

## ORIGINAL ARTICLE

# Prostate Volume and PSA Trends – Clinical Predictors of Malignancy in Benign and Malignant Prostatic Diseases

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**ABSTRACT**

**Background:** Prostate volume (PV) and prostate-specific antigen (PSA) are widely used clinical parameters in evaluating prostatic diseases. While PSA levels may increase in both benign and malignant conditions, smaller prostate volumes combined with elevated PSA improve malignancy prediction. Identifying reliable predictors is essential for timely diagnosis and appropriate management. **Aim of the study:** To evaluate the role of prostate volume and PSA trends as clinical predictors of malignancy in patients presenting with benign and malignant prostatic diseases. **Methods & Materials:** A prospective study was conducted at BIRDEM General Hospital, Dhaka, Bangladesh from July 2017 to June 2019. A total of 110 men aged  $\geq 50$  years with suspected prostatic disease underwent clinical assessment, transabdominal ultrasonography for prostate volume estimation, serum PSA measurement, and systematic prostate biopsy. Histopathology served as the diagnostic reference standard. Data were analyzed using SPSS version 26.0. Logistic regression identified independent predictors of malignancy. Diagnostic performance was evaluated through sensitivity, specificity, PPV, NPV, and accuracy.

**Result:** Malignancy was confirmed in 15.45% of participants. Malignant cases had significantly higher mean PSA levels ( $25.48 \pm 11.62$  ng/mL) and larger PV ( $57.4 \pm 16.2$  mL). PSA  $> 10$  ng/mL was the strongest predictor (OR 27.8;  $p < 0.001$ ), followed by PV Grade III/IV (OR 3.2;  $p = 0.02$ ). PSA  $> 10$  ng/mL demonstrated high specificity (94.6%) and accuracy (89.1%), while combining PSA  $> 10$  with PV Grade III/IV increased specificity to 97.8%.

**Conclusion:** PSA remains the strongest predictor of malignant prostatic disease, and incorporating prostate volume enhances diagnostic precision. Larger multicenter studies are encouraged.

**Keywords:** Prostate volume, PSA, Prostate cancer, Benign prostatic hyperplasia, Diagnostic predictors

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**INTRODUCTION**

Prostate volume (PV) measures the size of the prostate, usually in  $\text{cm}^3$  via imaging, while prostate-specific antigen (PSA) is a protein whose blood levels help screen for prostate conditions like benign prostatic hyperplasia (BPH) and prostate cancer. Globally, smaller prostate volumes, particularly those under  $45 \text{ cm}^3$  and more so below  $26 \text{ cm}^3$ , are associated with a significantly higher likelihood up to about 69% of prostate cancer when PSA density exceeds  $0.15 \text{ ng/mL/cm}^3$  [1]. In Bangladeshi, men evaluated for prostate disease, about 16% of prostate tissue specimens submitted for histopathology are found to be malignant, while roughly 82% are benign changes [2]. Prostate volume indicates the size of the prostate and can be measured via ultrasonography or MRI. Transrectal ultrasound (TRUS) estimates PV using the ellipsoid formula, while MRI employs semiautomatic or deep learning-based 3D segmentation for more precise measurements. Both methods slightly underestimate true

pathological volume, though MRI generally shows higher accuracy and stronger correlation with surgical specimens [3,4]. In benign prostatic hyperplasia, PV typically increases due to enlargement of the transition zone, whereas in prostate cancer, changes in zonal volumes, such as altered ratios between the peripheral and transition zones, can help differentiate malignant from benign conditions. Although larger prostate volume is often associated with benign disease, cancer can also occur in larger prostates, so PV alone is not definitive for diagnosis; it serves as a useful factor to stratify risk when combined with other clinical parameters like PSA levels and imaging biomarkers [5]. PSA is a protein biomarker secreted by prostate tissue, widely used in clinical practice to screen for and monitor prostate diseases. PSA levels correlate with prostate pathology, generally increasing in both benign conditions like BPH and malignant prostate cancer, but the patterns and implications differ [6]. Trends in PSA, such as rising levels over time (PSA velocity) or the ratio

