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Inflammatory Biomarkers Comparison Between Benign Prostatic Hyperplasia Versus Prostate Cancer Patient in Secondary Hospitals, Bogor, Indonesia

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Abstract:
This research aimed to compare inflammatory biomarkers derived from complete blood counts—namely, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI)—between BPH and prostate cancer patients. A retrospective study was conducted on 257 patients from two secondary hospitals in Bogor, Indonesia, between January 2021 and June 2025. Subjects were diagnosed with either BPH (n = 212) or prostate cancer (n = 45). Preoperative complete blood counts were used to calculate NLR, PLR, MLR, SII, and SIRI. Group comparisons were performed using the Mann–Whitney U test, and multivariate analysis of variance (MANOVA) was conducted to assess overall biomarker profile differences. Binary logistic regression was applied to evaluate the predictive value of individual biomarkers. PLR was significantly higher in prostate cancer patients (p = 0.007), while other biomarkers did not show significant intergroup differences in univariate analysis. MANOVA revealed a statistically significant difference in overall inflammatory profiles (Pillai's trace = 0.060, F(5, 251) = 3.208, p = 0.008). Logistic regression identified PLR (p < 0.001), SII (p = 0.035), and SIRI (p = 0.009) as independent predictors of prostate cancer. Inflammatory biomarkers—particularly PLR, SII, and SIRI—may serve as useful markers to differentiate prostate cancer from BPH and offer prognostic insight. These parameters are readily available from routine complete blood counts, making them valuable tools in clinical settings, especially in resource-limited areas. Further prospective studies are recommended to validate their utility and integration into standard diagnostic pathways.
***Keywords**: BPH; prostate cancer; inflammatory biomarker*

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a benign enlargement of the prostate and the most common cause of lower urinary tract symptoms (LUTS) in elderly patients (Ng et al., 2025). According to BPJS data in Indonesia, 97,403 BPH cases were recorded between 2016 and 2020, most commonly found among men aged 60–69 years (Tjahjodjati et al., 2021). The pathophysiology of BPH involves genetic, hormonal, metabolic, and inflammatory factors. Dihydrotestosterone (DHT) stimulates prostatic epithelial and stromal proliferation (Ng et al., 2025), while insulin and IGF-1 stimulate stromal growth and exert paracrine effects on epithelial cells. This mechanism links metabolic conditions such as obesity and diabetes to BPH (Devlin et al., 2021).

Prostate cancer is one of the most common types of cancer in men and ranks as the fifth leading cause of cancer-related death (Elmehrath et al., 2021; Ye et al., 2022). In 2020, 1.4 million new cases and 375,000 deaths due to prostate cancer were reported worldwide, especially in developed countries (Leslie et al., 2025). In Indonesia, prostate cancer incidence has tripled in recent years due to an aging population and increased PSA screening, with over 50% of new cases diagnosed at an advanced stage (Safriadi et al., 2022). Risk factors include genetic mutations, family history, and chronic inflammation (Fernandes et al., 2023).

Inflammation plays a key role in both BPH and prostate cancer. In BPH, fibroblast-derived growth factors and increased macrophage recruitment promote stromal proliferation through androgen pathways (Devlin et al., 2021). A shift in immune cells and the release of reactive oxygen species (ROS) further promote tissue remodelling and hyperplasia. In prostate cancer, chronic inflammation leads to DNA damage, genetic mutation, and tumor progression (Tanagho & McAninch, 2008). Chronic inflammation is characterized by a shift in balance toward tumor-promoting innate immune cells (macrophages, mast cells, and neutrophils) and away from the tumor-killing activity of adaptive immune cells (subclasses of T and B lymphocytes) (Zhou et al., 2021).

In recent years, inflammatory markers derived from complete blood counts such as the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI) have emerged as cost-effective indicators of systemic immune activation and potentially possess prognostic value in neoplastic diseases, including prostatic conditions. NLR reflects the balance between neutrophil and lymphocyte activity. Elevated NLR is linked to increased intravesical prostatic protrusion, higher International Prostate Symptom Scores (IPSS), and increased risk of BPH progression (Tanik et al., 2014; Chung et al., 2020). In prostate cancer, higher NLR is associated with poorer prognosis, reduced survival, and limited treatment response, especially in castration-resistant prostate cancer (Huszno et al., 2022; Lorente et al., 2015). This immune imbalance may reflect age-related immunosenescence contributing to inflammation and tumor-promoting microenvironments.

