



Correlation of Hematological Parameters with Specific Antigen Concentration and Prostate Volume in Benign Prostatic Hyperplasia: A Retrospective-Analytical Study

Arian Karimi Rouzbahani ^{1,2}, Firozeh Khosravinia ³, Samaneh Tahmasebi Ghorabi ⁴, Parastoo Baharvand ⁵, Behzad Yousefi Yeganeh ^{6,*}

¹ Razi Herbal Medicines Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran

² Surgery Education and Researching Network (SERGN), Universal Scientific Education and Research Network (USERN), Khorramabad, Iran

³ Student Research Committee, Lorestan University of Medical Sciences, Khorramabad, Iran

⁴ USERN Office, Lorestan University of Medical Sciences, Khorramabad, Iran

⁵ Social Determinants of Health Research Center, School of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran

⁶ Department of Surgery, School of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran

*Corresponding Author: Department of Surgery, School of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran. Email: byyyyyyb@yahoo.com

Received: 21 October, 2024; Revised: 12 October, 2025; Accepted: 9 November, 2025

Abstract

Background and Objectives: This study investigates the relationship between prostate volume, blood prostate-specific antigen (PSA) concentration, and 12 hematological variables in patients with benign prostatic hyperplasia (BPH).

Methods: Data for 12 hematological traits were extracted from the records of 166 hospitalized patients at Ashayer Hospital in Khorramabad during 2021-2022 and analyzed using correlation and regression procedures in SAS statistical software.

Results: Significant correlations were identified between PSA concentration and mean corpuscular volume (MCV), platelet count, and red cell distribution width (RDW). The highest correlation coefficients for PSA were with MCV (0.316) and platelet count (0.305). Multiple linear regression models identified key variables, including patient age, white blood cell (WBC) count, platelet count, and RDW. Models for estimating PSA concentration demonstrated higher statistical validity ($R^2 = 0.510$ to 0.540) than those for prostate volume, likely due to stronger phenotypic associations with hematological traits. Specific hematological traits with the lowest tolerance and highest variance inflation factor (VIF) included neutrophil percentage, lymphocyte percentage, red blood cell (RBC) count, hemoglobin concentration, and hematocrit percentage.

Conclusions: Hematological parameters were less effective in predicting prostate volume but valuable for estimating serum PSA concentration, offering potential insights for diagnostic models in BPH. However, these findings should be interpreted cautiously given study limitations, such as the retrospective design.

Keywords: Hematological Parameters, Prostate-Specific Antigen, Prostate Volume, Benign Prostatic Hyperplasia

1. Background

Prostate cancer (PCa) is the most prevalent non-skin cancer affecting men worldwide (1). Despite advances in the diagnosis and treatment of PCa, there are still 1,600,000 cases and 366,000 deaths reported annually in the United States alone (2). The prevalence varies among countries with diverse cultures and climates; for

example, it is 5.13% in Turkey, 7.23% in Egypt, and 8.23% in the Arab Gulf states collectively (3).

This disease is characterized by high occurrence, with approximately 80 - 85% of PCa originating from the peripheral zone of the prostate gland. In addition, metastatic PCa ranks as the third-leading cause of cancer-related deaths (1, 4). Over 80% of men diagnosed with PCa also exhibit histological evidence of benign prostatic hyperplasia (BPH), either with or without

clinical symptoms (4). The BPH is the most common urological condition in elderly males globally. The BPH leads to an increase in prostate size and is associated with bladder outlet obstruction and various lower urinary tract symptoms (5). The BPH can also result in the decline of urinary function and quality of life, as well as a higher risk of urinary tract infection (UTI) and acute urine retention, often requiring surgical intervention. Furthermore, the costs associated with BPH management are substantial, even though many men go undiagnosed and receive inadequate treatment (6).

Prostate-specific antigen (PSA) is a serine protease produced by prostate epithelial cells under androgen regulation, belonging to the tissue kallikrein family. Elevated serum PSA levels are common in PCa and other conditions, making it a key marker for prostate diseases. The PSA expression is primarily regulated by androgens via the androgen receptor (7). In BPH, prostate volume and serum PSA levels are critical progression factors, with volumes greater than 30 mL and PSA greater than 1.5 ng/mL posing the highest risks (8). The PSA levels are relevant to BPH diagnosis as they reflect prostate epithelial activity and hyperplasia, while hematological parameters [e.g., those from complete blood count (CBC)] may indicate underlying inflammation or systemic responses often associated with BPH progression. Focusing on hematological traits is rational because they are routinely measured, cost-effective, and may serve as accessible biomarkers in resource-limited settings, potentially correlating with PSA and prostate volume through shared inflammatory pathways (9).

Various diagnostic methods for BPH rely on PSA measurement and ultrasound-based prostate volume assessment, supplemented by digital rectal examination. However, there is a need for simpler and more affordable alternatives, particularly in under-equipped facilities. Routine CBC-differential tests, part of initial assessments, could provide phenotypic correlations with PSA and prostate volume, aiding evaluation when ultrasound or PSA testing is unavailable. Predictive models based on these parameters might reduce the frequency of repeated tests.

2. Objectives

This study hypothesizes that hematological parameters correlate with serum PSA concentration and prostate volume in BPH patients, potentially enabling

predictive models to improve PSA estimation and elucidate the hematological impacts on BPH. We aimed to explore these correlations in patients admitted to the urology department of Ashayer Hospital in 2021 - 2022, focusing on both prediction enhancement and mechanistic insights.

3. Methods

3.1. Study Design and Participants

An analytical retrospective study was conducted using a census method, including all patients diagnosed with BPH admitted to the Urology Department of Ashayer Hospital between January 1, 2021, and January 1, 2022.

3.2. Inclusion and Exclusion Criteria

Patients diagnosed with BPH at Ashayer Hospital with complete medical records, including hematological parameters, serum PSA levels, and prostate volume assessed by transabdominal ultrasound, were included. Exclusion criteria comprised patients with hematological diseases, chronic conditions (e.g., chronic kidney disease), incomplete records, recent use of prostate-reducing drugs (e.g., 5-alpha reductase inhibitors), smokers, vegetarians, hereditary disorders (e.g., thalassemia minor), or those expressing dissatisfaction with laboratory or ultrasound results.

