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Neutrophil-to-Lymphocyte Ratio (NLR) and suicidal ideation: A potential inflammatory indicator in affective disorders

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ABSTRACT

Background: Inflammation is increasingly recognized as a key factor in the pathophysiology of mental disorders, including affective disorders. Evidence suggests that elevated inflammation markers may be associated with a higher risk of suicidal ideation in patients with conditions such as depression and bipolar disorder. Cost-effective and accessible biomarkers are needed to identify individuals at high risk. The Neutrophil-to-Lymphocyte Ratio (NLR) is an easily obtainable inflammatory biomarker that may serve as a predictor of suicidal ideation in this population.

Objectives: To evaluate the predictive performance of NLR for suicidal ideation in patients with affective disorders.

Methods: A cross-sectional, retrospective study was conducted using secondary data from medical records of inpatients at Dr. Sardjito General Hospital, Yogyakarta, between January and December 2023. Eighty patients diagnosed with affective disorders were selected through consecutive sampling based on predefined inclusion and exclusion criteria. Participants were classified into two groups: those with suicidal ideation and those without. Categorical variables were comparedusing the Chi-square test and numerical variables analyzed using the Mann-Whitney U test or independent t-test, as appropriate. Receiver Operating Characteristic (ROC) curve analysis was performed to assess the predictive performance of NLR, with the Area Under the Curve (AUC), sensitivity, specificity, and optimal cut-off values reported.

Results: The mean NLR was significantly higher in patients with suicidal ideation (3.55) than in those without (2.46)(p=<0.001). ROC curve analysis yielded an AUC value of 0.783 (p=<0.001). The optimal cut-off for NLR was 2.77, with a sensitivity of 72.5%, specificity of 72.5%, and accuracy of 72.5%. An odds ratio of 6.95 (95% CI) was observed, indicating a significant association between elevated NLR and suicidal ideation.

Conclusion: A relationship exists between NLR and suicidal ideation in patients with affective disorders.

INTRODUCTION

Suicide is a complex phenomenon influenced by neurobiological, psychological, sociocultural, and environmental factors. It is defined as the deliberate termination of one's own life and ranks as the 14th leading cause of death worldwide. According to World Health Organization estimates, approximately 700,000 people die by suicide each year, althoughthe



Copyright © 2025 Ronny Tri Wirasto, Maharani Primastuti Arganist. Licensee Universitas Islam Indonesia actual number likely higher.² Globally, suicide is more common in low-and middle-income countries, where access to mental health services is often limited.³ Factors, such as poverty, unemployment, social stress, and restricted availability of mental health care contribute to the elevated risk in this population.⁴ In Indonesia, suicide is remains a significant public health concern, withcases from 613 in 2021 to 826 in 2022.⁵ Suicide attempts are estimated to be 10–20 times more frequent than completed suicides.²

Suicidal ideation, defined as persistent thoughts about ending one's life, is a criticalpredictor of suicide attempts and deaths. Identifying this stage early is essential for timely intervention.⁴ Suicidal ideation is a specific thought that an individual has about ending his or her life. It is one of many thoughts about death that exist.⁶ In the case of suicide, suicidal ideation is an important predictor to consider.⁷ The stages of suicide consist of a suicide plan, a suicide attempt, and a complete suicide. A person who has had suicidal ideation is at greater risk of progressing to the next stage, which is a suicide attempt to complete suicide.^{4,8} Suicide deaths and suicide attempts are acts of deep psychological despair and represent an emotional burden for the relatives and friends of the victim.⁶ Several studies have demonstrated that suicidal ideation and suicide attempts are highly prevalent in affective disorders, particularly depression and bipolar disorder.⁹ Moreover, accumulating evidence indicates associations between elevated pro-inflammatory markers and suicide ideation in patients with affective disorders.^{10,11} These findings underscore the need for diagnostic approaches that integrate both behavioral and biological indicators to improve risk identification.¹²

The neutrophil-to-lymphocyte ratio (NLR) is a commonly utilized inflammatory marker that has proven useful in evaluating inflammation in several diseases. The NLR is a hematologic parameter derived from the ratio of neutrophil to lymphocyte counts in peripheral blood tests. He has been studied across a range of medical conditions and is increasingly recognized as relevant to psychiatric disorders. Elevated NLR is has been reported inneuropsychiatric conditions such as alzheimer's disease, schizophrenia, depression, and bipolar disorder. Currently, NLR is also associated with mortality rates in patients with mental disorders. NLR inexpensive, easily obtained, and is accepted as a reliable clinical marker of systemic inflammation. Markey of systemic inflammation.