PLR is also a useful marker, where elevated platelet counts may indicate increased production of angiogenic growth factors such as VEGF and PDGF. In BPH, elevated PLR and SII are associated with increased disease prevalence and symptom severity (Shi et al., 2024). Elevation of pro-inflammatory cytokines such as IFN-γ and IL-17 promotes the secretion of growth factors by prostatic epithelial and stromal cells (Shi et al., 2024). Higher PLR is associated with poor survival and increased mortality in prostate cancer patients, especially when PLR exceeds 150 (Li et al., 2015). MLR similarly reflects the pro-inflammatory role of monocytes relative to the tumor-suppressive function of lymphocytes. In BPH patients, particularly those with type 2 diabetes, elevated MLR is positively associated with prostate volume (Chen & Feng, 2023). In prostate cancer, MLR has been proposed as a predictor of disease progression, particularly in patients with elevated PSA levels and larger prostate volume (Wang et al., 2024).

The SII, which incorporates neutrophils, lymphocytes, and platelets, also reflects the balance between innate and adaptive immune responses. Higher SII levels are associated with larger prostate volume, higher IPSS, and clinical progression in BPH (Ahmed et al., 2023; Liu et al., 2024). In prostate cancer, elevated SII is associated with advanced disease and higher mortality, particularly in high-risk populations such as African Americans (Horsanali et al., 2023; Bailey-Whyte et al., 2023). Lastly, the SIRI, which is calculated using neutrophils, monocytes, and lymphocytes, reflects a shift toward innate immune responses when elevated. Higher SIRI levels are independently associated with LUTS progression in BPH (Horsanali et al., 2023). However, its diagnostic relevance in BPH remains inconsistent

compared to other markers such as SII and PLR (Shi et al., 2024). SIRI has also been linked to poor survival outcomes and increased mortality in cancer cases, including prostate cancer (Zhou et al., 2021; Bailey-Whyte et al., 2023).

This study aims to compare inflammatory biomarkers, including NLR, MLR, PLR, SIRI, and SII, between patients with BPH and prostate cancer. Evaluating these biomarkers may provide insight into the role of inflammation in both diseases. The findings of this research are expected to contribute both theoretically and practically. Theoretically, this study enriches the scientific literature on the role of inflammatory biomarkers in differentiating BPH and prostate cancer, as well as their potential as prognostic indicators. Practically, the results may assist clinicians, particularly in secondary hospitals with limited resources, in utilizing routine complete blood count data as a cost-effective tool to support diagnostic processes and predict disease progression. Furthermore, this study can serve as a foundation for future research exploring the integration of inflammatory biomarkers into standard clinical pathways for prostate disease management.

METHOD

This retrospective study included patients that were categorized based on pathological diagnosis as prostate cancer and benign prostatic hyperplasia. Research data were obtained from medical records from January 2025 until June 2025. The study was conducted at Ciawi General Hospital between March 2025 and June 2025. Inflammatory biomarkers, including NLR, MLR, PLR, SIRI, and SII were obtained from complete blood counts before patient underwent surgery for treatment and diagnosis.

Data analysis was done using SPSS version 29. The normality of data distribution was assessed using Shapiro-Wilk test, which resulted in non-normal distribution. Comparison between two groups were analyzed using the Mann-Whitney U test. Statistical significance was set at $p < 0.05$. Multivariate analysis of variance (MANOVA) was performed to assess the overall difference in combined inflammatory biomarker profiles between groups. Additionally, binary logistic regression analysis was performed to assess the predictive value of each biomarker in identifying prostate cancer.

RESULTS AND DISCUSSION

A total of 257 patients were included in this study, consisting of 212 patients with BPH and 45 patients with prostate cancer. Histopathological examination was used to determine the diagnosis of the patients. The distribution of age was confirmed using Shapiro-Wilk test for both groups ($p > 0.05$). Independent t-test was performed to compare baseline age between the BPH and prostate cancer groups. The difference in mean age was not statistically significant ($p = 0.395$), indicating that baseline age characteristics were comparable between groups. Inflammatory biomarkers including NLR, PLR, MLR, SII, and SIRI were obtained from patients' electronic medical record and were used in data analysis. Descriptive statistic showed that the mean values for inflammatory biomarkers were higher in the prostate cancer group compared to the BPH group.

Table 1. Baseline Characteristics and inflammatory biomarker values

	Diagnosis	Mean	Std. Deviation	p-value (MWU)
Age	BPH	68.84	8.42	
	PCa	67.67	8.42	
Hb (g/dL)	BPH	12.91	1.71	
	PCa	12.27	2.09	
WBC	BPH	9.66	3.53	
(10^3/uL)	PCa	8.93	3.65	
NLR	BPH	3.71	3.38	0.149
	PCa	3.75	2.76	
PLR	BPH	161.14	90.15	0.007
	PCa	192.45	86.09	
MLR	BPH	0.39	0.23	0.247
	PCa	0.44	0.26	
SII	BPH	1106.84	1072.81	0.066
	PCa	1188.88	924.51	
SIRI	BPH	2.91	3.35	0.678
	PCa	3.19	4.38	