3.3. Data Collection Instruments

Data were collected from laboratory tests and transabdominal ultrasound reports. Hematological parameters were measured uniformly using standard laboratory protocols upon hospital admission, employing automated analyzers following institutional guidelines to ensure consistency. Prostate volume was calculated using the ellipsoid formula from ultrasound dimensions.

3.4. Procedure

After obtaining ethical approval from Lorestan University of Medical Sciences ([IR.LUMS.REC.1401.310](#)), patient files were retrieved from hospital archives. Data, including hematological parameters, serum PSA levels, prostate volume, and demographics (e.g., age), were extracted using a standardized checklist and entered into Excel for initial organization, then transferred to SAS software. Missing data were supplemented via

telephone or in-person document review; unsuccessful cases were excluded. Hematological data and PSA measurements were validated through cross-checking with original laboratory reports for accuracy. Informed consent was waived due to the retrospective nature of the study, as approved by the ethics committee.

3.5. Data Analysis

Analyses were performed using SAS software (SAS Institute, 2003). The steps included:

- UNIVARIATE procedure to check normality (using skewness and kurtosis); non-normal data (e.g., neutrophil and lymphocyte percentages) were log-transformed.
- PROC MEANS for descriptive statistics (mean, variance, standard deviation, standard error).
- PROC REG for linear regression coefficients between prostate volume/PSA (dependent variables) and 12 hematological parameters (independent variables), with plots and statistics.
- PROC CORR for Pearson correlation coefficients.
- PROC REG for tolerance testing and variance inflation factor (VIF) to assess multicollinearity; variables with tolerance less than 0.1 or VIF greater than 10 were considered collinear.
- PROC REG with stepwise, forward, and backward selection methods to build multiple linear regression models, selecting based on maximum R^2 and $P < 0.05$ for variable entry/retention; model validity prioritized higher R^2 and lower multicollinearity.

4. Results

4.1. General Examination of Traits in the Target Population

In this study, 15 quantitative variables were evaluated in patients with BPH. The basic statistics related to these variables are presented in Table 1. All variables exhibited considerable variance (standard deviation squared), indicating potential influences by various physiological or environmental factors. Notably, the average prostate volume and PSA concentration were 82.66 mL and 3.76 units, respectively, in the study population with an average age of 71.75 years (861 months). It was anticipated that the average PSA concentration in this cohort would be higher. The results of the normality test using the UNIVARIATE procedure demonstrated that all data, except for the percentage of neutrophils and lymphocytes, deviated from a normal distribution. For

these variables, the data were log-transformed to approximate a normal distribution.

4.2. Investigating Linear Dependence of Prostate Volume and Prostate-Specific Antigen Level on the Evaluated Hematological Traits

The simplest measure to assess the relationship between two variables is their covariance. Biologically, covariance represents the part of the variance of two traits created by common factors. However, the unit of covariance is the product of the units of the two variables, which complicates interpretation. To address this, the covariance of two traits is divided by the variance of the independent trait, resulting in the coefficient of correlation, which essentially expresses the covariance between two traits as a relative proportion of the variance of the independent trait. The unit of this coefficient is the unit of the dependent variable divided by the unit of the independent variable. In Tables 2, the coefficients of correlation for the variables of prostate volume and PSA (as dependent variables) from 13 hematologic traits (as independent variables) are presented, showing statistically significant relationships in the respective models.

Among the studied traits, the linear correlation of prostate volume was significant with patient age, red blood cell (RBC) count, hemoglobin concentration, hematocrit percentage, neutrophil percentage, and red cell distribution width (RDW, $P < 0.05$). In contrast, the linear correlation of PSA blood level was significant with mean corpuscular volume (MCV), platelet count, and RDW.

Figures 1 to 6 illustrate linear relationships between all studied traits and the two variables, prostate volume and PSA blood level. Although, in clinical settings, an increase in PSA secretion is indicative of benign or malignant hyperplasia of the prostate, the results showed that the linear correlation between both variables was very weak. The coefficient of correlation for a dependent variable from an independent variable indicates the number of units of change in the dependent variable per unit change in the independent variable. In this study, the highest coefficient of correlation for prostate volume was observed, in descending order, for RBC count, RDW, hemoglobin concentration, and white blood cell (WBC) count. Meanwhile, the highest coefficient of correlation for PSA concentration was observed, in descending order, for RBC count, RDW, mean corpuscular hemoglobin concentration (MCHC), and MCV.

Table 1. Review of Simple Statistics for Studied Traits in the Statistical Population

Variables	Number	Mean \pm SD	SE	Variance	Skewness	Kurtosis
Prostate volume	133	82.66 \pm 38.08	3.30	1449.89	1.24	2.19
PSA	164	3.76 \pm 3.26	0.25	10.60	1.60	3.18
Age	164	860.82 \pm 133.04	10.39	17695.75	-0.05	-0.81
WBC	164	7.14 \pm 2.47	0.19	6.10	1.27	3.41
RBC	165	4.77 \pm 0.70	0.05	0.50	0.18	0.55
Hb	165	14.14 \pm 2.08	0.16	4.31	-0.12	0.01
HCT	165	42.02 \pm 5.53	0.43	30.60	-0.04	0.14
MCV	165	88.63 \pm 6.75	0.53	45.54	-1.14	2.54
MCH	165	29.87 \pm 2.68	0.21	7.17	-1.21	4.85
MCHC	165	33.61 \pm 1.94	0.51	3.77	0.77	4.12
PLT	165	231.15 \pm 78.71	6.13	6196.02	1.18	2.04
Nutr	153	64.17 \pm 12.26	0.99	150.42	0.30	-0.41
Lymph	157	27.60 \pm 10.76	0.86	115.81	-0.20	-0.63
MXD	146	8.81 \pm 3.75	0.31	14.05	0.52	0.66
RDW	155	12.77 \pm 2.20	0.18	4.85	-0.45	2.97

Abbreviations: PSA, prostate-specific antigen; WBC, white blood cell; RBC, red blood cell; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration; RDW, red cell distribution width.