Despite growing evidence of inflammatory dysregulation in psychiatric conditions, relatively few studies have explored the association between NLR and suicidal ideation, especially in patients with affective disorders in low- and middle-income countries. Although immune system abnormalities are hypothesized to contribute to suicidal ideation, the underlying pathophysiological mechanisms remain unclear. Further research is needed to clarify these mechanisms and evaluate the potential utility of NLR as a biomarker for suicide risk. This study aims to investigate the relationship between NLR values and suicidal ideation in patients with affective disorders.

METHODS

Study design

This study employed a cross-sectional design with a retrospective approach. Samples were collected using a consecutive sampling technique. Data were obtained from medical records of inpatients diagnosed with affective disorders at Dr. Sardjito Central General Hospital, Yogyakarta, Indonesia, between January and December 2023. Extracted data included included demographic characteristics, clinical diagnoses, documentation of suicidal ideation, and results of routine complete blood count (CBC) tests, including neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio PLR. All data were securely stored and only established method were applied.

Population and sample

A total of 80 patients were selected based on the Slovin formula, with equal allocation to the suicidal ideation group (n = 40) and the non-suicidal ideation group (n = 40). Inclusion criteria were: (1) age >18 years, (2) diagnosis of affective or mood disorders (ICD-10 codes F30–F39), (3) hospitalization in the psychiatric unit, (4) availability of complete NLR data, and (5) clear documentation of suicidal ideation in the medical record. Exclusion criteria were: (1) pregnancy

or recent childbirth, (2) severe or acute medical comorbidities that could influence hematological parameters, and (3) incomplete medical record data.

Study variables

Suicidal ideation was defined as the presence of suicidal thoughts documented during psychiatric clinical interviews. Patients with suicide attempts or behaviors were excluded. Documentation was based on clinician notes and intent differentiation, without the use of a standardized questionnaire. Non-suicidal self-injury was excluded when intent to die was absent. The independent variable was the NLR, while the dependent variable was the presence or absence of suicidal ideation. Covariates included demographic and clinical data. Numerical variables were age, NLR, and PLR. Categorical variables were gender, marital status, readmission status, diagnosis, NLR cutoff, and PLR cutoff. Suicidal ideation status served as the grouping variable in analyses.

Laboratory analysis

Peripheral venous blood samples were collected at admission. All laboratory results were recorded in standard metric units. NLR was calculated using an automated hematology analyzer available in the hospital laboratory by dividing the absolute neutrophil count by the absolute lymphocyte count. The absolute neutrophil and lymphocyte counts were obtained from complete blood count (CBC) tests and expressed in cells per microliter (cells/ μ L). NLR is reported as a unitless value.

Data analysis

All data were analyzed using SPSS version 29.0. Numerical variables were are presented as mean and standard deviation (SD), while categorical variables were presented as frequency and percentage. Data normality was assessed with the Shapiro-Wilk test. Group comparisons were performed using the chi-square test for categorical variables, the independent t-test for normally distributed continuous variables, andthe Mann-Whitney test for non-normally distributed variables. Receiver Operating Characteristic (ROC) curve analysis was conducted to evaluate the predictive performance of NLR in identifying suicidal ideation. The optimal cut-off value along with area under the curve (AUC), sensitivity, specificity, and overall accuracy. All statistical tests were performed with a significance level of 5% (α = 0.05), so a p-value < 0.05 was considered to indicate a statistically significant difference. The results of this analysis were used to provide data-driven conclusions regarding the relationship between the study variables and to determine the potential of NLR as a predictor of suicidal ideation.

Ethical statement

This study received ethical approval from the Research Ethics Committee of Gadjah Mada University with letter number KE/0960/06/2024.