of free to total PSA, help improve malignancy prediction beyond a single measurement, with PSA density providing additional risk stratification [7]. Combining prostate volume with PSA measurements, especially PSA density, improves the prediction of malignancy and helps guide biopsy decisions, as higher PSA density is associated with more aggressive cancer and advanced pathological stages [8]. However, challenges remain, including variability in PSA due to non-cancer factors and limitations in imaging accuracy for PV measurement, which can affect PSA density calculations [6]. While MRI offers more precise prostate volume measurements than ultrasound, limited availability makes ultrasound more common; combining PSA, PV, and other biomarkers improves early detection and risk stratification, but must be interpreted cautiously to prevent overdiagnosis [9]. Although national surveys report on NCDs, nutrition, and demographics in Bangladesh, detailed population-specific data across regions and subgroups remain limited, with urban-rural disparities often masked by aggregated national statistics [10]. This study aimed to evaluate the role of prostate volume and PSA trends as clinical predictors of malignancy in patients with benign and malignant prostatic diseases.

## MATERIALS & METHODS

This study, conducted from July 2017 to June 2019 at BIRDEM General Hospital, Dhaka, Bangladesh. The study aimed to evaluate prostate volume and PSA trends as predictors of malignancy in patients presenting with suspected prostatic disease. A total of 110 consecutive male patients were enrolled. Patients were clinically evaluated and categorized into:

- Benign prostatic disease group (n=93)
- Malignant prostatic disease group (n=17)

Diagnosis was confirmed by histopathological examination following prostate biopsy.

### Inclusion Criteria

- Men aged 50 years and above
- Patients with symptoms of elevated PSA
- Patients who underwent biopsy with available histopathology reports

### Exclusion Criteria

- Prior history of prostate cancer
- Patients who received 5-alpha reductase inhibitors, androgen therapy, or previous prostate surgery
- Active urinary tract infection or prostatitis at the time of evaluation

### Ethical Considerations

Ethical approval was obtained from the Institutional Review Board of BIRDEM General Hospital. Written informed consent was collected from all participants.

### Biopsy and Histopathological Processing

All patients underwent systematic prostate biopsy following clinical and radiological evaluation. The biopsy specimens were immediately fixed in 10% formalin and submitted to the Department of Pathology for histopathological examination. Tissue samples were processed using the routine paraffin-embedding technique, which included overnight fixation, graded dehydration through ascending concentrations of alcohol, clearing in xylene, and embedding in paraffin wax. Paraffin blocks were sectioned at a thickness of 3–5  $\mu\text{m}$  using

a rotary microtome, and the sections were mounted on glass slides. The slides were subsequently deparaffinized in xylene, rehydrated through graded alcohol, and stained using Harris's hematoxylin followed by differentiation in acid alcohol and counterstaining with eosin. After staining, the sections were dehydrated, cleared, and mounted using DPX. Microscopically, nuclei stained blue, cytoplasm appeared pink to red, collagen and muscle fibers showed pink coloration, and red blood cells appeared bright red. Final histopathological diagnosis of benign or malignant prostatic disease was made based on evaluation of glandular architecture, cellular morphology, and nuclear atypia and was considered the reference standard for disease classification.

### Data Collection

Data were collected prospectively. Demographic data included age at presentation. Clinical data were obtained through direct patient interviews and physical examination and included the presence of lower urinary tract symptoms such as burning sensation during micturition, increased urinary frequency, dribbling of urine, fever, hesitancy, urgency, and acute urinary retention. Laboratory data included serum prostate-specific antigen (PSA) levels, measured using a standardized immunoassay protocol in the hospital laboratory. PSA values were documented as continuous variables and further categorized into three groups (0–5 ng/mL, 5.1–10 ng/mL, and >10 ng/mL) for analysis. Radiological data consisted of prostate volume measurements obtained by transabdominal ultrasonography (USG). Prostate size values were recorded in milliliters and classified into four grades: Grade I (20–30 g), Grade II (31–50 g), Grade III (51–80 g), and Grade IV (>80 g). Histopathological data were obtained from prostate biopsy specimens processed in the Department of Pathology. Final diagnosis was categorized as either benign prostatic disease or malignant prostatic adenocarcinoma and used as the reference standard for statistical analysis. All collected data were cross-checked for completeness and accuracy before statistical entry.