Hb: Haemoglobin; WBC: white blood count; NLR: Neutrophil-Lymphocyte Ratio; PLR: Platelet-Lymphocyte Ratio; MLR: Monocyte-Lymphocyte Ratio; SII: systemic immune-inflammation index (platelet count x neutrophil count / lymphocyte count); SIRI: systemic inflammation response index (neutrophil count x monocyte count / lymphocyte count); MWU: Mann-Whitney U Test

Source: Primary data processed, 2025

Mann-Whitney U test was performed to analyze each individual biomarkers. The result demonstrated that only PLR showed statistically significant difference between the two groups (p = 0,007) with higher values in the prostate cancer group.

Table 2. Multivariate Analysis of Variance (MANOVA)

	Value	F	df	p-value	Partial Eta Squared
Pillai's Trace	0.060	3.208	5, 251	0.008	0.060
Wilks' Lambda	0.940	3.208	5, 251	0.008	0.060
Hotelling's Trace	0.064	3.208	5, 251	0.008	0.060
Roy's Largest Root	0.064	3.208	5, 251	0.008	0.060

Source: Primary data processed, 2025

MANOVA was performed to assess whether the combined inflammatory biomarkers differed significantly between BPH and prostate cancer patients. Pillai's trace analysis demonstrated a statistically significant overall difference in inflammatory biomarkers between the two groups (Pillai's trace = 0.060, F(5, 251) = 3.208, p = 0.008). The partial eta squared for this model was 0.060, suggesting that approximately 6% of the variance in the combined inflammatory biomarkers is explained by diagnostic category, which reflects a modest effect size. Other multivariate test statistics (Wilks' Lambda, Hotelling's Trace, and Roy's Largest Root) also showed similar significance (p = 0.008), supporting the robustness of the finding. In summary, the MANOVA indicates that the overall inflammatory biomarker

signature differs significantly between patients with BPH and those with prostate cancer, even though not all biomarkers individually reached significance in univariate comparisons.

Table 3. Logistic Regression Analysis

	B (SE)	OR (Exp(B))	95% CI	p-value
NLR	-0.267	0.766	0.543	0.129
PLR	0.15	1.016	1.006	<0.001
MLR	-2.424	0.089	0.004	0.114
SII	-0.001	0.999	0.997	0.035
SIRI	0.508	1.663	1.136	0.009

Source: Primary data processed, 2025

Furthermore, binary logistic regression showed that PLR ($p < 0.001$), SII ($p = 0.035$), and SIRI ($p = 0.009$) were statistically significant independent predictors of prostate cancer. Odds ratios (OR) provided further insight into the predictive strength of each biomarker. PLR had an OR of 1.016 (95% CI 1.006–1.025, $p < 0.001$). This indicates that for every unit increase in PLR, the odds of prostate cancer increased by 1.6%. Similarly, SIRI was found to be an independent predictor with an OR of 1.663 (95% CI 1.136–2.433, $p = 0.009$), indicating that patients with higher SIRI values had a 66% increased odds of prostate cancer. Lastly, SII had an OR of 0.999 (95% CI 0.997–1.000, $p = 0.035$), showing that it has statistical significance but minimum effect size.

Discussion

Inflammation plays a crucial role in the pathophysiology of both Benign Prostatic Hyperplasia (BPH) and prostate cancer. This study was conducted to investigate the differences in inflammatory biomarkers between BPH and prostate cancer patients, as well as to evaluate the predictive potential of these biomarkers in differentiating the two conditions. Our findings showed that the mean values of inflammatory biomarkers were higher in the prostate cancer group, with MANOVA showing a significant difference in the overall inflammatory profile. However, when evaluating each biomarker individually, only PLR showed a statistically significant elevation in the prostate cancer group. Additionally, binary logistic regression analysis suggested that PLR, along with SII and SIRI, were independent predictors of prostate cancer.

The MANOVA result ($p = 0.008$) supports the hypothesis that inflammation, as a hallmark of cancer, plays a role in disease progression and tumor survival. Tumor cells can trigger an inflammatory response by releasing chemotactic factors such as damage-associated molecular patterns and by acidifying the microenvironment (Zhou et al., 2021). Activated tumor-promoting inflammatory cells such as macrophage subtypes, mast cells, neutrophils, and certain subclasses of T and B lymphocytes can promote angiogenesis, stimulate tumor proliferation, and facilitate tissue invasion. Conversely, adaptive immune cells, including other T- and B-cell subsets, can elicit tumor-killing responses (Zhou et al., 2021). An imbalance in immune cell activity due to chronic inflammation may therefore contribute to tumor progression in prostatic diseases, particularly prostate cancer. However, the lack of

significance for most individual biomarkers in the Mann–Whitney U tests highlights variability and overlapping values in clinical presentations.

