

MLR and Survival in CKD Patients on Regular Hemodialysis at Tabanan Hospital (2023-2025)

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Abstract

Chronic kidney disease (CKD) is often accompanied by persistent low-grade inflammation, which can be challenging to characterize as infectious or non-infectious due to elevated inflammatory markers such as C-reactive protein (CRP), monocyte chemoattractant protein-1 (MCP-1), IL-6, IL-8, and TNF-alpha. The monocyte-lymphocyte ratio (MLR) has emerged as a biomarker specifically indicative of chronic inflammation and has been shown to correlate with worsening kidney function in CKD patients, suggesting its potential to predict disease severity. This observational analytical study examined CKD patients undergoing regular hemodialysis, collecting MLR data and analyzing survival outcomes. Survival analysis was performed using Kaplan–Meier survival curves, Cox regression, and Log-Rank tests. The study found significant differences in survival rates among patients with mild, moderate, and high MLR values. Moreover, MLR was statistically significant in predicting the occurrence of death, with each incremental increase in MLR associated with a heightened risk of mortality. These findings highlight the clinical utility of MLR as a prognostic biomarker in CKD, providing a simple, cost-effective tool for assessing chronic inflammation and guiding risk stratification in patients undergoing hemodialysis.

Keywords: CKD, MLR, Survival

INTRODUCTION

Chronic Kidney Disease (CKD) has become one of the diseases with the highest morbidity and mortality worldwide. Epidemiological data indicate that around 850 million people suffer from CKD, especially in low- and middle-income countries. This number has increased alongside the rise in obesity, diabetes mellitus, and hypertension, which are notable risk factors for CKD (Bello et al., 2024; Kovesdy, 2022). Chronic Kidney Disease (CKD) is defined as an abnormality in kidney structure or function lasting at least three months, meeting at least one criterion for kidney damage markers or a reduced Glomerular Filtration Rate (GFR). Markers of kidney damage include persistent albuminuria ($\text{ACR} \geq 30 \text{ mg/g}$ [$\geq 3 \text{ mg/mmol}$]), abnormalities in urine sediment, sedentary hematuria, electrolyte or tubular disorders, histological abnormalities, structural abnormalities identified through imaging, and history of kidney transplant. The criterion for decreased GFR is a value of less than $60 \text{ ml/min per } 1.73 \text{ m}^2$ (Kidney Disease Improving Global Outcomes, 2024). CKD etiologies are generally divided into two categories: primary and secondary. The primary causes originate from the kidneys themselves, such as Polycystic Kidney Disease, Glomerulonephritis, and

Pyelonephritis. Secondary etiologies stem from systemic diseases impacting kidney function, including diabetes mellitus, hypertension, NSAID use, urinary tract obstruction, and autoimmune diseases (Gupta et al., 2023).

Low-grade inflammation occurs due to factors such as uremia, metabolic syndrome, malnutrition, dyslipidemia, and consequences of kidney replacement therapies like hemodialysis and CAPD (Kadatane et al., 2023; Liao et al., 2022; Zhou et al., 2024). Kidney damage results from chronic pathological processes that alter the kidney's architecture and develop into fibrosis. Healthy kidneys can physiologically regulate these inflammatory markers. Causes of impaired inflammation regulation related to CKD etiology include diabetes and incomplete recovery from acute kidney injury (AKI) (Kadatane et al., 2023).