Table 2. Regression Coefficients: Prostate Volume and Prostate-Specific Antigen Level Among the Evaluated Hematological Traits

Variables	Prostate Volume		PSA	
	Citizenship Coefficient	P-Value	Citizenship Coefficient	P-Value
Prostate volume	-	-	0.242	0.8085
PSA	0.242	0.8085	-	-
Age	0.082	0.0008	-0.001	0.5642
WBC	2.707	0.487	0.044	0.7263
RBC	-8.674	0.0602	0.721	0.0891
Hb	-3.396	0.0275	-0.123	0.3902
HCT	-1.337	0.0214	-0.076	0.1549
MCV	-0.139	0.7709	-0.182	0.0001
MCH	-0.303	0.7925	-0.169	0.1072
MCHC	-1.274	0.4572	0.286	0.0672
PLT	0.0096	0.8100	0.016	0.0001
Nutr	0.542	0.0456	-0.010	0.6834
Lymph	-0.730	0.0191	0.004	0.8986
MXD	0.154	0.8546	0.039	0.6098
RDW	3.713	0.0065	0.292	0.0204

Abbreviations: PSA, prostate-specific antigen; WBC, white blood cell; RBC, red blood cell; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration; RDW, red cell distribution width.

4.3. Investigating Pearson Correlation Between Prostate Volume, Prostate-Specific Antigen Level, and Evaluated Hematological Traits

Because the unit of the coefficient of correlation is expressed as the ratio of the dependent variable unit to the independent variable unit, physiological interpretation is not straightforward. Therefore,

another measure, the correlation coefficient, is used. It is obtained by dividing the covariance between the two variables by the product of their standard deviations. This measure is dimensionless and provides a simple representation of the relationship between two variables (Table 3).

Prostate volume showed a significant correlation with patient age, RBC count, WBC count, hemoglobin

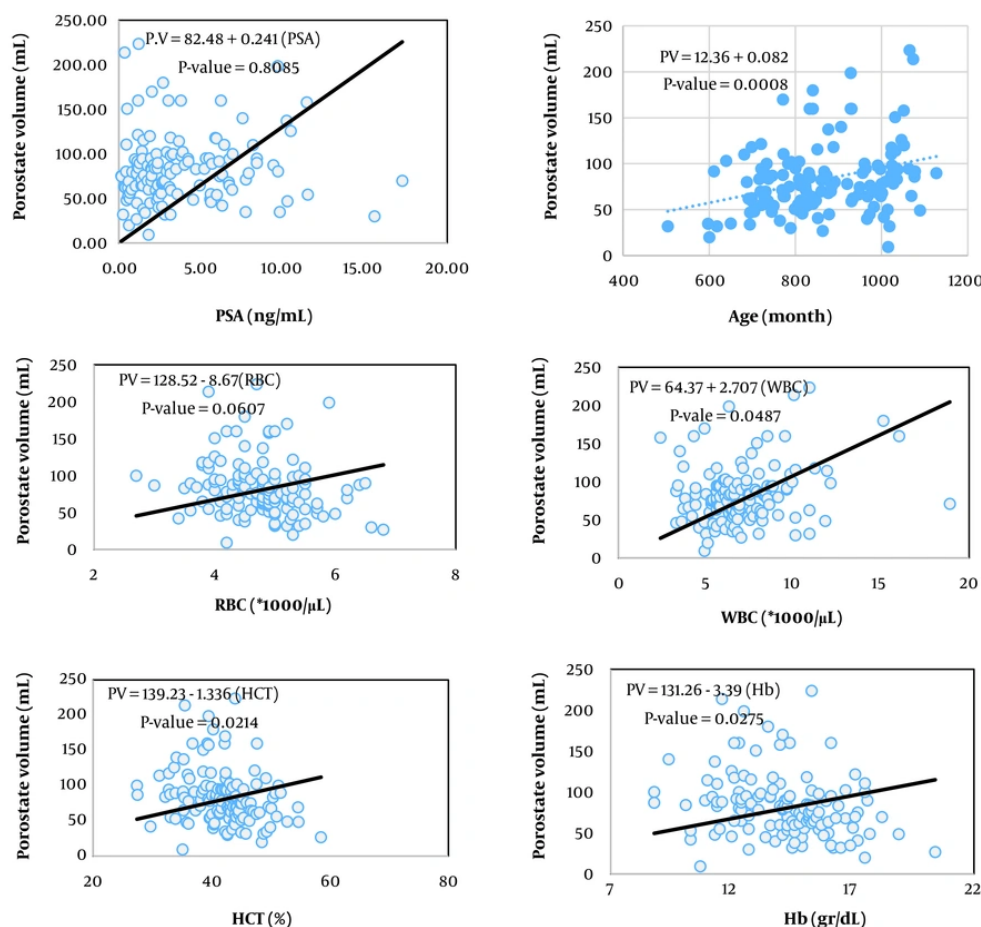


Figure 1. Relationships of prostate volume with age, prostate-specific antigen (PSA) concentration, red blood cell (RBC) count, hemoglobin concentration, and hematocrit percentage in patients with benign prostatic hyperplasia (BPH) and their related models

concentration, hematocrit percentage, neutrophil count, and RDW ($P < 0.05$). The highest correlations were, in descending order, with patient age, hemoglobin concentration, and hematocrit percentage. The correlation coefficient of prostate volume with most traits related to RBCs and hemoglobin was negative.

The Pearson correlation coefficients between RBC count, hemoglobin concentration, MCV, platelet count, neutrophil percentage, and RDW were significant. Although all correlation coefficients were statistically described as low, the correlation coefficient between PSA and MCV and platelet count was higher than for other traits. Similar to prostate volume, the correlation coefficient between PSA and most traits related to hemoglobin concentration was negative. Among the set

of traits studied, the correlation coefficients between RBC count, hemoglobin concentration, lymphocyte percentage, and RDW with both prostate volume and PSA level were significant and mostly had the same sign and numerically consistent, suggesting the possibility of shared physiological pathways for changes in both traits.

