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Evaluation of Neutrophil-Lymphocyte Ratio and Platelet-Lymphocyte Ratio in Diabetic Kidney Disease Patients: A Hospital-Based Cross-Sectional Analysis

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ABSTRACT

Background: Diabetes mellitus represents a chronic metabolic disorder with globally increasing prevalence and is one of the leading causes of microvascular complications such as diabetic kidney disease (DKD). Chronic inflammation plays a crucial role in DKD pathogenesis, prompting exploration of simple inflammatory markers such as neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR). This study aimed to determine the relationship between NLR and PLR values with the incidence of DKD.

Subject and Methods: This cross-sectional study employed consecutive non-random sampling technique. The study population consisted of all patients visiting Cinta Kasih Tzu Chi Cengkareng Hospital from January to April 2025, totaling 128 respondents. Secondary data from medical records were analyzed using Chi-Square test to determine associations between NLR and PLR (categorized as high vs low) with diabetic kidney disease incidence. Statistical analysis employed Chi-Square test with significance set at $p<0.050$.

Results: Among 128 respondents, 64 (50.00%) were diagnosed with diabetic kidney disease. High NLR group comprised 101 respondents (78.90%), with 50 (39.10%) having DKD. High PLR group totaled 32 respondents (25.00%), with 19 (14.80%) having DKD. NLR demonstrated no significant association with DKD incidence (PR= 0.96; CI95% 0.48 to 1.41; p=0.828). PLR also showed no significant association with DKD incidence (PR= 0.89; CI95% 0.52 to 1.53; p=0.552).

Conclusion: Neither NLR nor PLR demonstrates a significant relationship with diabetic kidney disease incidence at Cinta Kasih Tzu Chi Cengkareng Hospital. These findings suggest that NLR and PLR cannot be used as standalone predictors for DKD and should be considered alongside other clinical parameters in comprehensive diabetes management protocols.

Keywords: Diabetic nephropathy, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, diabetes mellitus

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BACKGROUND

Diabetes mellitus represents a chronic metabolic disorder characterized by inap/-propriate elevation of blood glucose levels. Several types of diabetes exist, including type 1 diabetes mellitus, type 2 diabetes mellitus, maturity-onset diabetes of the young (MODY), gestational diabetes, neonatal diabetes, and secondary causes due to endocrinopathies, steroid use, and

other factors. However, type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) constitute the main subtypes, where T1DM is caused by imperfect insulin secretion and T2DM is caused by suboptimal insulin action (Sapra and Bhandari, 2017).

The International Diabetes Federation (IDF) in the 10th edition Atlas reports that an estimated 537 million people aged 20-79 years currently have diabetes, representing 10.5% of the global population in this age group. This number is projected to increase over time, with estimates of 643 million (11.3%) by 2030 and 783 million (12.2%) by 2045 (Magliano and Boyko, 2021).

In 2021, the number of diabetes cases among adults in Indonesia was 19,465,102 people, representing 10.8% of the total adult population in Indonesia (International Diabetes Federation, 2024). This alarming trend is consistent with global patterns showing diabetes as a leading cause of morbidity and mortality worldwide (Zheng, Ley and Hu, 2018).

This concerning trend aligns with evidence that diabetes has become a major non-communicable disease priority in Indonesia, contributing significantly to the national disease burden (Mboi et al., 2022; Wahidin et al., 2024). Given this continuously increasing prevalence, diabetes has become a global concern. One microvascular complication of diabetes is diabetic kidney disease (DKD).

As diabetes prevalence increases worldwide, the number of people affected by diabetic kidney disease complications also rises. DKD not only affects kidney risk but significantly increases infection rates and cardiovascular events that can reduce patients' quality of life. DKD has multifactorial causes, with chronic inflammation playing an important role in its onset and progression. Diabetic patients experience metabolic dysfunction and activate inflammatory signals in the body, leading to increased levels of several inflammatory factors that promote inflammation and are involved in kidney damage (Rumondang, Bisuk and Umboh, 2022).