Low-grade inflammation, as seen in CKD, plays a crucial role in the initiation and progression of the disease. Inflammatory markers associated with CKD include C-reactive protein, Interleukin-8 (IL-8), TNF receptor, and pentraxin (Kadatane et al., 2023; Liao et al., 2022). Recent scientific advances show that inflammatory markers such as the monocyte-lymphocyte ratio (MLR), neutrophil-lymphocyte ratio (NLR), and platelet-lymphocyte ratio (PLR) can be obtained from routine blood tests (Zhang et al., 2020). These markers are commonly used to predict cardiovascular disease and tumors due to their ability to reflect low-grade systemic inflammation. Monocyte-Lymphocyte Ratio (MLR) is calculated by dividing the absolute monocyte count by the total lymphocyte count. Monocytes, derived from myeloid progenitors and including macrophages and dendritic cells, tend to increase with CKD (Patel et al., 2017; Yona & Gordon, 2015). Research indicates a significant reduction in B and T lymphocyte percentages in patients with advanced CKD, a finding consistent across age, comorbidities, and gender. Uremia is suggested to be a dominant factor in the reduction of B cells (Xiang et al., 2016; Betjes & Litjens, 2015).

MLR reflects chronic inflammatory processes generally (Xu et al., 2021; Liu et al., 2024). Whereas pro-inflammatory cytokines tend to rise, T lymphocytes marked by CD4 and CD8 actually decrease. Monocytes and neutrophils increase during inflammation. Monocytes contribute to activation of innate and adaptive immunity through phagocytosis, antigen presentation, and production of pro-inflammatory cytokines, whereas lymphocytes tend to decrease. This reciprocal relationship between monocyte and lymphocyte counts forms the basis of the MLR (Carrillo-Palau et al., 2023; Hua et al., 2023). Studies have linked MLR with the incidence of new CKD and identified it as a biomarker for inflammatory activity and disease severity, including CKD (Xu et al., 2021; Zhou et al., 2024; Qiu et al., 2023). High MLR correlates with increased inflammation in CKD, poorer kidney function, and can predict CKD severity (Zhou et al., 2024). Furthermore, elevated MLR is a strong predictor of all-cause mortality and cardiovascular death (Hua et al., 2023). In CKD patients with diabetes mellitus, high MLR is associated with increased mortality risk within 90 days of ICU treatment (Qiu et al., 2023). Among peritoneal dialysis patients, MLR associates with all-cause mortality and cardiovascular events (Xiang et al., 2018; Yang et al., 2023).

Prior studies by Wang et al. (2020) demonstrated that elevated MLR is significantly associated with inflammation and poorer renal function in CKD, suggesting its potential as a prognostic biomarker. Gu et al. (2021) further identified MLR as a strong predictor of all-cause mortality and cardiovascular events in CKD patients, including those on dialysis. However, these studies had limitations related to sample diversity, stage-specific CKD analysis, and longitudinal survival evaluation, leaving gaps in understanding MLR's predictive utility across different CKD severities in hemodialysis patients.

This study aims to address these gaps by analyzing the association between MLR and survival outcomes in CKD patients undergoing regular hemodialysis, employing Kaplan–Meier survival curves, Cox regression, and Log-Rank tests. This will provide evidence on the prognostic value of MLR for risk stratification and clinical decision-making in CKD

management. The findings are expected to improve patient monitoring, guide early interventions, and enhance survival predictions in this CKD population.

RESEARCH METHOD

This research is an observational analytical research where the researcher only collects secondary data and then conducts statistical tests on the data. This study included a retrospective cohort. Researchers try to see and review exposure to variables that occurred in the past and then observe the results in the present. This research was conducted in the Medical Records of Tabanan Hospital by taking patient data from 2023 to 2025. The population in this study includes the target population and the affordable population. The target population is CKD patients undergoing regular Hemodialysis, while the affordable population includes patients diagnosed with CKD and undergoing regular hemodialysis starting from 2023-2025 whose medical records are recorded in the Medical Record Unit of Tabanan Hospital. The sample used is the affordable population of the study, namely patients diagnosed with CKD and undergoing regular hemodialysis starting from 2023-2025 who meet the inclusion and exclusion criteria and their medical records are recorded in the Medical Record unit of Tabanan Hospital.

Sampling uses a total sampling technique where the researcher takes all samples that meet the inclusion and exclusion criteria.