4.4. Investigating Linear Alignment Among the Evaluated Hematological Trait Variables

Tolerance test results are presented in Table 4. The lowest tolerance and highest VIF were observed for neutrophil percentage, lymphocyte percentage, RBC count, hemoglobin concentration, and hematocrit percentage, indicating high collinearity. Values near 1

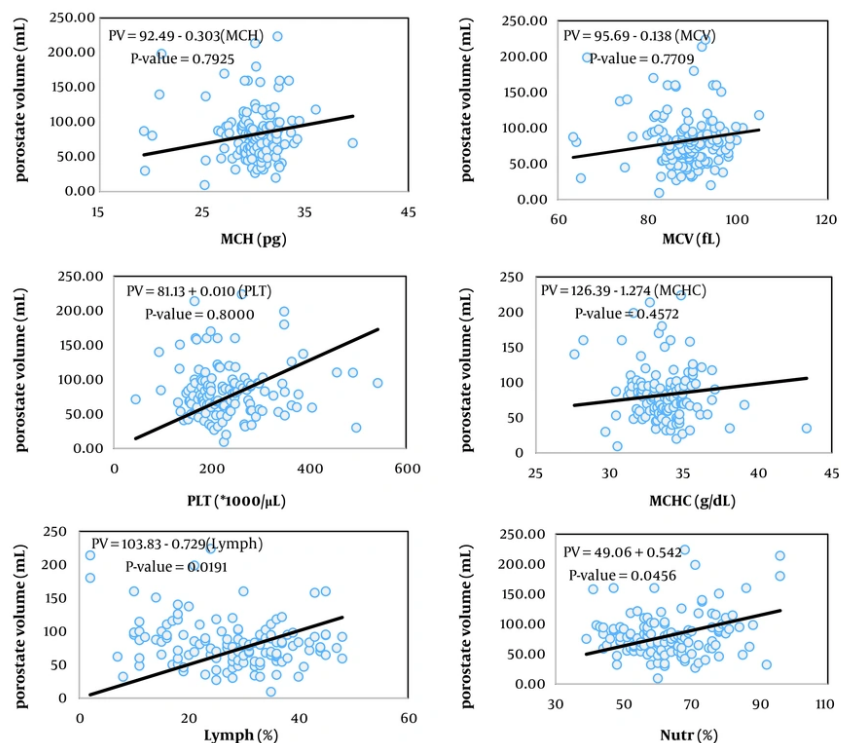


Figure 2. Correlation lines of prostate volume with mean corpuscular volume (MCV), MCH, mean corpuscular hemoglobin concentration (MCHC), platelet count, neutrophil percentage, and lymphocyte percentage in patients with benign prostatic hyperplasia (BPH) and related models

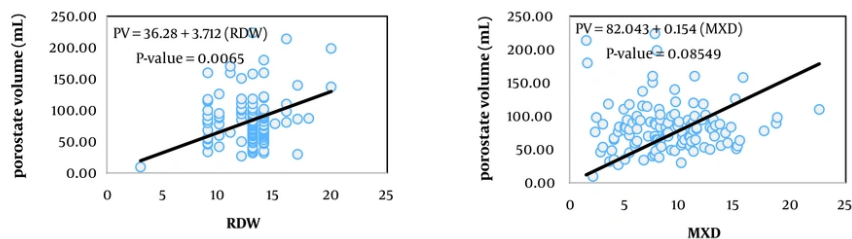


Figure 3. Dependence curves of prostate volume on MXD and red cell distribution width (RDW) in patients with benign prostatic hyperplasia (BPH) and related models

for age, WBC count, platelet count, and RDW indicated low collinearity and thus suitability for inclusion in models.

4.5. Linear Multivariate Regression Models to Estimate Prostate Volume and Prostate-Specific Antigen Level Using Evaluated Hematological Traits

Table 5 presents the best multivariable linear models (based on the coefficient of determination, R^2) for estimating prostate volume and PSA concentration using various modeling methods in the software employed. For prostate volume, the maximum R^2 was 0.22 (forward method); stepwise and backward methods yielded similar results with four variables. For PSA, R^2

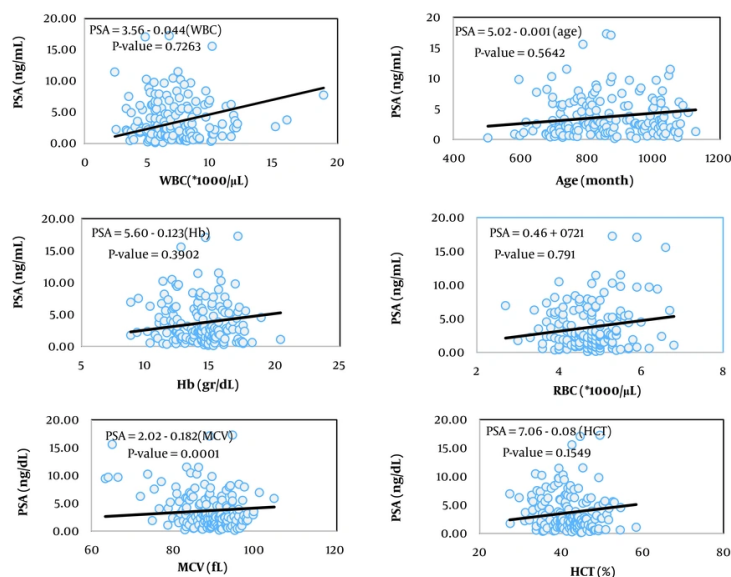


Figure 4. Prostate-specific antigen (PSA) concentration curves based on age, white blood cell (WBC) count, red blood cell (RBC) count, hemoglobin concentration, hematocrit percentage, and mean corpuscular volume (MCV) in patients with benign prostatic hyperplasia (BPH) and related models