However, DKD screening is not performed routinely due to cost issues and technical constraints in clinical application. Additionally, care costs for patients with DKD are extremely high, causing increased economic burden. The economic impact of diabetic complications, particularly nephropathy, represents a significant healthcare challenge globally (Bommer et al., 2018). Therefore, various early detection indicator methods for DKD have begun to be developed and have become research priorities in the field of diabetes complications. One cost-effective and easily measured indicator used to detect inflammatory status is the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR). Although NLR and PLR have been proven to have close relationships with the development and prognosis of various diseases, research on their relationship with DKD remains very limited and has not been clinically and significantly established (Li, Shen and Rao, 2022).

Previous studies have demonstrated correlations between NLR and diabetic control levels (Duman et al., 2019), while other research has shown associations between these inflammatory markers and various complications in diabetic patients (Akmal TH et al., 2024). Recent studies have also explored NLR in diabetic patients with concurrent infections, showing significant correlations with disease severity (Findi Z et al., 2023). Some studies have explored PLR as a marker for kidney damage in other conditions (Tolla et al., 2019), and research has indicated potential

relationships between inflammatory ratios and various clinical conditions beyond diabetes (Firdaus DY et al., 2022), and research has indicated potential relationships between inflammatory ratios and diabetic complications (Khairani et al., 2022).

The hospital setting provides valuable opportunities for examining diabetes epidemiology and inflammatory markers. Hospital-based studies offer advantages including access to comprehensive medical records, standardized diagnostic procedures, and diverse patient populations. Understanding the relationship between inflammatory markers and diabetic complications in specific healthcare settings enables targeted prevention strategies and improved clinical management protocols. This study aimed to investigate the relationship between NLR and PLR with diabetic kidney disease incidence at Cinta Kasih Tzu Chi Cengkareng Hospital, contributing to the growing body of evidence on inflammatory markers in Indonesian healthcare settings.

SUBJECTS AND METHOD

1. Study Design

This was a cross-sectional study to examine the relationship between neutronphil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) with diabetic kidney disease incidence. Cross-sectional studies are particularly suitable for assessing prevalence and associations between variables at a single point in time. The study was conducted at Cinta Kasih Tzu Chi Cengkareng Hospital, Jakarta, Indonesia, from January to April 2025, including preparation, data collection, and report compilation phases.

2. Population and Sample

The target population consisted of all patients diagnosed with diabetic kidney disease (DKD). The source population (accessible population) comprised all patients visiting Cinta Kasih Tzu Chi Cengkareng Hospital during the study period. Sample size was determined using the formula for comparing two proportions, with significance level (α) 0.05 and power (1-β) 0.80 and effect size of 0.5, resulting in a minimum requirement of 64 respondents per group, totaling 128 respondents.

Consecutive non-random sampling technique was employed, where all patients meeting criteria were included sequentially until the sample size was reached. Inclusion criteria comprised: (1) patients diagnosed with type 1 or type 2 diabetes mellitus based on medical examination; (2) age ≥18 years; (3) available NLR and PLR laboratory data in medical records; and (4) agreement to participate by providing informed consent. Exclusion criteria included: (1) patients with non-diabetic kidney disease; (2) patients with acute infection or active systemic inflammatory conditions; and (3) patients with hematological disorders such as severe anemia or significant leukocytosis.

3. Study Variables

The dependent variable in this study was diabetic kidney disease incidence. The independent variables were neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR). Confounding variables controlled included age, gender, diabetes duration, HbA1c, blood pressure, BMI, smoking history, medication use, and other comorbidities.

4.Operational Definition of Variables

Diabetic kidney disease was defined based on DKD diagnosis documented in medical records. NLR and PLR were calculated from complete laboratory data recorded in patient medical records. NLR and PLR measurement scales were numeric, while

DKD was categorized as "present" or "absent."

5. Study Instruments

Data on type 2 diabetes mellitus diagnosis were obtained from medical records based on clinical documentation and laboratory results. Patient demographic data including age and gender were collected from medical record documentation. All data were extracted using a standardized data collection form designed specifically for this study to ensure consistency and completeness of information.