PLR emerged as the most consistent biomarker, demonstrating both significant intergroup differences and predictive value in logistic regression. PLR has been associated with poorer overall and cancer-specific survival in several urologic malignancies (Huszno et al., 2022). A previous study comparing PLR among healthy controls, BPH patients, and prostate cancer patients also showed significantly higher PLR values in the prostate cancer group. Moreover, prostate cancer patients with higher PLR (>150) exhibited significantly higher mortality during a three-year follow-up compared to those with lower PLR (<150) (Li et al., 2015). A meta-analysis further showed that elevated PLR correlated with poor disease-free and overall survival in prostate cancer patients, underscoring its prognostic significance (Wang et al., 2018). These findings suggest that platelets play a role in cancer growth, dissemination, and angiogenesis through platelet-derived TGF-β. Interactions between cancer cells and platelets activate the TGF-β/Smad and NF-κB pathways, which enhance metastasis. Additionally, platelet aggregation around cancer cells may protect them from lysis by NK cells. Conversely, tumor-infiltrating lymphocytes (CD8+ and CD4+) are known to play important roles in anti-tumor activity. Therefore, PLR not only provides prognostic information in cancer patients but is also readily available in daily practice as part of a routine complete blood count (Wang et al., 2018).

SII and SIRI, though not showing significant intergroup differences in the Mann–Whitney U test, were identified as significant predictors of prostate cancer in this study. Both indices are calculated from multiple blood cell components and thus can provide a more comprehensive representation of immune system status. SII highlights platelet activity in inflammation, while SIRI focuses on monocyte-driven systemic inflammation and immune activation. Both markers have been described as prognostic indicators in various cancer types, cardiovascular diseases, and inflammatory disorders (Marchi et al., 2024). A meta-analysis reported that high SII was associated with poorer outcomes across multiple cancer types, including urological malignancies. Proposed mechanisms include tumor-induced thrombopoietin leading to thrombocytosis, the pro-tumor roles of platelets and neutrophils, and the suppression of lymphocyte-mediated anti-tumor activity (Yang et al., 2018). In prostate cancer, elevated SII levels combined with a high Ki-67 index have been linked to poorer prognosis, higher Prostate-Specific Antigen (PSA), Gleason score, and lymph node metastasis (Wu et al., 2023).

SIRI has also been shown to serve as a prognostic tool in several malignancies. High pre-treatment SIRI levels are correlated with reduced overall and disease-free survival across various cancers, including prostate cancer (Zhou et al., 2021). In prostate cancer, SIRI—alongside NLR—has been identified as a strong prognostic biomarker, associated with increased all-cause and cancer-specific mortality (Bailey-Whyte et al., 2023). Recent findings suggest that SIRI may not only reflect a systemic pro-inflammatory state but also indicate transitions in neutrophil subtypes and their activity. Under certain conditions, neutrophils may exert anti-tumor effects by promoting cancer cell apoptosis and cooperating with T cells. However, they can also secrete pro-inflammatory cytokines, reactive oxygen species (ROS), and neutrophil extracellular traps (NETs) that foster tumor metastasis and angiogenesis (Tang

et al., 2024). Monocytes differentiate into tumor-associated macrophages (TAMs), which can exhibit either anti- or pro-tumor effects depending on signals from the tumor microenvironment. SIRI may thus indicate monocyte responses and holds potential as a therapeutic target when combined with immunotherapy (Tang et al., 2024).

Our findings showed that although the mean NLR and MLR levels were higher in the prostate cancer group, these differences were not statistically significant compared with the BPH group.

This study has several limitations. The sample size was particularly limited for the prostate cancer group (n = 45) due to the lower incidence of this disease compared with BPH in the general population. A limited sample size may reduce statistical power and generalizability. Furthermore, the retrospective study design restricts causal inference and is prone to information and selection bias. Confounding variables such as undiagnosed infections and comorbidities could have influenced inflammatory biomarker levels but were not fully controlled for. Future prospective studies with larger sample sizes are recommended to validate these findings and to further explore the clinical utility of inflammatory biomarkers in prostatic disease management.

CONCLUSION

This study demonstrated significant differences in inflammatory profiles between BPH and prostate cancer patients. Among the evaluated biomarkers, PLR showed a significant difference between the two groups and was also an independent predictor of prostate cancer, along with SII and SIRI. These findings highlight the role of inflammation in prostatic diseases. Additionally, inflammatory biomarkers derived from routine blood tests might be utilized as a cost-effective prognostic tool and potentially help in predicting prostatic disease progression especially in resource-limited settings. Further prospective study should explore their prognostic value and their integration with existing clinical parameters to improve early detection in prostate cancer.

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