The following biomarkers were recorded; Total PSA (TPSA), Free PSA (FPSA), Percentage free PSA and PSA density. Product: Snibe Diagnostic Maglumi 800, Model: Maglumi 800: Full automated chemiluminescence immunoassay (CLIA) analyzer designed for high-throughout clinical laboratory testing (PSA Testing). This equipment was manufactured in China on 20th March, 2021. Features; throughout: up to 180 tests/hour, 24 hours ready to use and time to first result: 17minutes. Specifications: Principle of luminescence, non-enzyme involved flash chemiluminescence long stability of reagents, and ABEl label, stable in acid and alkaline solution. Modes of operation: Random, Batch and STAT

Sample loading: Upto 40 sample tubes, continuous loading, STAT available, analyzer auto numbered, LIS connection and refrigerated sample area with independent power supply.

Reagent loading: Nine (9) reagents on board, continuous loading, RFID reading all info of reagents and refrigerated reagent area.

System Specifications: Dimension:145cm(W)x 75cm(D)x 135cm(H), Weight: Approximately 250kg (551Ibs) Power consumption 2.5kw , operating temperature: 20^{o}c to 30^{o}c (68^{o}F to 86^{o}F) and humidity: 50% to 80% RH

Procedure for data Collection

Data were collected on demographic characteristic using semi-structured questionnaires

3.10.2 PRE-EXAMINATION PREPARATION

Participants were instructed to empty their urinary bladder prior to scanning. They were asked to change into a hospital gown for the ultrasound procedure.

3.10.2.1 TRUS Examination Workflow

The participant was positioned in the left lateral decubitus position with knees flexed toward the chest. A sterile transducer sheath was placed over the TRUS probe, with ultrasound gel applied internally and externally to improve image quality and minimize discomfort. The probe was gently introduced through the anus under minimal pressure. The prostate was visualized in both axial and sagittal planes. Standardized measurements of length, width, and height were obtained. Prostate volume was calculated using the manually using the ellipsoid formula.

Prostate volume =$\frac{\pi}{6}$x height (anteroposterior) x width (transversal) x length (cephalocaudal)[15].

3.10.2.2 PSA Sample Collection Workflow:

Blood was drawn before prostate volume determination.

i. About 3–5 mL of venous blood was collected into serum separator tubes.
ii. Samples were centrifuged, and serum was analyzed within 2–3 hours.
iii. Total PSA and free PSA were quantified using CLIA.
iv. Percentage PSA and PSA density were computed.

Data Recording:

For each participant, the following were documented: Age, TRUS prostate measurements and calculated volume, TPSA, FPSA, %PSA, PSAD, Clinical diagnosis (Normal, BPH, Prostatitis, or

Prostate Cancer). Data were checked for accuracy before entry.

Methods of data analysis.

Data were analyzed using the SPSS Statistics Version 24 (IBM, Chicago, IL, USA). Descriptive statistical tools (mean, standard deviation, Median, mode, ranges, percentage, table, and figure. Inferential analysis: Pearson correlation was used assessed linear associations between PSA, age, and prostate volume, Natural log transformation was used to normalized highly skewed PSA and PV values to meet regression assumptions. Regression Models A and B quantified the influence of age and PV on PSA and showed that PV is the major predictor. Collinearity diagnostics ensured predictor stability. ANOVA confirmed the regression models were statistically significant. ROC analysis evaluated diagnostic performance of PSA and PSAD. Statistical significance was set at $p < 0.05$**.**

RESULTS

Table 1. Frequency and percentage distributions of demographic variables of the participants

Age Group (Years)	Number of participant	Percentage (%)
40-49	32	17.2
50-59	41	22.2
60-69	68	36.8
70-79	37	20.0
80-89	7	3.1
Total	**185**	**100**

From table 1 above, the highest proportion 68 (36.8%) of patients falling within the 60–69 years age category and the least 7(3.1%) are within age bracket of 80-89years**.** This distribution reflects the increased prevalence of prostate-related disorders with advancing age

Table 2. Presents descriptive statistics for prostate dimensions and volume, including mean ± SD, mode, median, range, and selected percentiles (5th, 25th, 75th, 95th).