6. Data Analysis

Data analysis utilized prevalence ratio calculations to determine associations between independent variables (NLR and PLR) and the dependent variable (diabetic kidney disease incidence). Statistical analysis was performed using Chi-Square test with significance set at $p<0.050$. Confidence intervals were calculated at 95% level. The strength of association was measured using prevalence ratio with 95% confidence interval. All statistical analyses were conducted using SPSS version 26.0 software.

7. Research Ethics

Research ethical issues including informed consent, anonymity, and confidentiality were addressed carefully during the study process. This study utilized secondary data from medical records with appropriate institutional approval from Cinta Kasih Tzu Chi Cengkareng Hospital. Patient confidentiality was maintained throughout data collection and analysis by using coding systems and removing personal identifiers. The study protocol adhered to Declaration of Helsinki principles for medical research involving human subjects. Research ethical clearance approval was obtained from the Health Research Ethics Committee, Faculty of Medicine, Tarumanagara University, Indonesia, No. 588/KEPK/FK/UNTAR/II/-2025.

RESULTS

1. Sample Characteristics

Among 128 respondents examined in this study, the mean age was 58.45 years (SD= 14.513 years) with age range from 25 to 78 years. Gender distribution showed male predominance with 67 respondents (52.30%) compared to female respondents totaling 61 (47.70%). Overall, 64 respondents (50.00%) were diagnosed with diabetic kidney disease, while 64 respondents (50.00%) did not have DKD diagnosis (see Table 1).

Table 1. Sample Characteristics of Study Population (N=128)

Characteristics	Category	Frequency	Percentage
Age	<45 years	21	16.40%
	45-65 years	68	53.10%
	>65	39	30.50%
Gender	Male	67	52.30%
	Female	61	47.70%

2. Neutrophil-Lymphocyte Ratio (NLR) Distribution

Analysis revealed that the majority of respondents had high NLR values, comprising 101 respondents (78.90%), while respondents with low NLR values totaled 27 respondents (21.10%) (see Table 2).

Table 2. Neutrophil-Lymphocyte Ratio (NLR) Distribution

Variable	Frequency	Percentage
Low NLR	27	21.10%
High NLR	101	78.90%
Total	**128**	**100%**

3. Platelet-Lymphocyte Ratio (PLR) Distribution

Analysis showed that the majority of respondents had low PLR values, comprising 96 respondents (75.00%), while respondents with high PLR values totaled 32 respondents (25.00%) (see Table 3).

Table 3. Platelet-Lymphocyte Ratio (PLR) Distribution

Variable	Frequency	Percentage
Low PLR	96	75.00%
High PLR	32	25.00%
Total	**128**	**100%**

4. Bivariate Analysis

Relationship between Neutrophil-Lymphocyte Ratio (NLR) and Diabetic Kidney Disease

The analysis demonstrated no significant association between NLR and diabetic kidney disease incidence. Among respondents in the high NLR group, 50 out of 101 (49.50%) had DKD compared to 14 out of 27 (51.85%) in the low NLR group. This association was not statistically significant (PR= 0.96; 95% CI= 0.48 to 1.41; p=0.828), indicating that individuals with high NLR were not significantly more likely to develop diabetic kidney disease compared to those with low NLR (see Table 4).

Table 4. Relationship between Neutrophil-Lymphocyte Ratio (NLR) and Diabetic Kidney Disease Incidence

NLR	DM	%	DKD	%	Total	%	p	PR
Low	13	10.20%	14	10.90%	27	21.10%		
High	51	39.80%	50	39.10%	101	78.90%	**0.828**	**0.96**
Total	**64**	**50.00%**	**64**	**50.0%**	**128**	**100%**		

Relationship between Platelet-Lymphocyte Ratio (PLR) and Diabetic Kidney Disease

PLR analysis revealed no significant association with diabetic kidney disease incidence. Among respondents with high PLR, 19 out of 32 (59.38%) had DKD compared to 45 out of 96 (46.88%) in the low PLR group. This difference was not statistically significant (PR= 0.89; 95% CI= 0.52 to 1.53; p=0.552), indicating that PLR is not a significant predictor of diabetic kidney disease development in this population (see Table 5).