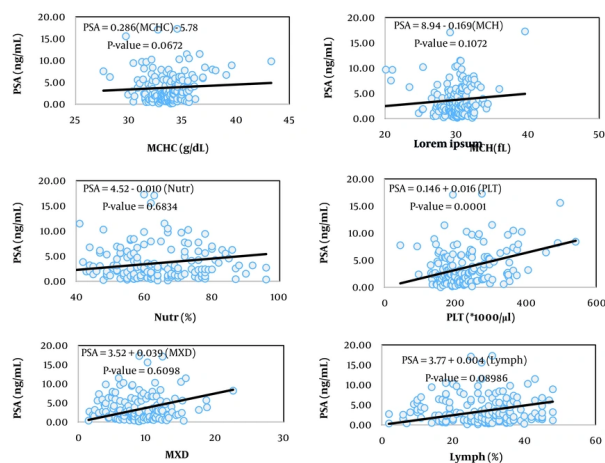


Figure 5. Dependence curves of prostate-specific antigen (PSA) concentration on MCH, mean corpuscular hemoglobin concentration (MCHC), platelet count, neutrophil percentage, lymphocyte percentage, and MXD in patients with benign prostatic hyperplasia (BPH) and related models

ranged from 0.51 to 0.54 across methods (indicating higher validity than prostate volume models, likely due to stronger correlations); common variables included RBC count, MCH, MCHC, platelet count, hemoglobin,

and RDW. Patient age was not included in PSA models. Orthogonal modeling did not improve R^2 .

The orthoreg modeling method is used to construct linear statistical models when the predictor variables

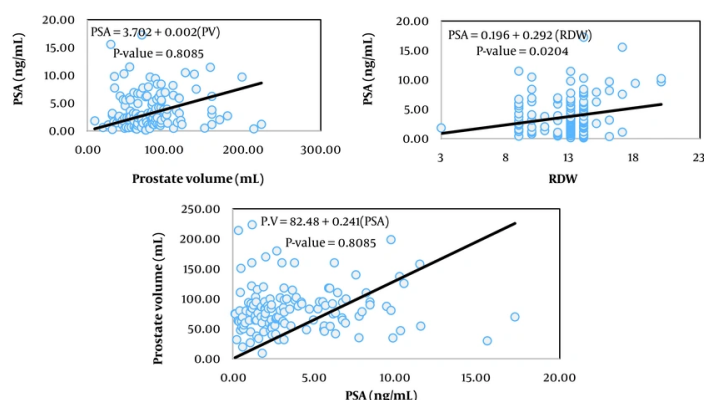


Figure 6. Dependence curves of prostate-specific antigen (PSA) concentration on age and prostate volume, and dependence curves of prostate volume on PSA concentration in patients with benign prostatic hyperplasia (BPH) and related models

Table 3. Pearson's Correlation Coefficients between Prostate Volume, Prostate-Specific Antigen Level, and Evaluated Hematological Traits

Variables	Prostate Volume		PSA	
	R	P-Value	R	P-Value
Prostate volume	1.000	-	0.063	0.475
PSA	0.063	0.475	1/000	-
Age	0.278	0.001	0.026	0.741
WBC	0.218	0.012	0.007	0.930
RBC	-0.201	0.021	0.145	0.061
Hb	-0.251	0.003	-0.070	0.031
HCT	-0.250	0.772	-0.111	0.155
MCV	-0.037	0.673	-0.316	0.0001
MCH	-0.025	0.772	-0.111	0.155
MCHC	-0.139	0.112	-0.139	0.081
PLT	-0.034	0.670	0.305	0.0001
Nutr	0.184	0.040	0.038	0.647
Lymph	-0.240	0.006	-0.240	0.006
MXD	0.024	0.789	0.077	0.357
RDW	0.198	0.026	0.198	0.026

Abbreviations: PSA, prostate-specific antigen; WBC, white blood cell; RBC, red blood cell; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration; RDW, red cell distribution width.

exhibit high linear collinearity. This approach generates a model for estimating the target dependent variable by incorporating all available predictor variables. The results presented in Table 5 indicate that the models developed using this method do not demonstrate a higher coefficient of determination for predicting prostate volume and PSA concentration.

5. Discussion

5.1. Correlation Between Prostate Volume and Prostate-Specific Antigen with Hematological Traits

This study examined relationships between prostate volume, serum PSA, and 12 hematological variables in BPH to develop predictive models for resource-limited settings. Mean prostate volume (82.66 mL) and PSA (3.76 ng/mL) at mean age 71.75 years were lower than expected, supporting the limited reliability of PSA in

Table 4. Results of the Tolerance Test to Check Linear Alignment or Orthogonality Between Age and Evaluated Hematological Traits

Variables	Parameter Estimation	SE	t-Value	Significant Probability	Tolerance	Variance Inflation
Age	0.073	0.025	2.88	0.0048	0.824	1.212
WBC	1.192	1.453	1.51	0.1344	0.760	1.316
RBC	-6.407	35.903	-0.18	0.8587	0.014	71.208
Hb	-5.154	11.930	-0.43	0.6666	0.014	70.133
HCT	0.909	4.292	0.21	0.8328	0.016	63.750
MCV	-1.861	1.991	-0.93	0.3520	0.048	20.911
MCH	4.868	4.723	1.03	0.3050	0.050	20.084
MCHC	1.091	3.469	0.31	0.7538	0.205	4.885
PLT	0.011	0.043	0.26	0.7917	0.713	1.403
Nutr	2.390	2.570	0.93	0.3544	0.009	105.535
Lymph	2.119	2.550	0.83	0.4078	0.013	78.290
MXD	3.123	2.648	1.18	0.2409	0.085	11.834
RDW	4.810	1.457	3.30	0.0013	0.757	1.321

Abbreviations: WBC, white blood cell; RBC, red blood cell; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration; RDW, red cell distribution width.