Variable	Mean ± SD	Mode	Median	Minimum	Maximum	5^{th} Centile	25^{th} Centile	75^{th} Centile	95^{th} Centile
Prostate length(cm)	3.8 ± 1.4	3.0	3.4	1.3	9.2	2.1	2.8	4.5	6.4

Prostate width (cm)	4.8 ± 1.2	4.5	4.6	1.8	9.3	3.4	4.0	5.2	6.96
Prostate height (cm)	4.8 ± 1.1	4.0	4.6	2.4	9.2	3.4	4.0	5.4	6.94
prostate volume(cm^3)	54.5 ± 53.5	15.7	36.3	2.9	400.4	14.7	24.2	57.6	137.93

In table 2 above, the mean prostate volume was 54.5 ± 53.5, with a median of 36.3 cm^3 and an interquartile span from 24.2cm^3 (25^{th} percentile) to 57.6 cm^3(75^{th} percentile). The total range of observed volumes was from 2.9–400.4cm^3, which indicates substantial variation in gland size across the cohort. Linear dimensions averaged 3.8 ± 1.4 (length), 4.8 ± 1.2 (width), and 4.8 ± 1.1 (height), consistent with a cohort enriched for prostate-related conditions where enlargement is common.

Table 3 Descriptive statistics of prostate volume and ultrasound dimensions by diagnostic group

Diagnosis Group	**Number**	**Mean PV/STD (cm^3)**	**Minimum (cm^3)**	**Maximum (cm^3)**	**Mean Length/STD (cm)**	**Mean Width/STD (cm)**	**Mean Heigth/STD(cm)**
BPH	73	91.90±65.30	33.45	400.42	4.85±1.34	5.75±1.04	5.67±1.03
Cancer	13	57.08±47.15	16.82	181.82	3.98±1.39	4.85±1.18	4.88±1.10
Normal	62	24.01±9.33	2.94	49.38	2.87±0.64	3.90±0.62	3.96±0.54
Prostatitis	37	31.13±14.77	13.83	103.15	3.13±0.86	4.30±0.54	4.32±0.70

From the Benign Prostatic Hyperplasia (BPH) group (n=73), the mean prostate volume was 91.90 ml (SD = 65.30), with a minimum of 33.45 ml and a maximum of 400.42 ml. The mean prostate length was 4.85cm (SD=1.34, range =2.90-9.20cm), mean width was 5.75cm (SD=1.04, range=4.30-9.30cm), and mean height was 5.67cm (SD=1.03, range =4.20-9.20cm). From the Cancer group (n= 13), the mean prostate volume was 57.08 ml (SD = 47.15), with a minimum of 16.82 ml and a maximum of 181.82 ml.

The mean prostate length was 3.98cm (SD=1.39, range =2.20-6.50cm), mean width was 4.85cm (SD=1.18, range= 3.20-7.50cm), and mean height was 4.88cm (SD=1.10, range =3.50-7.40cm). Their mean gland measurements remained relatively lower than BPH but higher than normal prostates. From the Normal group (n= 62), the mean prostate volume was 24.01 ml (SD = 9.33), with a minimum of 2.94 ml and a maximum of 49.38ml. The mean prostate length was 2.87cm (SD=0.64, range =1.30-4.60cm), mean width was 3.90cm (SD=0.62, range= 1.80-5.20cm), and mean height was 3.96cm (SD=0.54, range =2.40-5.40cm). From the Prostatitis group (n= 37), the mean prostate volume was 31.13 ml (SD = 14.77), with a minimum of 13.83 ml and a maximum of 103.15ml. The mean prostate length was 3.13cm (SD=0.86, range =1.90-5.80cm), mean width was 4.30cm (SD=0.54, range= 2.80-cm), and mean height was 3.96cm (SD=0.54, range =2.40-5.40cm).

Table 4 Descriptive Analysis of Antigen Parameters (PSA Metrics) : summaries the distribution of antigen parameters—Total PSA, Free PSA, % Free PSA and PSA Density (PSAD)—with counts, mean ± SD, mode, median, range, and selected percentiles (5th, 25th, 75th, 95th).