### Statistical Analysis

Data analysis was performed using SPSS version 26.0. Continuous variables were summarized as mean  $\pm$  standard deviation and compared between benign and malignant groups using the independent samples t-test. Categorical variables were presented as frequencies and percentages and analyzed using the chi-square test or Fisher's exact test when appropriate. Binary logistic regression was employed to identify independent predictors of malignant disease, and results were expressed as adjusted odds ratios (OR) with 95% confidence intervals (CI). The diagnostic accuracy of major predictors was evaluated by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) using standard 2 $\times$ 2 contingency tables. A p-value of <0.05 was considered statistically significant.

### RESULT

Figure 1 shows that most patients had benign prostatic diseases 74.55%, while malignant prostatic disease accounted for 25.45%. Similarly benign cases had a mean age of 67.1 $\pm$ 9.0 years, while malignant cases were slightly older at 70.5 $\pm$ 7.8 years (p=0.12) (Table I). Increased frequency appeared in 100% of both groups. Burning sensation was reported by 50.54% of benign vs 64.71% of malignant cases (p=0.32). Fever was notably lower in malignant (5.88%) than benign (24.73%) (p=0.08). Other symptoms dribbling (86.02% vs 88.24%), hesitancy (80.65% vs 88.24%), urgency (93.55% vs

88.24%) and urinary retention (79.57% vs 88.24%) were similar between groups.

Table II indicates that among the patients were more frequent in Grade I at 37.63% and Grade II at 41.94%, while malignant cases were higher in Grade III at 47.06% and Grade IV at 11.76%. Mean prostate volume was greater in malignant at 57.4 ± 16.2 mL compared to 44.8 ± 18.5 mL in benign. PSA trends showed 81.72% of benign in the 0–5 range, 12.90% in 5.1–10, and 5.38% above 10, whereas malignant patients had 23.53% in 0–5, 11.76% in 5.1–10, and 64.71% above 10, with a significantly higher mean PSA of 25.48±11.62 ng/mL.

PSA above 10 ng/ml showed the strongest association with malignancy, with an odds ratio of 27.8 and a confidence interval of 7.9–97.5 (Table III). Prostate Grade III or IV also increased risk, with an odds ratio of 3.2 and a confidence interval of 1.2–8.4. Age over 70 years (OR 1.7, 0.6–5.0), burning sensation (OR 1.8, 0.6–5.5), and urinary retention (OR 1.5, 0.4–5.1). Table IV demonstrates that PSA above 10 ng/ml showed good diagnostic performance, with a sensitivity of 64.7%, specificity of 94.6%, positive predictive value of 68.8%, negative predictive value of 93.3%, and overall accuracy of 89.1%. Prostate Volume Grade III/IV had moderate sensitivity of 58.8% and specificity of 79.6%, with PPV of 34.5%, NPV of 91.3%, and accuracy of 76.4%. Combining PSA above 10 ng/ml with Grade III/IV increased specificity to 97.8% and PPV to 80%, with overall accuracy of 89.1%.

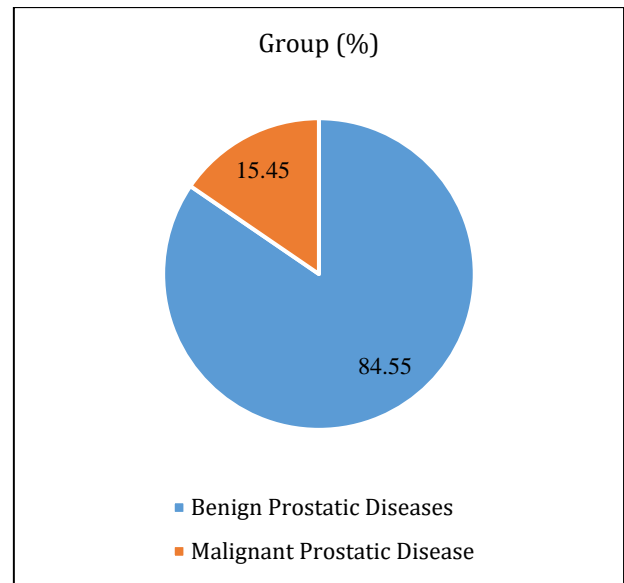


Figure - 1: Distribution of study participants by group (n=110)