Table 5. Statistical Models to Estimate Prostate Volume and Plasma Prostate-Specific Antigen Level Using Hematological Variables

Estimation Methods	The Dependent Variable	Estimation Model	R ² (P > 0.05)
Stepwise	Prostate volume	(Age × 0.083) + (WBC × 2.466) + (RDW × 3.684) - 52.099	0.22 (< 0.0001)
Forward	Prostate volume	(Age × 0.086) + (WBC × 2.641) + (MCH × 0.879) + (MXD × 0.567) + (RDW × 3.665) - (-89.96)	0.24 (0.0004)
Backward	Prostate volume	(Age × 0.083) + (WBC × 2.466) + (RDW × 3.684) - 52.10	0.22 (< 0.0001)
Stepwise	PSA	(MCH × 0.673) - (MCV × 0.358) + (PLT × 0.014) + (RDW × 0.208) - 9.467	0.349 (< 0.0001)
Forward	PSA	(Age × 0.002) + (MCH × 0.710) - (WBC × 0.093) + (PLT × 0.015) + (RDW × 0.217) - (MCV × 0.366) + 7.667	0.54 (< 0.0001)
Backward	PSA	(MCH × 10.673) - (MCV × 0.358) + (PLT × 0.014) + (RDW × 0.208) - 9.467	0.51 (< 0.0001)
Orthoreg ^a	Prostate volume	(Age × 0.0743) + (WBC × 2.234) + (HCT × 1.456) + (MCH × 2.768) + (MCHC × 0.936) + (Nutr × 2.635) + (Lymph × 2.366) + (MXD × 3.312) + (RDW × 4.683) - (PLT × 0.003) - (MCV × 1.934) - (RBC × 22.564) - 183.935	0.25 (0.0025)
Orthoreg	PSA	(Age × 0.001) + (WBC × 0.05) + (RBC × 10.622) + (MCH × 1.579) + (MCHC × 0.533) + (PLT × 0.011) + (RDW × 0.169) - (MXD × 0.195) - (Lymph × 0.246) - (Nutr × 0.262) - (MCV × 0.212) - (Hb × 3.268) - 35.411	0.54 (< 0.0001)

Abbreviations: WBC, white blood cell; RDW, red cell distribution width; PSA, prostate-specific antigen; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration; RBC, red blood cell.

^a This option of linear modeling is used for situations where the independent variables used have linear alignment.

BPH diagnosis (10-12). Variance in variables suggests multifactorial influences (13). Covariance and regression analyses showed that prostate volume was correlated with age, RBC count, hemoglobin, hematocrit, neutrophil percentage, and RDW (P < 0.05). This is consistent with inflammatory processes involving neutrophils and blood changes (14). Unexpected RBC-related correlations align with studies showing lower hemoglobin and hematocrit in high-PSA groups (15) or treated PCa (16).

The PSA showed weaker correlations, significant only with MCV, platelet count, and RDW. Shared RDW correlations indicate links to anisocytosis. Biologically, MCV (reflecting RBC size) may correlate with PSA via chronic inflammation altering erythropoiesis and prostate epithelium; platelet count could relate to thrombocytosis in BPH inflammation, promoting PSA release through cytokine pathways. Pearson correlations were weak (absolute value less than 0.3), with the highest values for prostate volume-age (0.285) and PSA-MCV/platelet count (0.316/0.305), consistent

with prior age-corrected correlations (17). Our negative RBC/hemoglobin correlations match Nigerian findings (15) and hormonal therapy studies (16), but discrepancies (e.g., lack of strong WBC-PSA link) may stem from population differences.

5.2. Linear Alignment Among Hematological Traits

Weak relationships may reflect collinearity (18-20). The lowest tolerance and highest VIF for neutrophil and lymphocyte percentages, RBC count, hemoglobin, and hematocrit indicate redundancy; age, WBC, platelet count, and RDW exhibited low collinearity, enhancing model utility.

5.3. Applied Linear Statistical Models

No viable prostate volume models were found (R^2 less than 0.22); PSA models had higher R^2 values (0.51 - 0.54), excluding age, with shared variables (RBC count, MCH, MCHC, platelet count, hemoglobin, RDW). Higher PSA model validity likely results from stronger correlations. Similar modeling approaches are used to estimate glomerular filtration rate or cancer outcomes (17, 21, 22).

5.4. Comparison with Emerging Biomarkers

While this study focuses on conventional biomarkers (PSA, hematological parameters) in BPH, prostate diseases, including cancer, also involve advanced biomarkers such as noncoding RNAs (ncRNAs). In cancers (e.g., lung, hepatocellular carcinoma, glioma), circular RNAs (circRNAs) regulate Wnt/ β -catenin and PI3K/Akt pathways, influencing progression, apoptosis, and inflammation (23-34). Long ncRNAs in acute myeloid leukemia and bladder cancer modulate STAT3, apoptosis, and drug resistance (25, 27). MicroRNAs such as miR-489 suppress tumors via apoptosis induction and Wnt inhibition (24). These findings contrast with our routine CBC-based approach for BPH but highlight the potential for ncRNA integration in prognostic models assessing malignant transformation risk.

5.5. Clinical Applications and Limitations

The findings suggest that hematological parameters may be useful for PSA estimation in early diagnosis, patient stratification, or resource optimization in low-access settings. However, limitations include the retrospective design (potential bias), single-center data (limited generalizability), unmeasured confounders (e.g., comorbidities), and excluded cases due to

incomplete records. Future research should validate these findings prospectively, explore additional parameters, or integrate ncRNAs for comprehensive models.

5.6. Conclusions

Linear regressions showed that prostate volume was associated with age, RBC count, hemoglobin, hematocrit, neutrophil percentage, and RDW; PSA was associated with MCV, platelet count, and RDW. Correlations were weak, with no strong phenotypic links. Hematological parameters failed to predict prostate volume (R^2 less than 0.22) but showed promise for PSA ($R^2 = 0.52$). These insights may aid diagnostic models, but claims are tempered by limitations such as retrospective bias and single-center scope, warranting cautious application.

5.7. Limitations

Main limitations include incomplete clinical/laboratory data leading to exclusions, retrospective design introducing selection bias, single-center scope limiting generalizability, and potential unmeasured confounders (e.g., diet, medications).

Acknowledgements

The authors would like to thank the patients for their willingness to participate in this study.

Footnotes

Authors' Contribution: Conceptualization and study design: B. Y. Y. and A. K. R.; Data acquisition: F. Kh.; Introduction and discussion writing: S. T. Gh.; Data analysis/interpretation: P. B.; Statistical analysis: B. Y. Y. All authors contributed critically to the revision of the manuscript for important intellectual content. The final manuscript was read and approved by all authors.

Conflict of Interests Statement: The authors declare no conflict of interest.

Data Availability: The data supporting the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Ethical Approval: This study was approved by the Lorestan University of Medical Sciences Ethics

Committee ([IR.LUMS.REC.1401.310](https://doi.org/10.1186/1475-2875-1401310)).