Table 5. Relationship between Platelet-Lymphocyte Ratio (PLR) and Diabetic Kidney Disease Incidence

PLR	DM	%	DKD	%	Total	%	P Value	PR
Low	16	12.50%	19	14.80%	35	27.30%		
High	48	37.50%	45	35.20%	93	72.70%	**0.552**	**0.89**
Total	**64**	**50.00%**	**64**	**50.00%**	**128**	**100%**		

5. Multivariate Analysis

Relationship between demographic and inflammatory markers with Diabetic Kidney Disease

Binary logistic regression was conducted to assess the independent association of demographic variables (age and gender) and inflammatory markers (NLR and PLR) with diabetic kidney disease. The results demonstrated that none of these variables were significantly associated with DKD. Female respondents had lower odds compared to males (aOR= 0.82; 95% CI= 0.40 to 1.68; p = 0.592). Respondents aged <45 years and 45–65 years did not show significant differences compared to those aged >65 years (aOR= 1.40; 95% CI = 0.473 to 4.15; p= 0.54 and aOR = 0.93; 95% CI= 0.43 to 2.21; p= 0.947, respectively). Similarly, high PLR (aOR= 1.25 95% CI = 0.52 to 3.01; p= 0.621) and high NLR (aOR= 1.03; 95% CI= 0.40 to 2.67; p= 0.945) were not significantly associated with DKD incidence. These findings indicate that neither demographic variables nor inflammatory markers were independent predictors of diabetic kidney disease in this study population (see Table 6).

Table 6. The results of binary logistic regression of Diabetic Kidney Disease (n=128)

Independent variables	aOR	Diabetic Kidney disease 95% CI		p
		Lower Bound	Upper Bound	
Gender				
Male	Ref.			
Female	0.82	0.40	1.68	0.592
Age				
<45 years old	1.40	0.47	4.15	0.543
45-65 years old	0.97	0.43	2.21	0.947
>65 years old	Ref.			
PLR				
Low	Ref.			
High	1.25	0.52	3.02	0.621
NLR:				
Low	Ref.			
High	1.03	0.40	2.67	0.945

DISCUSSION

The findings of this study demonstrate no significant association between neutrophil-to-lymphocyte ratio (NLR) and diabetic kidney disease incidence, with a prevalence ratio of 0.96 (95% CI= 0.48 to 1.41; p= 0.828). Similarly, platelet-to-lymphocyte ratio (PLR) showed no significant association with DKD incidence (PR= 0.89; 95% CI= 0.52 to 1.53; p= 0.552). These

findings contrast with some previous research suggesting that inflammatory markers could serve as predictors of diabetic complications.

In our multivariate logistic regression, after adjusting for age and gender, neither NLR nor PLR were found to be independent predictors of DKD (Table 6), indicating limited discriminatory value when demographic factors are considered.

The absence of significant association between NLR and DKD in this study may be attributed to several factors. While NLR has been established as an inflammatory marker, its sensitivity and specificity as a standalone predictor for diabetic complications remain limited. Research indicates that NLR values can be influenced by various factors including acute infections, medications, and other comorbidities that may not directly relate to kidney function deterioration (Khandare et al., 2017).

Elevated neutrophils contribute to oxidative stress and release of pro-inflammatory cytokines such as IL-6 and TNF-α, which in turn accelerate podocyte injury and glomerulosclerosis. Conversely, reduced lymphocyte counts may represent impaired adaptive immunity, further exacerbating tissue injury (Huang et al., 2015; Zhao et al. 2020). These mechanisms suggest that while NLR can reflect systemic inflammatory burden, it may not directly translate into kidney-specific outcomes in all populations. The hospital-based study design may have introduced selection bias, as patients with more severe conditions or those requiring immediate medical attention might be overrepresented.