RESULTS

Characteristics of Research Subjects

Among the 80 participants, most were female (91.3%), the average patient age was 24.11 years, the marital status was mostly unmarried (96.3%), the diagnosis was mostly severe depressive episode with psychotic symptoms (38.8%). The test used is the chi square test for categorical data and the Mann-Whitney U test for numerical data that is not normally distributed. The results of statistical tests showed that the characteristics of the study subjects based on gender, age, marital status, paranoid ideation, and readmission did not show significant differences (p>0.05) (Table 1).

Statistical comparisons were performed to analyze the differences in NLR and PLR values between patients with and with no suicidal ideation. Normality tests were conducted prior to selecting appropriate statistical tests. The Mann–Whitney U test was used for NLR due to nonnormal distribution, while the independent t-test was used for PLR.

Table 2 shows that the laboratory examination results of NLR (p=<0.001) showed significantly different results between patients with no suicidal ideation and patients with suicidal ideation, where patients with suicidal ideation had higher NLR values (mean=3.55) compared to patients with no suicidal ideation (mean=2.46). Analysis of Platelet to Lymphocyte Ratio (PLR) (p=0.023) showed significantly different results between patients with no suicidal ideation and patients with suicidal ideation, where patients with suicidal ideation had higher PLR values (mean=174.78) compared to patients with no suicidal ideation (mean=149.10).

Receiver operating characteristic (ROC) and area under curve (AUC) analysis of NLR and PLR as predictors of suicidal ideation

The ROC curve was used as an analysis to see the cut-off of NLR and PLR as predictors of suicidal ideation. Figure 1 shows the NLR parameter has an AUC value of 0.783 with p=<0.001 and PLR has an AUC value of 0.637 with p=0.036. The cut-off obtained for NLR is 2.77 with a sensitivity of 72.5% and a specificity of 72.5% with an accuracy of 72.5%, while for PLR, a cut-off of 149.00 is obtained with a sensitivity of 65.5% and a specificity of 55.0% and an accuracy of 60.0%. After determining the cut-off value of NLR and PLR as predictors of suicidal ideation, the analysis was then re-analyzed using chi-square, and the odds ratio (OR) value was determined to determine the magnitude of the risk. The results of the analysis can be seen in Table 3.

Table 1. Characteristics of Research Subjects

	Takal	Suicide Ideation		
Characteristic	Total	No SI	SI	p-value
	N (%)	N (%)	N (%)	_
Gender				1.000a
Woman	73(91.3)	36(90.0)	37(92.5)	
Man	7(8.8)	4(10.0)	3(7.5)	
Age	24.11(8.04)	23.40(5.98)	24.83(9.71)	0.839b
Marital Status				1.000a
Not Married	77(96.3)	38(95.0)	39(97.5)	
Married	3(3.8)	2(5.0)	1(2.5)	
Readmission				0.499^{a}
No	70(87.5)	34(85.0)	36(90.0)	
Yes	10(12.5)	6(15.0)	4(10.0)	
Diagnosis				
Bipolar affective disorder, current episode manic with psychotic symptoms	1(1.3)	1(2.5)	0(0.0)	
Bipolar disorder, current episode depressed, severe, without psychotic features	5(6.3)	3(7.5)	2(5.0)	
Bipolar disorder, current episode depressed, severe, with psychotic features	20(25)	10(25)	10(25.0)	0.035a
Bipolar affective disorder, current episode mixed	5(6.3)	4(10.0)	1(2.5)	
Major depressive disorder, single episode, severe without psychotic features	18(22.5)	14(32.5)	5(12.5)	
Major depressive disorder, single episode, severe with psychotic features	31(38.8)	9(22.5)	22(55)	

Note: ^aChi-Square test; ^bMann-Whitney U test; SI: Suicidal Ideation; No SI: No Suicidal Ideation

Table 2. Analysis of NLR and PLR Test on Suicidal Ideation

	To	Total		Suicide Ideation			
Variable	'-		No	SI	S	I	p-value
	Mean	SD	Mean	SD	Mean	SD	
NLR	3.01	1.18	2.46	0.99	3.55	1.12	<0.001*b
PLR	161.94	50.85	149.10	43.88	174.78	54.53	0.023*a

Note: aIndependent t-test; bMann-Whitney U; *significant at p<0.05; NLR: Neutrophil to Lymphocyte Ratio; PLR: Platelet to Lymphocyte Ratio; SI: Suicidal Ideation; No SI: No Suicidal Ideation.