Parameter	Mean ± SD	Mode	Median	Minimum	Maximum	P5	P25	P75	P95
Total PSA (ng/mL)	14.56 ± 45.20	0.36	2.25	0.06	400.00	0.26	0.92	7.41	57.19
Free PSA (ng/mL)	2.47 ± 7.23	0.04	0.50	0.01	60.00	0.08	0.26	1.09	9.16
% Free PSA (%)	25.84 ± 15.33	15.00	21.90	5.30	85.30	7.40	14.80	33.30	57.62
PSA Density (ng/mL/mL)	0.23 ± 0.55	0.11	0.06	0.00	3.86	0.01	0.03	0.15	0.93

From table 4 Total PSA showed 14.56 ± 45.20 with a median of 2.25 and a range of 0.06–400.00 ng/mL. Free PSA had 2.47 ± 7.23 and a median of 0.50 ng/mL; dispersion (P25–P75) was 0.26–1.09 ng/mL. % Free PSA centred on a median of 21.90% with interquartile spread 14.80–33.30%. PSA density (PSAD) averaged 0.23 ± 0.55 with median 0.06 and ranges 0.00–3.86 ng/mL/mL.

Table 5 PSA and PSAD by prostate related conditions

Condition Group	Number	Mean TPSA(ng/mL)	Mean PSAD ($ng/mL/cm^3$)	Mean %free PSA
Cancer	13	76.9	1.38	14.7
BPH	73	19.8	0.19	21.3
Normal	62	2.29	0.10	24.9
Prostatitis	37	2.94	0.10	40.4

From table 5 Mean total PSA was highest among patients with prostate cancer (M = 76.9 ng/mL), followed by those with BPH (M = 19.8 ng/mL), prostatitis (M = 2.94 ng/mL), and normal prostates (M = 2.29 ng/mL). PSA density showed a similar pattern, with the highest values observed in cancer (M = 1.38 ng/mL/cm³) and intermediate values in BPH (M = 0.19 ng/mL/cm³), whereas normal and prostatitis groups had comparatively low densities (both ≈ 0.10 ng/mL/cm³). Percentage free PSA was highest in prostatitis (M = 40.4%) and lowest in cancer (M = 14.7%).

Table 6 Cross –Tabulation of Age Groups with Mean Prostate Volume, Total PSA, PSAD Density.

Age Group (years)	Number	Mean Prostate Volume(cm^3)	Mean Total PSA (ng/mL)	Mean PSAD Density ($ng/mLcm^3$)
40-49	32	28.9	1.43	0.051
50-59	41	38.7	3.55	0.091
60-69	68	67.8	22.51	0.192
70-79	37	93.2	18.67	0.148
80-89	7	112.9	20.36	0.181
Total	**185**	**54.5**	**14.60**	**0.226**

From the table 6, the mean of prostate volume increased from 28.9 cm^3 in the 40-49 year group to 112.9 cm^3in the 80-89year group, demonstrating a clear age-related trend of prostatic enlargement. The results indicate a progressive increase in prostate volume and PSA indices with advancing age. Similarly, the mean PSA level raised significantly with age, from 1.43ng/mLin the youngest eligible

group (40-49 years) to 20.36ng/mL among patients aged 80-89 years. PSA density showed a related pattern, increasing from 0.051 ng/mL/cm^3 in the 40-49 year age group to 0.181ng/mL/cm^3 in those aged 80-89 years. The highest PSA density values were recorded in the 60-69 year group (0.192 ng/mL/cm^3), which also had the largest number of prostate cancer cases. This suggests that both PSA and PSA density increase with age, but their diagnostic utility may peak in the 60-69 year range, which is also the group most affected by malignant prostate pathology.

Table 7 Correlations between PSA and age and prostate volume

Pair	Pearson r	Pearson p-values
TPSA vs Age	0.2216	0.0024
TPSA vs PV	0.4029	0.001

TPSA versus Age: There was a weak positive correlation between participant's serum PSA and age. The pearson correlation coefficient (r) is 0.2216, and the p-value is 0.0024.This means that as age increases, PSA levels tend to increase, but the relationship is not extremely strong(Table7)

TPSA versus Prostate Volume: There was a moderate positive correlation between participants PSA levels and prostate volume. The Pearson correlation coefficient (r) is 0.4029, and the p-value is 0.001.