Inclusion Criteria

1. Adult patient is > 18 years old
2. Started diagnosed with CKD in January 2023 – May 2025
3. Have undergone Regular Hemodialysis
4. Recorded in medical records and complete blood test results available

Exclusion Criteria

1. Suffering from malignant diseases as the main etiology of CKD suffered
2. Medical records are inaccessible or corrupted
3. No complete blood test results available on medical records
4. Complete blood test results, especially Lymphocyte and Monocyte values = 0

The Monocyte-Lymphocyte Ratio (MLR) used in this study was divided into 3 groups, namely: High: > 0.35 , Medium: $0.23-0.35$, Low: $< 0.23.22$ The survival analysis was carried out through the Kaplan-Meier curve, the Log-Rank test and the Cox Regression test. The Kaplan-Meier curve is a curve that describes the survival time in subjects who are censored (do not experience events) and those who experience events/events that in this study are the events of death. Cox Regression was used in this study to determine the influence of an independent variable, namely MLR on the time of occurrence of a death event, while Log-rank aims to compare between 2 or more groups, whether there is a difference between groups on survival time. In this study, it was analyzed whether there was a difference between low, medium, and high MLR values on survival of CKD patients.

RESULTS AND DISCUSSION

There was a total of 98 respondents who met the research inclusion criteria. These respondents are CKD patients who have begun to be diagnosed and undergo regular hemodialysis therapy starting from 2023 to mid-2025. In this study, the dominant patient was male, which was 55.1%. From several etiologies underlying the development of CKD in respondents, DKD was ranked first with a percentage of 34.7% of all cases, followed by

Nephrosclerosis as much as 31%. During the follow-up time, there were 31 respondents who experienced an event that in this study was death.

Table 1. Characteristics of Research Respondents

Variable	Category	n (%)
Age	≥ 60	50 (51)
	<60	48 (49)
Gender	Man	54 (55,1)
	Woman	44 (44,9)
Etiology	DKD	34 (34,7)
	Nefrosclerosis	31 (31,6)
	PNC	20 (20,4)
	GNC	1 (1,0)
	Nephropathy Obstructive	7 (7,1)
	Nephropathies Vein	2 (2,0)
Patient Status	Polycystic Kidney Disease	3 (3,1)
	Censored	67 (68,4)
	Uncensored (<i>Event</i>)	31 (31,6)

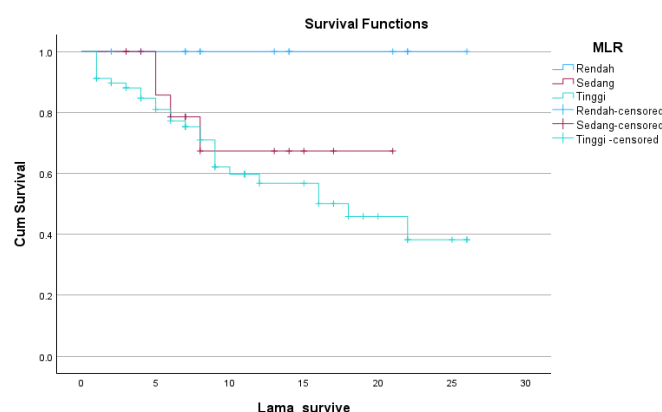


Figure 1. Kaplan-Meier Curve

Survival in this study is described by the Kaplan-Meier Curve. There is a sharp curve decline on the line that represents a high MLR value. This is interpreted as the number of respondents who experience events (deaths) have a high MLR. Meanwhile, on the line representing low MLR, the decline of the curve tends to be slow, which is interpreted as the amount of data that is censored (does not experience events). The lowering of the curve explains the decrease in the probability of survival over time. In contrast to high and medium MLR lines, the lines representing low MLR tend to be constant, this means that the probability of survival of respondents with low MLR is still high.