The NLR and PLR cut-off of the ROC curve were analyzed for suicidal ideation using the chi-square test. Odd Ratio (OR) values were analyzed to determine the odds of risk. Based on table 3, it is known that patients who do not have suicidal ideation are mostly known with NLR <2.77 (72.5%), then patients with suicidal ideation are mostly with NLR>2.77 (72.5%), OR value = 6.95, which means that patients with NLR>2.77 have a risk of having suicidal ideation 6. 95 times greater than patients with NLR <2.77. Statistical test results get a value of p = <0.001 (p <0.05), which means that NLR is significantly associated with suicidal ideation, thus, NLR can be a predictor of suicidal ideation.

Patients who do not have suicidal ideation are known to be mostly with PLR < 149 (55.0%), then patients with suicidal ideation are mostly with PLR > 149 (65.0%), OR value = 2.27 and the statistical test results get a value of p = 0.072 (p>0.05), which means that PLR is not significantly associated with suicidal ideation, thus PLR cannot be a predictor of suicidal ideation.

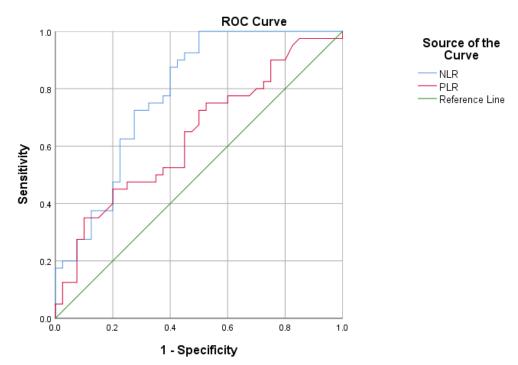


Figure 1. ROC curves of NLR and PLR based on suicidal ideation. NLR (AUC=0.783; p=<0.001*); PLR (AUC=0.637; p=0.036*)

Table 3. ROC Curve Cutoff Analysis

	Suicide	Ideation	OD (OF)/ CD		
Variable	No SI	SI	OR (95% CI)	p-value	
	N (%)	N (%)			
NLR			6.95 (2.60- 18.55)	<0.001*	
<2.77	29(72.5)	11(27.5)			
<u>≥</u> 2.77	11(27.5)	29(72.5)			
PLR			2.27 (0.923- 5.58)	0.072	
<149.00	22(55.0)	14(35.0)			
≥149.00	18(45.0)	26(65.0)			

Notes: Chi-Square test/Fisher exact test; OR: Odd ratio; CI: Confidence interval; *Significant at p<0.05; NLR: Neutrophil to Lymphocyte Ratio; PLR: Platelet to Lymphocyte Ratio; SI: Suicidal Ideation; No SI: No Suicidal Ideation.

Based on the analysis, NLR is better than PLR as a predictor of suicidal ideation, where NLR as a predictor of suicidal ideation has an accuracy of 72.5%, while PLR has an accuracy of 65.0%.

DISCUSSION

This study demonstrates that NLR significantly associated with suicidal ideation among patients with affective disorders. NLR value were higher in individuals with suicidal ideation compared with those without, consistent with prior studies showing elevated NLR in patients with depression and bipolar disorder.²⁰ Another study also mentioned that the NLR value in depressed patients who committed suicide was significantly higher than in depressed patients who did not commit suicide.²¹ The NLR has advantages over other blood tests that it can be obtained from a simple routine blood test. The NLR is derived from the ratio of neutrophil count to lymphocyte count obtained from standard blood testing.^{17,22} Elevated NLR scores correlate with suicidal ideation and suicidal behavior in individuals diagnosed with affective disorders, including depression and bipolar disorder.^{6,20} The normal range of NLR values is between 1-2. NLR values above 3.0 and below 0.7 in adults may indicate a pathological condition. The NLR values between 2.3-3.0 are a sign of conditions such as cancer, infection, inflammation, or mental disorders, including Bipolar and Depression.²³ It has been theorized that stress and depression elevate leukocyte and neutrophil counts while diminishing lymphocyte levels.²⁴