Funding/Support: The present study received no funding/support.

References

- Yamashiro JR, de Riese WTW. Any Correlation Between Prostate Volume and Incidence of Prostate Cancer: A Review of Reported Data for the Last Thirty Years. *Res Rep Urol*. 2021;**13**:749-57. [PubMed ID: 34676178]. [PubMed Central ID: PMC8518471]. <https://doi.org/10.2147/RRU.S331506>.
- Wang G, Zhao D, Spring DJ, DePinho RA. Genetics and biology of prostate cancer. *Genes Dev*. 2018;**32**(17-18):1105-40. [PubMed ID: 30181359]. [PubMed Central ID: PMC6120714]. <https://doi.org/10.1101/gad.315739.118>.
- Noweir A, Abusamra A, Al Zarooni A, Binbay M, Doble A, Tariq L, et al. Prevalence of benign prostatic hyperplasia among the adult general population of five Middle Eastern Countries: Results of the SNAPSHOT programme. *Arab J Urol*. 2022;**20**(1):14-23. [PubMed ID: 35223105]. [PubMed Central ID: PMC8881068]. <https://doi.org/10.1080/2090598X.2021.2010451>.
- Liu FC, Hua KC, Lin JR, Pang ST, Yu HP. Prostate resected weight and postoperative prostate cancer incidence after transurethral resection of the prostate: A population-based study. *Medicine (Baltimore)*. 2019;**98**(3). e13897. [PubMed ID: 30653095]. [PubMed Central ID: PMC6370121]. <https://doi.org/10.1097/MD.00000000000013897>.
- Inamura S, Ito H, Shinagawa T, Tsutsumiuchi M, Taga M, Kobayashi M, et al. Prostatic stromal inflammation is associated with bladder outlet obstruction in patients with benign prostatic hyperplasia. *Prostate*. 2018;**78**(10):743-52. [PubMed ID: 29608020]. <https://doi.org/10.1002/pros.23518>.
- He H, Wu S, Hao J, Wang L, Ai K, Zhu X, et al. Serum omentin-1 level in patients with benign prostatic hyperplasia. *BMC Urol*. 2020;**20**(1):52. [PubMed ID: 32375790]. [PubMed Central ID: PMC7203873]. <https://doi.org/10.1186/s12894-020-00623-4>.
- Huang SF, Yu YL, Cui YF, Lou YM, Liao MQ, Wang CY, et al. Association between serum prostate-specific antigen concentrations and the risk of developing type 2 diabetes mellitus in Chinese men: A cohort study. *J Diabetes Investig*. 2021;**12**(9):1560-8. [PubMed ID: 33544958]. [PubMed Central ID: PMC8409830]. <https://doi.org/10.1111/jdi.13521>.
- Aigbe E, Irekpita E, Ogbetere FE, Alili UI. Correlation between prostate volume and prostate-specific antigen in Nigerian men with symptomatic histologically-diagnosed benign prostatic hyperplasia. *Niger J Clin Pract*. 2022;**25**(9):1523-8. [PubMed ID: 36149214]. https://doi.org/10.4103/njcp.njcp_67_22.
- Shi C, Cao H, Zeng G, Yang L, Wang Y. The relationship between complete blood cell count-derived inflammatory biomarkers and benign prostatic hyperplasia in middle-aged and elderly individuals in the United States: Evidence from NHANES 2001-2008. *PLoS One*. 2024;**19**(7). e0306860. [PubMed ID: 38980876]. [PubMed Central ID: PMC1233019]. <https://doi.org/10.1371/journal.pone.0306860>.
- Kazemi Rashed F, Zomrrodi A, Nabavi S. [Evaluation of the Relation between Bladder Wall Thickness Changes and Clinical Findings in Patients with Benign Prostatic Hyperplasia Before and After Prostatectomy]. *Med J Tabriz Univ Med Sci*. 2011;**33**(4):60-3. FA.
- Hassanzadeh K, Salami M. [Relation between Histological Types of Benign Prostatic Hyperplasia and Clinical Symptoms]. *Med J Tabriz Univ Med Sci*. 2015;**37**(2):12-5. FA.
- Gilfrich C, Leicht H, Fahlenbrach C, Jeschke E, Popken G, Stolzenburg JU, et al. Morbidity and mortality after surgery for lower urinary tract symptoms: a study of 95 577 cases from a nationwide German health insurance database. *Prostate Cancer Prostatic Dis*. 2016;**19**(4):406-11. [PubMed ID: 27502738]. <https://doi.org/10.1038/pcan.2016.33>.
- Moller A, Jennions MD. How much variance can be explained by ecologists and evolutionary biologists? *Oecologia*. 2002;**132**(4):492-500. [PubMed ID: 28547634]. <https://doi.org/10.1007/s00442-002-0952-2>.
- Mendonca R, Silveira AA, Conran N. Red cell DAMPs and inflammation. *Inflamm Res*. 2016;**65**(9):665-78. [PubMed ID: 27251171]. <https://doi.org/10.1007/s00011-016-0955-9>.
- Obeagu E, Gi A, Obeagu G, Ugwuja S, Agbo E. Evaluation of Impact of Level of Prostate Specific Antigen on Haematological Parameters of Men in Owerri, Nigeria. *J Biomed Sci Appl*. 2017;**1**:3.
- Torricelli P. Preventive Effects of A Mixture of Micronutrients with Antioxidative Properties on Experimentally Induced Prostate Hyperplasia. *Am J Life Sci*. 2013;**1**(1). <https://doi.org/10.11648/j.ajls.2013010114>.
- Kim Y, Kwon S, Heun Song S. Multiclass sparse logistic regression for classification of multiple cancer types using gene expression data. *Comput Stat Data Anal*. 2006;**51**(3):1643-55. <https://doi.org/10.1016/j.csda.2006.06.007>.
- Morrissey MB, Ruxton GD. Multiple Regression Is Not Multiple Regressions: The Meaning of Multiple Regression and the Non-Problem of Collinearity. *Philos Theory Pract Biol*. 2018;**10**(20220112). <https://doi.org/10.3998/ptpbio.16039257.0010.003>.
- McGiffen ME, Carmer SG, Ruesink WG. Diagnosis and Treatment of Collinearity Problems and Variable Selection in Least-Squares Models. *J Econ Entomol*. 1988;**81**(5):1265-70. <https://doi.org/10.1093/jee/81.5.1265>.
- Midi H, Sarkar SK, Rana S. Collinearity diagnostics of binary logistic regression model. *J Interdiscip Math*. 2010;**13**(3):253-67. <https://doi.org/10.1080/09720502.2010.10700699>.
- Boateng EY, Abaye DA. A Review of the Logistic Regression Model with Emphasis on Medical Research. *J Data Anal Inf Process*. 2019;**7**(4):190-207. <https://doi.org/10.4236/jdaip.2019.74012>.
- Howell P, Davis S. Predicting persistence of and recovery from stuttering by the teenage years based on information gathered at age 8 years. *J Dev Behav Pediatr*. 2011;**32**(3):196-205. [PubMed ID: 21336144]. <https://doi.org/10.1097/DBP.0b013e31820fd4a9>.
- Alimohammadi M, Gholinezhad Y, Mousavi V, Kahkesh S, Rezaee M, Yaghooobi A, et al. Circular RNAs: novel actors of Wnt signaling pathway in lung cancer progression. *EXCLI J*. 2023;**22**:645-69. [PubMed ID: 37636026]. [PubMed Central ID: PMC10450211]. <https://doi.org/10.17179/excli2023-6209>.
- Paskeh MDA, Mirzaei S, Orouei S, Zabolian A, Salehi H, Azami N, et al. Revealing the role of miRNA-489 as a new onco-suppressor factor in different cancers based on pre-clinical and clinical evidence. *Int J Biol Macromol*. 2021;**191**:727-37. [PubMed ID: 34562537]. <https://doi.org/10.1016/j.ijbiomac.2021.09.089>.
- Kirtonia A, Ashrafzadeh M, Zarrabi A, Hushmandi K, Zabolian A, Bejandi AK, et al. Long noncoding RNAs: A novel insight in the leukemogenesis and drug resistance in acute myeloid leukemia. *J Cell Physiol*. 2022;**237**(1):450-65. [PubMed ID: 34569616]. <https://doi.org/10.1002/jcp.30590>.
- Mafi A, Rismanchi H, Malek Mohammadi M, Hedayati N, Ghorbanhosseini SS, Hosseini SA, et al. A spotlight on the interplay between Wnt/beta-catenin signaling and circular RNAs in hepatocellular carcinoma progression. *Front Oncol*. 2023;**13**:1224138.