Table 2. comparison of censored data and events at low, medium, and high MLR values

MLR	Total N	N of Events	Censored	
			N	Percent
Low	13	0	13	100.0%

MLR	Total N	N of Events	Censored	
			N	Percent
Medium	17	4	13	76.5%
High	68	27	41	60.3%
Overall	98	31	67	68.4%

Statistically, it is necessary to prove whether the three MLR groups above provide a significant difference in survival rate, therefore a log rank test was also carried out in this study. From the log rank test, a p value of 0.28 (<0.05) was obtained, which means that there was a significant difference in the survival rate of mild, medium, and high MLR.

Table 3. Cox-Regression Test Results

	Hazard Ratio	P-Value	95% CI
MLR	2.78	0.019	1.18-6.55

The Cox-Regression test was carried out in this study to determine the significance of the research variable, which in this case is the MLR value in relation to the occurrence of events. Hazard ratio >1 which means that every increase in the MLR value increases the risk of events (deaths). The risk of death in this study increased 2.78 times higher at higher hazards, which in this case was a higher MLR. In this Cox-regression test, a P value of <0.05 was obtained, indicating that the MLR value is statistically significant in relation to the occurrence of the event (death).

Discussion

The kidneys in normal circumstances play a role in maintaining the homeostasis of the immune system by the mechanism of clearing excess cytokines and antigens from the circulation. The kidneys receive about 25% of the body's bloodstream but lack the protective, detoxifying, and antioxidant mechanisms that are essential to fight the inflammatory processes and free radicals that are caused by them like the other organs of the liver which have all these mechanisms. People with CKD tend to experience low-degree inflammation that lasts chronically. Inflammatory dysregulation causes ongoing kidney injury and progresses to CKD. Some of the conditions that can cause dysregulation include diabetes, uremia, AKI that is not resolved properly, etc. In the condition of infection (pyelonephritis) there is an increase in pro-inflammatory markers such as TNF-Alpha, Monocyte chemoattractant-1 (MCP-1), IL-8, IL-6, all of which can activate immune cells. MCP-1 specifically attracts monocytes and macrophages to the site of injury. Studies show MCP-1 is associated with worsening renal fibrosis (Kadatane et al., 2023; Heine et al., 2012).

MLR is used to describe inflammatory processes in general, particularly chronic inflammation (Xu et al., 2021; Liu et al., 2024). Studies show MLR is associated with the incidence of new CKD. MLR was found to be higher in populations with CKD compared to those without CKD. MLR is also linked to several diseases such as autoimmune, malignancy, and cardiovascular (Xu et al., 2021; Qiu et al., 2023). Another study found that high MLR is a strong predictor of all cause and death from cardiovascular disease. A high MLR in CKD patients with comorbid DM was also significantly associated with an increased risk of death

within 90 days of ICU treatment (Hua et al., 2023; Yang et al., 2023; Qiu et al., 2023). Comparative studies of MLR in CKD and non-CKD populations found that MLR in CKD populations was higher than in non-CKD and positively associated with an increased risk of death. 14 Studies related to chronic diseases such as COPD stated that MLR was proven to be an independent predictor of patient mortality (Liu et al., 2024). Similar results were also obtained from this study where high MLR was related to the occurrence of events (deaths). The higher the MLR value, the higher the risk of death for sufferers. Some of the weaknesses in this study include the possibility of bias in the selection of respondents because it was carried out retrospectively in one health center. Other factors can include the use of certain medications and other comorbidities in patients, so to confirm the results of this study, a wider range of studies is needed covering several health centers by considering the right inclusion and exclusion criteria.

CONCLUSION

This study found that the monocyte-lymphocyte ratio (MLR) is significantly associated with survival in CKD patients undergoing regular hemodialysis, with distinct differences in survival rates observed among patients with mild, moderate, and high MLR levels. Higher MLR values were statistically linked to an increased risk of death, indicating that each incremental rise in MLR elevates the likelihood of mortality events. Future research should investigate the mechanistic pathways by which MLR influences patient outcomes and explore its predictive value across diverse CKD populations and hemodialysis protocols to optimize risk stratification and personalized treatment approaches.

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