The NLR was a good predictor of suicidal ideation, and this finding was statistically significant. The cutoff value obtained for NLR was 2.77 (Area under the curve = 0.783) with high sensitivity, specificity, and accuracy (72.5%). The odds ratio (OR) for NLR > 2.77 was 6.95, signifying that patients above this threshold were almost seven times more likely to display suicidal ideation. These results align with research done by Amitai et al, where the NLR cutoff for suicidal ideation was 1.76 (area under the curve=0.75) with a sensitivity of 73% and specificity of 71%.²⁰ Another study conducted in Europe showed similar results where the optimal cut-off value for NLR in predicting suicidal ideation was 1.59 (area under the curve = 0.593, sensitivity = 60%, and specificity = 58%).²⁵ The differences might result from variations in the study populations, as our sample comprised acutely psychiatric inpatients, whereas other studies encompassed a more diverse cohort of both outpatients and inpatients. Variations in clinical severity, regional immunological profiles, and methodology may also have a role. There are The ROC curve is widely used in other studies to see the NLR cutoff in mental disorders. The NLR cutoff was found to be 1.8-1.98.²² Some of the most important indicators of chronic inflammation are subtype and white blood cell (leukocyte) count. The NLR has been suggested as a good predictor of inflammatory processes. NLR is an attractive biomarker of systemic inflammation because it is fast, affordable, and easy to obtain from routine blood tests.^{26,27}

Increased neutrophil counts and decreased lymphocyte counts in suicidal ideation may be caused by inflammation or chronic stress that triggers cellular immunosuppression.^{20,26} One of

the immune systems that plays a role in the inflammatory system is neutrophils. Neutrophils are nonspecific inflammatory mediator that will produce various inflammatory substances as a body defense mechanism. The imbalance in the natural immune system is shown in the increased NLR, where neutrophils serve as the initial defense in the natural immune system, whereas lymphocytes are essential to the adaptive immune response.^{20,28} The ratio between neutrophils and lymphocytes, as indicated by the neutrophil to lymphocyte ratio (NLR), may provide significant insights into an individual's inflammatory state and its potential correlation with depressive disorders.^{12,22}

Our finding that 91.3% of patients were female with high suicidal ideation (92.5%) aligns with prior research showing a higher risk of suicide ideation among women with affective disorders. This may be linked to psychosocial and hormonal factors, as suggested in previous literature.^{3,22} Mental health factors, educational qualifications, social support, marital status, and unpleasant experiences during childhood significantly increase the likelihood of women expressing suicidal thoughts compared to men.²⁹ Young adult patients in this study dominated the age at which suicidal ideation was found. Our study aligns with another study that mentions the average age of depression and bipolar patients in Indonesia is young adulthood.^{30,31} Suicidal ideation was also found to be most prevalent in unmarried depression and bipolar patients.³¹ Marriage can reduce the prevalence of depression by 5.38%. Unmarried or divorced patients have a greater prevalence of depression than married patients.³² In Indonesia, marriage is believed to reduce the psychological effects of other problems experienced by the individual.^{32,33}

This study also found that suicidal ideation was prevalent in depression and bipolar disorder. A person diagnosed with depression often experiences hopelessness, which can increase suicidal thoughts compared to a person who has bipolar disorder. The chronic nature of depression can make suicidal ideation common in patients.³⁴ Inflammatory mediators are elevated in patients with neuropsychiatric disorders.³⁵ Severe depressive symptoms and other symptoms such as pessimism, social anxiety, and helplessness increase the likelihood of suicidal ideation.³⁶ Research shows that the prevalence of suicidal ideation among individuals with bipolar disorder and depression in low-income countries reaches 67%²³, whereas the prevalence of suicidal ideation in depression is 37.7%.³⁷