REGRESSION EQUATION:

Using TPSA as the dependent variable and AGE + PROSTATE VOLUME (PV) as predictors:

TPSA=−20.37+0.289(Age)+0.317(PV)

TABLE 8a. MODEL SUMMARY

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	0.408	0.166	0.157	40.41

- R = 0.408
- R^2 = 0.166 → Age + PV together explain 16.6**%** of the variance in TPSA.
- Adjusted R^2 = 0.157

TABLE 8b. (Coefficient table)

Mode A: PSA~Age +PV (Linear OLS)

Predictor	B (Coeff.)	Std.Error	T	Sig.(p)	95% Cl for B (Lower, Upper)
Constant	-20.37	18.29	-1.11	0.266	(-56.40,15.65)
Age	0.289	0.312	0.93	0.357	(-0.33, 0.91)
PV	0.317	0.067	4.74	<0.001	(0.19, 0.44)

As shown in table 8a and 8b above, the overall regression model was statistically significant, indicating that age and prostate volume together significantly predicted TPSA levels ($F(2, 182) = 18.15$, $p < 0.001$). The model accounted for 16.6% of the variance in TPSA ($R = 0.408$, $R^2 = 0.166$, Adjusted $R^2 = 0.157$). This shows that, although the model significantly explains variation in TPSA, a substantial proportion of the variability is attributable to other factors not included in the model. The estimated regression equation for the prediction of TPSA was:

TPSA=−20.37+0.289(Age)+0.317(Prostate Volume)

As shown by the regression coefficients, prostate volume was a statistically significant independent predictor of TPSA levels ($B = 0.317$, $t = 4.74$, $p < 0.001$). This implies that, after controlling for age, each 1 cm^3 increase in prostate volume was associated with an average increase of approximately 0.317 ng/mL in TPSA. In contrast, age did not emerge as a statistically significant predictor of TPSA in the presence of prostate volume ($B = 0.289$, $t = 0.93$, $p = 0.357$). This suggests that, when prostate volume is held constant, increasing age alone does not significantly change TPSA levels in this study population. The regression analysis demonstrates that prostate volume has a significant positive influence on serum TPSA, whereas age does not independently predict TPSA when prostate volume is taken into account. This finding supports the view that prostate size is an important determinant of PSA production and should be considered when interpreting PSA values in clinical practice.

Model B: ln(PSA) ~ Age + ln(PV) (Linear OLS)

(Log transformed Regression)

Using all 185 patients and taking natural logs of PSA and prostate volume (PV):

Regression equation (Model B), $\ln(PSA)=\beta0+\beta1(Age)+\beta2\ln(PV)$

Estimated coefficients (rounded):

- Intercept (β_0) = −5.581
  - SE = 0.824
  - t = −6.78
  - $p < 0.001$
  - Age (β_1) = 0.035 per year, SE = 0.009, $t = 3.68$, $p < 0.001$, ln(PV) (β_2) = 1.218, SE = 0.133,$t = 9.17$, $p < 0.001$

Model fit: $n = 185$, $R^2 = 0.460$, Adjusted $R^2 = 0.453$, $F(2, 182) = 77.48$, $p < 0.001$
After natural log transformation of serum PSA and prostate volume, multiple linear regression demonstrated that both age and ln(prostate volume) were independent predictors of ln(PSA). The overall

model was statistically significant ($F(2,182) = 77.48$, $p < 0.001$) and explained approximately 46.0% of the variance in ln(PSA) ($R^2 = 0.460$, adjusted $R^2 = 0.453$). An increase of one year in age was associated with an average increase of 0.035 units in ln(PSA) ($p < 0.001$), while a one-unit increase in ln(prostate volume) was associated with an average increase of 1.218 units in ln(PSA) ($p < 0.001$), after controlling for age.