Table - I: Baseline characteristics by disease group (n=110)

Variable	Benign (n=93)		Malignant (n=17)		P-value
	n	%	n	%	
Age (years), Mean ± SD	67.1 ± 9.0		70.5 ± 7.8		0.12
<b>Complications</b>					
Burning sensation	47	50.54	11	64.71	0.32
Increased frequency	93	100.00	17	100.00	1
Dribbling of urine	80	86.02	15	88.24	0.81
Fever	23	24.73	1	5.88	0.08
Hesitancy	75	80.65	15	88.24	0.5
Urgency	87	93.55	15	88.24	0.57
Urinary retention	74	79.57	15	88.24	0.48

Table - II: Prostate Volume (USG) and PSA Trends among patients (n=110)

Variable	Benign (n=93)		Malignant (n=17)		P-value
	n	%	n	%	
<b>Prostate USG</b>					
Grade I (20–30 g)	35	37.63	2	11.76	0.04
Grade II (31–50 g)	39	41.94	5	29.41	0.33
Grade III (51–80 g)	16	17.20	8	47.06	0.01
Grade IV (>80 g)	3	3.23	2	11.76	0.18
Prostate volume (mL), Mean ± SD	44.8 ± 18.5		57.4 ± 16.2		0.02
<b>PSA Trends (ng/mL)</b>					
0–5	76	81.72	4	23.53	<0.001
5.1–10	12	12.90	2	11.76	0.9
>10	5	5.38	11	64.71	<0.001
PSA level (ng/mL), Mean ± SD	6.42 ± 3.15		25.48 ± 11.62		<0.001

Table - III: Logistic regression for predictors of malignancy

Predictor	OR (95% CI)	P-value
PSA >10 ng/ml	27.8 (7.9–97.5)	<0.001
Prostate Grade III/IV	3.2 (1.2–8.4)	0.02
Age >70 years	1.7 (0.6–5.0)	0.32
Burning sensation	1.8 (0.6–5.5)	0.32
Urinary retention	1.5 (0.4–5.1)	0.48

**Table – IV: Diagnostic accuracy of key predictors**

Predictor	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
PSA >10 ng/ml	64.7	94.6	68.8	93.3	89.1
Prostate Volume Grade III/IV	58.8	79.6	34.5	91.3	76.4
PSA >10 ng/ml + Prostate Volume Grade III/IV	47.1	97.8	80	91.3	89.1