Another affordable biomarker is PLR. PLR showed no significant differences in results between patients with and with no suicidal ideation with p>0.05. In previous studies, no substantial difference was identified in PLR and suicidal ideation among individuals diagnosed with affective disorders. PLR is associated with stress. Stress causes endothelial permeability, platelet aggregation, and activation of the sympathetic nervous system. Peripheral inflammation is caused by the appearance of neutrophils and macrophages as a result of permeability. Serotonin is widely found on platelets. Serotonin receptors (5HT2A) and transporters located on the cell surface play a crucial role in the production, re-absorption, and metabolism of serotonin. Aggressiveness and impulsivity shown by a person with suicide attempts are related to the concentration of serotonin present on platelets, as well as the number of aggregated 5-HT2A receptors located on the platelet surface. Studies show that PLR is affected by various factors beyond inflammation. PLR is insufficient to account for the complex interactions between biological, psychological, and environmental factors that contribute to suicidal ideation, resulting in its lack of significance as a predictive measure for such behavior. Studies show the platelet surface as a predictive measure for such behavior.

There are several other confounding factors that can affect the NLR values. Age, gender, ethnicity, and use of antipsychotics are some of the factors that affect the NLR value.¹⁷ NLR and PLR levels are also impacted by these recurrent episodes, which may raise markers linked to apoptosis, neurotoxicity, impaired neuroplasticity, and increased oxidative damage.^{14,22}

In logistic regression, our findings reinforce NLR was a strongerpredictor than PLR for suicidal ideation in affective disorders.^{20,38} Another study also mentioned that NLR value can be a better predictor than PLR for suicidal ideation in depressed patients.¹⁴ Another study conducted in Asia showed that NLR had better results in differentiating suicide attempts in depressed patients. The area under the curve (AUC) for NLR was greater than 0.7 indicating its strong ability in this regard, while PLR did not show the same effectiveness.⁴⁰ NLR may indicate inflammatory dysregulation related to suicidal ideation and may explain stronger predictive ability when

compared to PLR.²⁰ The clinical implication of our findings is that NLR may function as a practical and accessible instrument for physicians to identify patients with affective disorders at an elevated risk of suicidal thoughts. It may facilitate early intervention and enhanced surveillance in psychiatric environments as part of a comprehensive clinical evaluation.

This study has several limitations. First, NLR and PLR were assessed only once at admission, without longitudinal follow-up to examine dynamic changes after stabilization. Second, NLR cutoff values vary across studies, and the cut-off of 2.77 identified in this study may generalize to other populations due to differences in methodology, population characteristics, and measurement timing. Third,incomplete or missing data in medical records posed potential bias. Future studies with larger, prospective, and multicenter designs are required to validate standardized cut-off values and clarify underlying biological mechanisms.

CONCLUSION

This study demonstrates a significant association between neutrophil-to-lymphocyte ratio (NLR) and suicidal ideation in patients with affective disorders. NLR, obtained from a simple routine blood test, may serve as a practical and cost-effective screening tool to help identify patients at elevated risk of suicide. Further prospective studies are warranted to validate these findings and to establish standardized cut-off values for clinical application.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGMENTS

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DATA AVAILABILITY

The data supporting the findings of this study were derived from medical records of inpatients diagnosed with affective disorders at Dr. Sardjito Central General Hospital, Yogyakarta, Indonesia, from January to December 2023. Due to patient confidentiality and institutional regulations, these data are not publicly available. Access may be granted upon reasonable request and with approval from the hospital's ethics committee.

SUPPLEMENTAL DATA

No additional supplemental data are provided for this study. All relevant data supporting the findings of this research are included within the main article.

AUTHOR CONTRIBUTIONS

MPA contributed to data collection, assessment, writing, and finalization; RTW provided advice during the research and draft of the manuscript.

DECLARATION OF USING AI IN THE WRITING PROCESS

During the preparation of this manuscript, the authors used DeepL to assist in text simplification and harmonization. All content was subsequently reviewed, edited, and approved by authors, who take full responsibility for the final version of the article.

LIST OF ABBREVIATIONS

NLR: Neutrophyl To Lymphocyte Ratio; PLR: Platelet To Lymphocyte Ratio; AUC: Area Under The Curve; ROC: Receiver Operating Characteristic, OR: Odd Ratio; CI: Confidence Interval, SI: Suicidal Ideation

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