Rewrite the equation:

$\ln(PSA) = -5.581 + 0.035 \times Age + 1.218 \times \ln(PV$

TABLE 10 ANOVA (Regression Significance test)

Source	Df	F	Sig.(p-value)
Regression	2	18.15	P<0.001
Residual	182		
Total	184		

The overall regression model is statistically significant ($F(2,182)=18.15$, $p<0.001$)

Table 11 Collinearity Diagnostics – Model A (Age and PV)

Predictor	VIF	Tolerance
Age	2.31	0.43
PV	2.31	0.43

Collinearity diagnostics for Model A, which included age and prostate volume as predictors, showed variance inflation factors (VIF) of 2.31 for both variables, with corresponding tolerances of 0.43. These values are below the commonly used VIF threshold of 10, indicating no serious multicollinearity between age and prostate volume in the untransformed model

Table 12 Collinearity Diagnostics – Model B (Age and ln(PV)

For Model B (predictors: Age and ln (PV)), the collinearity statistics were:

Predictor	VIF	Tolerance
Age	24.90	0.040
In(PV)	24.90	0.040

In contrast, collinearity diagnostics for Model B, which included age and the natural logarithm of prostate volume [ln(PV)], revealed marked multicollinearity. The VIF values for both age and ln(PV) were 24.90, with corresponding tolerances of 0.04. These values exceed the conventional VIF cut-off of 10 and tolerance cut-off of 0.1, suggesting that age and ln(PV) are highly collinear in this specification. Although Model B demonstrated good overall explanatory power for ln(PSA), the high collinearity between age and ln(PV) should be considered when interpreting individual regression coefficients.

Table 13 To establish evidence-based thresholds for PSA and PSAD that enhance diagnostic accuracy and reduce unnecessary interventions.

Marker	AUC	Optimal Threshold (Youden J)	Sensitivity @ Opt	Specificity @ Opt	Threshold @ 90% Sens
PSA	0.899	12.72	0.846	0.872	3.942
PSAD	0.941	0.214	1.0	0.884	0.214

Table 13 shows the performance of theses markers using various statistical measures. Analyses were conducted to determine optimal diagnostic cut-off values capable of distinguishing malignant from non-non-malignant prostate conditions. The convection PSA cut-off value of ≥ 4.0 ng/mL

demonstrated high sensitivity (92.3%) but low specificity (68.0%) leading to a high rate of unnecessary interventions. Increasing the PSA threshold to ≥ 12.72 ng/mL improved specificity to 87.2%, but sensitivity was slightly reduced to 84.6%, reducing false positive. PSA density (PSAD) at the common cut-off value of ≥ 0.15 ng/mLcm^3 yielded 100% sensitivity and 81.4 % specificity.

The optimal PSAD cut-off identified in this study was ≥ 0.214 ng/mL/cm^3, which achieved 100% sensitivity and 88.4% specificity, making it the most reliable single marker for distinguishing malignant cases. In this cohort, increasing PSAD cut-off from 0.15 to approximately 0.21 keeps sensitivity at 100% while improving specificity.

ROC Curves

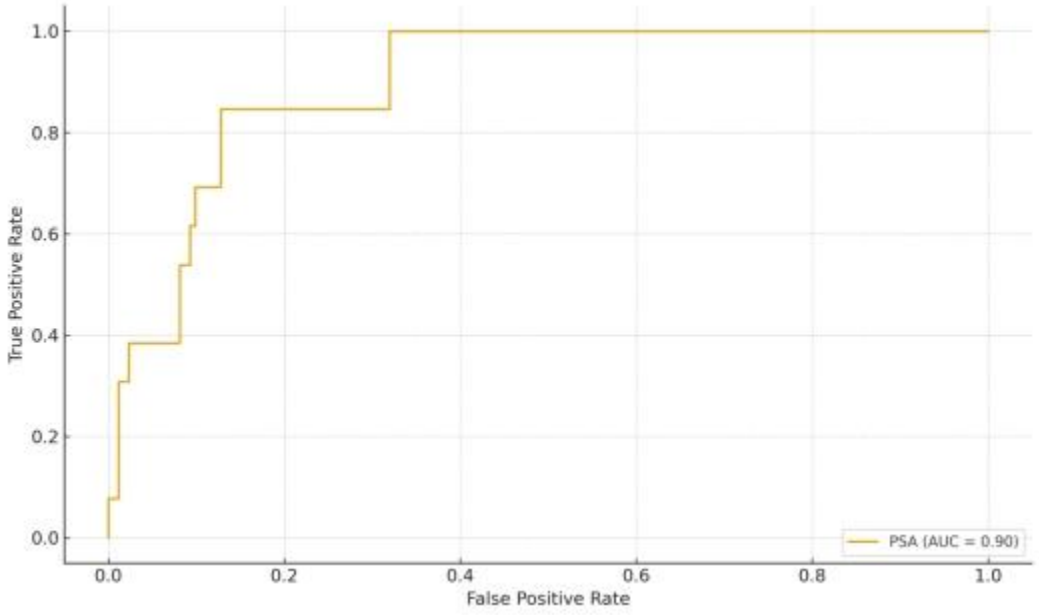

Figure 1. Receiver Operating Characteristic (ROC) for PSA.