Previous studies have suggested correlations between elevated NLR and diabetic complications, but the relationship appears to be complex and multifactorial. The pathogenesis of DKD involves multiple overlapping pathways, including hemodynamic alterations, metabolic dysregulation, and activation of pro-fibrotic signaling cascades. Recent studies emphasize the role of Wnt/β-catenin and TGF-β pathways in driving podocyte dysfunction, extracellular matrix accumulation, and eventual progression to proteinuria and renal fibrosis (Zhou and Liu, 2015; Samsu, 2021). These mechanisms underline that systemic markers like NLR and PLR only represent partial aspects of the inflammatory milieu and cannot capture the multifactorial biological processes of DKD.

Consistent with our multivariate regression, PLR also did not emerge as an independent predictor of DKD after adjusting for age and gender. This suggests that platelet-lymphocyte interactions, while potentially relevant in systemic inflammation, may not be specific enough to predict kidney complications in diabetic patients. PLR values can be influenced by various factors including medication use, particularly antiplatelet therapy commonly prescribed to diabetic patients, which could affect the reliability of PLR as a diabetic complication predictor (Li, Shen and Rao, 2022).

Beyond statistical associations, the biological role of platelets in DKD progression is increasingly recognized. Platelets release mediators such as platelet-derived growth factor (PDGF) and transforming growth factor-β (TGF-β), which stimulate mesangial proliferation, extracellular matrix accumulation, and renal fibrosis (Qiao et al., 2021). This pro-fibrotic activity links platelet activation with microvascular injury in diabetic kidneys, although clinical correlations using PLR remain inconsistent.

Taken together, our results reinforce that while NLR and PLR reflect systemic inflammation, they are insufficient as independent predictors of DKD. The study's findings indicate that both NLR and PLR,

while easily obtainable from routine blood tests, cannot serve as standalone diagnostic or predictive tools for diabetic kidney disease. This aligns with current clinical practice that emphasizes comprehensive assessment including multiple parameters such as estimated glomerular filtration rate (eGFR), albuminuria, duration of diabetes, glycemic control, and blood pressure management for DKD evaluation and management. Recent studies have emphasized the importance of multi-parameter approaches in diabetic nephropathy assessment and management (de Boer et al., 2020).

These findings are consistent with previous research demonstrating the complex nature of diabetic kidney disease pathogenesis (Alicic, Rooney and Tuttle, 2017). Some studies have suggested correlations between inflammatory markers and diabetic complications in specific populations (Lauddin et al., 2019), though results have been variable across different patient groups and study designs.

This study has several limitations that should be acknowledged. The cross-sectional design limits causal inference, and the hospital-based setting may not represent the general diabetic population. In addition, important confounding variables such as diabetes duration, glycemic control status, blood pressure levels, and medication use were not controlled for, which could significantly influence both inflammatory markers and kidney function, potentially confounding the observed associations. The relatively small sample size may also have reduced the statistical power to detect subtle associations.

Previous cross-sectional studies in Indonesian healthcare settings have reported varying results regarding inflammatory markers and metabolic conditions (Rias et al., 2020), underscoring the importance of population-specific research in this area.

In light of these limitations, future research should employ longitudinal designs with comprehensive risk factor assessment and larger, more diverse populations to better elucidate the complex relationships between inflammatory markers and diabetic complications. Moreover, the integration of multiple biomarkers and clinical parameters into predictive models may enhance accuracy in identifying DKD risk.

Despite these limitations, the present study contributes to the growing body of evidence on inflammatory markers in diabetic complications and provides context-specific insights for clinical practice in Indonesian healthcare settings. While NLR and PLR may not serve as standalone predictors, they may still be useful components of comprehensive inflammatory assessment protocols in diabetic patient management, particularly in resource-limited settings where cost-effective tools are needed.

AUTHORS CONTRIBUTION:

I Made Satya Pramana Jaya formulated the research concept, designed the cross-sectional study methodology, extracted and collected data from medical records, conducted statistical analysis using Chi-Square test, interpreted study findings, wrote the original manuscript draft, and finalized manuscript revisions. Lydia Tantoso supervised the overall research project, validated the study methodology and data collection procedures, guided statistical analysis and result interpretation, reviewed and revised the manuscript, and provided final approval for publication.

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CONFLICT OF INTEREST

The authors declare that the study was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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