- [PubMed ID: 37546393]. [PubMed Central ID: PMC10403753]. <https://doi.org/10.3389/fonc.2023.1224138>.
27. Mirzaei S, Paskeh MDA, Hashemi F, Zabolian A, Hashemi M, Entezari M, et al. Long non-coding RNAs as new players in bladder cancer: Lessons from pre-clinical and clinical studies. *Life Sci.* 2022;**288**:119948. [PubMed ID: 34520771]. <https://doi.org/10.1016/j.lfs.2021.119948>.
 28. Kahkesh S, Khoshnazar SM, Gholinezhad Y, Esmailzadeh S, Hosseini SA, Alimohammadi M, et al. The potential role of circular RNAs - regulated PI3K signaling in non-small cell lung cancer: Molecular insights and clinical perspective. *Pathol Res Pract.* 2024;**257**:155316. [PubMed ID: 38692125]. <https://doi.org/10.1016/j.prp.2024.155316>.
 29. Mafi A, Khoshnazar SM, Shahpar A, Nabavi N, Hedayati N, Alimohammadi M, et al. Mechanistic insights into circRNA-mediated regulation of PI3K signaling pathway in glioma progression. *Pathol Res Pract.* 2024;**260**:155442. [PubMed ID: 38991456]. <https://doi.org/10.1016/j.prp.2024.155442>.
 30. Ashrafizadeh M, Mohan CD, Rangappa S, Zarrabi A, Hushmandi K, Kumar AP, et al. Noncoding RNAs as regulators of STAT3 pathway in gastrointestinal cancers: Roles in cancer progression and therapeutic response. *Med Res Rev.* 2023;**43**(5):1263-321. [PubMed ID: 36951271]. <https://doi.org/10.1002/med.21950>.
 31. Mafi A, Mannani R, Khalilollah S, Hedayati N, Salami R, Rezaee M, et al. The Significant Role of microRNAs in Gliomas Angiogenesis: A Particular Focus on Molecular Mechanisms and Opportunities for Clinical Application. *Cell Mol Neurobiol.* 2023;**43**(7):3277-99. [PubMed ID: 37414973]. [PubMed Central ID: PMC11409989]. <https://doi.org/10.1007/s10571-023-01385-x>.
 32. Alimohammadi M, Rahimzadeh P, Khorrami R, Bonyadi M, Daneshi S, Nabavi N, et al. A comprehensive review of the PTEN/PI3K/Akt axis in multiple myeloma: From molecular interactions to potential therapeutic targets. *Pathol Res Pract.* 2024;**260**:155401. [PubMed ID: 38936094]. <https://doi.org/10.1016/j.prp.2024.155401>.
 33. Mirzaei S, Gholami MH, Ang HL, Hashemi F, Zarrabi A, Zabolian A, et al. Pre-Clinical and Clinical Applications of Small Interfering RNAs (siRNA) and Co-Delivery Systems for Pancreatic Cancer Therapy. *Cells.* 2021;**10**(12). [PubMed ID: 34943856]. [PubMed Central ID: PMC8699513]. <https://doi.org/10.3390/cells10123348>.
 34. Heydarnia E, Dorostgou Z, Hedayati N, Mousavi V, Yahyazadeh S, Alimohammadi M, et al. Circular RNAs and cervical cancer: friends or foes? A landscape on circRNA-mediated regulation of key signaling pathways involved in the onset and progression of HPV-related cervical neoplasms. *Cell Commun Signal.* 2024;**22**(1):107. [PubMed ID: 38341592]. [PubMed Central ID: PMC10859032]. <https://doi.org/10.1186/s12964-024-01494-0>.