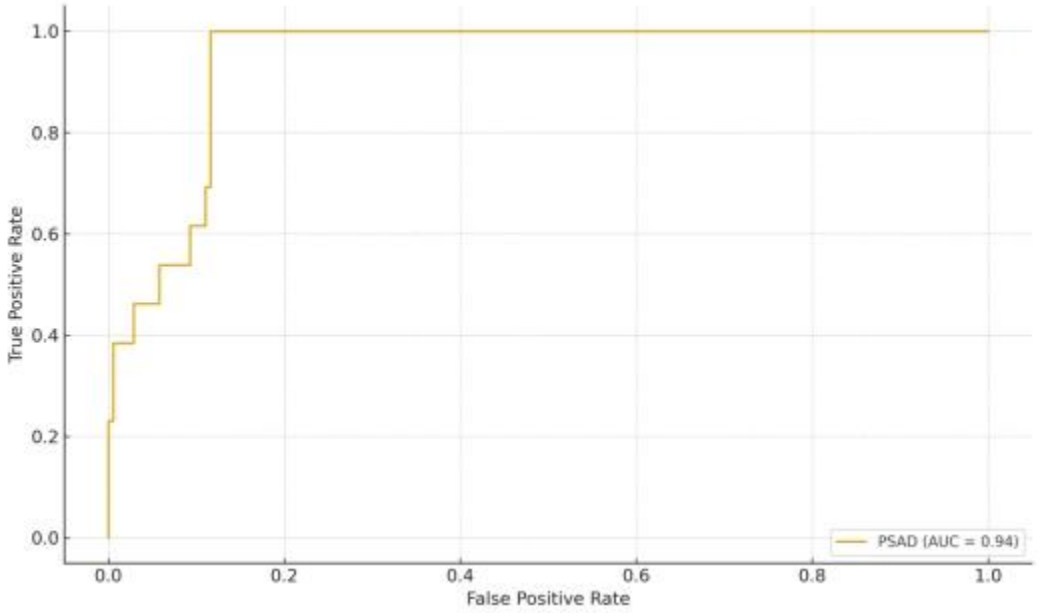

Figure 2. Receiver Operating Characteristic (ROC) for PSAD.

From the Receiver operating characteristic (ROC) curves analysis was performed to evaluate the diagnostic performance of TPSA and PSAD in distinguishing prostate cancer from benign conditions (BPH, prostatitis and normal prostates). Cancer status was coded as 1 and non-cancer as 0. The area under the ROC curve (AUC) for TPSA was 0.90, indicating excellent discriminatory ability. PSAD showed an even higher AUC of 0.94, suggesting superior performance compared with TPSA alone.

Using the Youden index, an optimal TPSA cut-off of approximately 12.7 ng/mL yielded a sensitivity of 84.6% and a specificity of 87.2%. For PSAD, the optimal threshold was about 0.21 ng/mL/cm³, which achieved 100% sensitivity and 88.4% specificity. Thus, PSAD demonstrated very high rule-out capacity, as no cancer cases in this cohort had PSAD values below 0.21 ng/mL/cm³. These results support the use of PSAD, with a threshold around 0.20–0.21 ng/mL/cm³, as an evidence-based clinical decision limit in this population, while a TPSA threshold in the range of 10–13 ng/mL also provides good discrimination between malignant and benign disease."

PROPOSED CLINIC THRESHOLDS ARE:

From ROC curve analysis, the evidence-based clinic thresholds derived in this cohort were a TPSA cut-off of about 12.7 ng/mL and a PSAD cut-off of about 0.21 ng/mL/cm³ **(**gave 100% sensitivity and high specificity) for discriminating prostate cancer from benign prostate conditions.