**DISCUSSION**

Prostate disorders encompass a spectrum of conditions, ranging from benign hyperplasia and chronic prostatitis to malignant neoplasms, each exhibiting distinct clinical and biochemical profiles [11]. In the study, the majority of patients presented with benign prostatic diseases accounting for 84.55%, whereas malignant prostatic disease constituted 15.45% of cases, similar to findings by Tolani et al., who reported that benign prostatic hyperplasia and prostate cancer were diagnosed in 71.40% and 28.60% of patients, respectively [12]. Muhammad et al. reported 64.00% benign prostatic hyperplasia and 20.00% prostate cancer [13]. Mean age was 67.1 ± 9.0 years in benign and 70.5 ± 7.8 years in malignant cases (p = 0.12). Islam et al stated that patients with prostate cancer were notably older than those with benign prostatic hyperplasia, with mean ages of 72 ± 4.4 versus 64 ± 6.6 years, respectively (p = 0.00001) [14]. Xing et al. reported a mean age of 65.9 ± 8.7 years (range 37–86 years) [15]. Increased frequency occurred in 100% of both groups. Burning sensation was 50.5% vs 64.7% (p = 0.32), fever 24.7% vs 5.9% (p = 0.08), while dribbling, hesitancy, urgency, and retention were similar (86.0–93.5% vs 88.2–88.2%). Mobley et al. reported that 15–25% of men experience lower urinary tract symptoms (LUTS), such as nocturia, urgency, frequency, incomplete bladder emptying, stop-start urination, straining, post-void urgency, and weak urinary stream [16]. Tolani et al. reported that difficulty in urination (91.4%), low back pain (44.8%), urinary retention (38.1%), erectile dysfunction (31.4%), hematuria (22.9%), and chronic renal failure (4.8%) was observed among patients [12]. Benign cases were mainly Grade I–II (37.6%–41.9%) and malignant cases Grade III–IV (47.1%–11.8%). Mean prostate volume was 44.8 ± 18.5 mL (benign) vs 57.4 ± 16.2 mL (malignant). PSA >10 ng/mL was seen in 5.4% of benign vs 64.7% of malignant cases, with mean PSA 25.48 ± 11.62 ng/mL in malignancy. Yamashiro et al. stated an inverse relationship between prostate volume and the risk of prostate cancer [17]. Al-Azab et al. reported that prostate volume is a stronger predictor of cancer than PSA alone, especially when PSA is in the lower to intermediate range (2–9 ng/mL), indicating that in smaller glands, cancer contributes relatively more to PSA elevation than benign enlargement [18]. Wolff et al. reported that mean PSA density was significantly higher in prostate cancer than BPH (0.46 vs. 0.116, p < 0.005), indicating that absolute PSA alone has limited specificity [19]. Erdogan et al. demonstrated that free/total PSA ratio, prostate volume, and PSA density differed significantly between prostate cancer and non-cancer cases (p < 0.001) [20]. PSA >10 ng/mL was most strongly associated with malignancy (OR 27.8, 95% CI 7.9–97.5), followed by Grade III–IV prostate (OR 3.2, 95% CI 1.2–8.4); age >70 y, burning, and retention showed weaker associations (OR 1.5–1.8). Hwang et al. identified elevated PSA as a significant risk factor, with higher PSA levels associated with increased prostate cancer incidence (HR 1.77, 95% CI 1.67–1.88) [21]. Al-Azab et al. reported that smaller prostate volume was the strongest predictor of a positive biopsy (OR 0.26, p < 0.001), indicating that larger prostates, likely due to BPH, were more often associated with benign findings [18]. Tiger et al. reported that each 10 mL increase in prostate volume was

associated with an approximately 30% lower risk of clinically significant prostate cancer [22]. PSA >10 ng/mL showed sensitivity 64.7%, specificity 94.6%, PPV 68.8%, NPV 93.3%, and accuracy 89.1%. Prostate volume Grade III/IV had sensitivity 58.8%, specificity 79.6%, PPV 34.5%, NPV 91.3%, and accuracy 76.4%. Combining PSA >10 ng/mL with Grade III/IV improved specificity to 97.8%, PPV to 80%, and overall accuracy remained 89.1%. Merriel et al. reported that PSA has high pooled sensitivity (~0.93) but low specificity (~0.20), indicating a substantial rate of false positives when used alone [23]. Saema et al. demonstrated that PSAD had superior discriminatory power over PSA, particularly in predicting cancer among patients with PSA in the ‘grey zone’ [24]. Khalid et al. demonstrated that MRI-derived PSAD with a cutoff of about 0.158 ng/mL/mL achieved 73.6% sensitivity and 92.7% specificity (AUC 0.83) for detecting prostate cancer [25].

**Limitations of the study:** This study has several limitations. The sample size was relatively small, particularly for malignant cases, which may limit generalizability. Prostate volume was measured using ultrasonography, which can underestimate true prostate size compared to MRI. Single-center design and lack of long-term follow-up restrict broader applicability and outcome assessment. PSA levels can be influenced by non-malignant factors such as inflammation or recent instrumentation, potentially confounding results. Additionally, other emerging biomarkers and imaging modalities were not evaluated, which may have enhanced diagnostic accuracy.

**CONCLUSION**

Prostate volume and PSA trends were shown to be significant clinical predictors of prostatic malignancy in this study. Patients with malignant disease had higher mean prostate volumes and markedly higher PSA levels compared to those with benign conditions. PSA above 10 ng/mL demonstrated the strongest association with malignancy, exhibiting high specificity and overall diagnostic accuracy. Prostate volume of Grade III/IV also contributed moderately to risk stratification, while combining elevated PSA with larger prostate grades further improved predictive specificity. These findings underscore the complementary value of integrating PSA trends and prostate volume assessment in clinical decision-making, enhancing early detection and guiding biopsy strategies in patients with suspected prostatic disease.

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**Conflict of interest:** None declared

**Ethical approval:** The study was approved by the Institutional Ethics Committee.

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