DISCUSSIONS

This study confirms that prostate-related disorders in this cohort are predominantly diseases of older men, with a mean age of 61.1±10.72 years and the highest burden in the 60–69 year group. This age pattern is consistent with international and regional data showing that the incidence and prevalence of benign prostatic hyperplasia (BPH) and prostate cancer rise steeply after the sixth decade of life[1,16,17] African series from Nigeria and other sub-Saharan settings similarly report peak presentation in the seventh

decade, often with advanced disease and large glands[15,18-20] . These parallels suggest that the age structure and clinical profile of the present cohort are broadly representative of men with prostate disease in comparable low- and middle-income settings.

The sonographic findings demonstrated marked heterogeneity in gland size, with an overall mean prostate volume of 54.5 ±53.5cm³ (range 2.9–400.4 cm³). As expected, volumes were largest in BPH (mean 91.9 cm³), intermediate in cancer (57.1 cm³), and lowest in normal prostates (24.0 cm³), with prostatitis occupying an intermediate range (31.1 cm³). This pattern agrees with reports from Abotsi et al.[8] in Ghana and Aisuodionoe-Shadrach et al.[21] in Nigeria, who documented mean prostate volumes exceeding 80 cm³ in BPH patients and approximately 20–30 cm³ in men with normal prostates. The present study therefore confirms that prostate volume alone is not a reliable discriminator of malignancy, as large prostate size is more strongly associated with benign hyperp. Age-related increases in prostate volume in this study—from 28.9 cm³ at 40–49 years to 112.9 cm³ at 80–89 years—mirror age-related growth curves reported in Asian and African populations [5,6,22]. Together, these findings reinforce that sonographic volume is a robust marker of age-related prostatic remodeling in this population.

The overall mean total prostate-specific antigen (TPSA) recorded in this study was 14.56 ± 45.20 ng/mL, with a median of 2.25 ng/mL, indicating a positively skewed distribution due to extremely high PSA values among cancer patients. With respect to antigenic markers, the study demonstrated a clear gradient in total PSA and PSA density (PSAD) across diagnostic groups. Mean total PSA was highest in cancer (76.9 ng/mL), followed by BPH (19.8 ng/mL), and was much lower in prostatitis (2.94 ng/mL) and normal prostates (2.29 ng/mL). PSA density showed an analogous trend, with cancer cases averaging 1.38 ng/mL/cm³ and BPH 0.19 ng/mL/cm³, whereas normal and prostatitis groups clustered around 0.10 ng/mL/cm³.These gradients are consistent with the biological expectation that malignant glands produce disproportionally higher PSA per unit volume than benign hyperplasia, while inflammatory and normal prostates generate lower PSA output, particularly when adjusted for gland size[5,10,23] . The markedly reduced percentage free PSA in cancer (mean 14.7%) compared with prostatitis (40.4%) in this cohort is also in line with reports that free-to-total PSA ratios are significantly lower in malignant disease and can complement PSAD in risk stratification[24,25]..

Correlation and regression analyses further underline the central role of prostate volume as a determinant of PSA biology. In this study, total PSA correlated only weakly with age ($r = 0.22$) but showed a moderate correlation with prostate volume ($r = 0.40$). In the multiple linear regression using untransformed variables, prostate volume was an independent predictor of PSA ($B = 0.317$, $p < 0.001$), whereas age lost significance when volume was included, and the model explained 16.6% of PSA variance. After log transformation, both age and ln(volume) became significant predictors of ln(PSA), and the model fit improved substantially ($R^2 = 0.46$).

These findings are in keeping with recent studies showing strong volume–PSA coupling in BPH and mixed cohorts, with age effects largely mediated through gland size[5,8,12,26-28],. Systematic reviews of age-specific PSA also indicate that while PSA tends to rise with age, the predictive value of age alone is modest, and adjustment for prostate volume yields more clinically meaningful risk estimates [6,29-31].

The collinearity diagnostics in this dataset are noteworthy. In the unlogged model (age and prostate volume in original units), variance inflation factors were modest (VIF = 2.31), indicating acceptable independence between predictors. However, when age and ln(volume) were combined in the log–linear model, VIF values increased markedly (24.9), reflecting strong collinearity between age and transformed prostate size. This statistical behavior reflects the biological reality that gland growth is strongly age-linked and cautions against over interpreting individual regression coefficients when both age and ln(volume) are included in the same model. Contemporary imaging-based studies that automate volume estimation for PSAD calculation also highlight the tight coupling of age, prostate size,

and PSA and recommend careful model specification to avoid instability in multivariable analyses [32,33].

The most clinically important contribution of this study is the evaluation of diagnostic thresholds for PSA and PSAD. In line with international guidelines, the conventional PSA cut-off of ≥ 4.0 ng/mL showed high sensitivity (92.3%) but limited specificity (68.0%), implying a substantial burden of unnecessary biopsies and anxiety [34]. Raising the PSA threshold in this cohort to approximately 12.7 ng/mL improved specificity to 87.2% while maintaining acceptable sensitivity (84.6%). This aligns with recent work suggesting that in high-prevalence, low-resource populations, higher PSA cut-offs may be appropriate to prioritise men at greatest risk of clinically significant cancer and reduce overdiagnosis [19]. PSA density performed even better than total PSA in this study. The AUC for PSAD (0.94) exceeded that of PSA (0.90), and the commonly used PSAD threshold of ≥ 0.15 ng/mL/cm³ achieved 100% sensitivity but only 81.4% specificity. The optimal PSAD cut-off in this cohort was about 0.21 ng/mL/cm³, which preserved 100% sensitivity and improved specificity to 88.4%; importantly, no cancer case had a PSAD below 0.21. These observations concur with multiple contemporary studies and meta-analyses showing that PSAD outperforms PSA alone for detecting clinically significant disease and can meaningfully reduce unnecessary biopsies, particularly in the PSA "grey zone[11,23,35,36]. Current guideline updates increasingly emphasise PSAD cut-offs of 0.15–0.20 ng/mL/cm³ when integrating MRI, biomarkers and risk calculators into biopsy decisions[32,33] . The slightly higher optimal cut-off identified in the present Nigerian cohort (≈0.21) may reflect differences in gland size, tumour biology, and referral patterns compared with Western populations and underscores the value of locally derived thresholds. The commonly used PSA threshold of 4.0 ng/mL demonstrated high sensitivity but poor specificity, confirming earlier reports by Chung et al.[37] . The higher PSA density threshold observed in this study is comparable to findings by Peng et al[38], who reported optimal PSAD cut-offs between 0.20 and 0.30 ng/mL/cm³, and supports the need for population-specific diagnostic thresholds.

Overall, the present findings support the central study objectives by demonstrating that prostate volume is the dominant structural correlate of PSA, that PSA and PSAD both rise with age and malignant pathology, and that PSAD, particularly around a threshold of 0.20–0.21 ng/mL/cm³, provides excellent discrimination between malignant and benign conditions in this population. When interpreted alongside recent regional and global literature, these results argue for routine incorporation of sonographic prostate volume and PSAD into diagnostic pathways, rather than reliance on total PSA alone, to improve risk stratification and reduce unnecessary interventions in men presenting with prostate-related symptoms.

CONCLUSION

This study confirms that prostate volume strongly influences PSA levels and improves diagnostic accuracy when combined with PSA as PSA density. Prostate cancer patients tend to have disproportionately higher PSA and PSAD irrespective of gland size, distinguishing them from BPH and normal cases. While age alone was not a strong predictor of PSA, its effect was mediated through increasing prostate volume. These findings underscore the importance of incorporating prostate volume (sonographically measured) into diagnostic protocols to avoid unnecessary biopsies, particularly in borderline PSA (4–10 ng/mL) cases. The study proposes locally relevant diagnostic thresholds**:** PSAD ≥ 0.21 ng/mL/cm³ — highly predictive of prostate cancer in this population.PSA ≥ 12.7 ng/mL — Increased specificity for malignancy in the Nigerian cohort. These thresholds offer improved risk stratification compared to the conventional PSA ≥ 4 ng/mL worldwide standard. Incorporating PSAD, %fPSA, and prostate volume improves diagnostic accuracy and reduces overtreatment.

Conflict of interest: None declared among the authors

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