Neutrophil-Lymphocyte Ratio and Procalcitonin as Predictors of the Severity of Acute Pancreatitis

Iriana D[1], Kartini A[2], Widaningsih Y[1], Abdullah AA[1,2]

[1] Department of Clinical Pathology, Faculty of Medicine, Hasanuddin University/Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia.
   E-mail: dessyiriana19@gmail.com
[2] Labuang Baji General Hospital, Makassar, Indonesia

ABSTRACT

The Neutrophil-Lymphocyte Ratio (NLR) and procalcitonin are used to indicate systemic inflammation in various medical disorders. Both parameters were determined in this study to predict the severity of acute pancreatitis. This study was a cross-sectional study using a retrospective approach to patients diagnosed with acute pancreatitis by using medical record data from patients at Dr. Wahidin Sudirohusoso Hospital, Makassar, from January 2014 to May 2019. This study comprised 35 patients hospitalized with acute pancreatitis, with a similar proportion of males and females. This study discovered that the mean age in this study was 44.17±12.9 years. The most prevalent cause was Gallstones (77.1%), the most severe degree was mild (54.2%), and the highest outcome was survival (77.1%). The NLR (9.93±11.19, p=0.011) increased in proportion to severity. However, additional analysis based on classification of disease severity revealed that only mild-severe NLR was significant (p=0.005). Procalcitonin (8.13±11.25, p=0.001) increased along with the increased disease severity, and the subsequent analysis showed that the distribution of severity was similar. The NLR can predict the severity of acute pancreatitis but is less effective than procalcitonin. This study required a more proportional subject population and consideration of other factors.

Keywords: Acute pancreatitis, neutrophil-lymphocyte ratio, procalcitonin, severity degree

INTRODUCTION

Acute pancreatitis is one of the most common gastrointestinal hospitalizations, with the acute inflammatory process beginning with a local acinar lesion. Persistent inflammation can cause hypoxia, which can lead to organ failure and death. Gallstones and alcohol abuse remain the most prevalent etiological factors.[1-5]

The global incidence of acute pancreatitis is about 73 incidents per 100,000 people per year. Acute pancreatitis may vary from a minor, self-limiting illness that needs supportive treatment to severe disease with life-threatening consequences. About 25% of patients with acute pancreatitis may develop severe disease with hemodynamic instability and multiorgan failure, causing admission to an intensive treatment unit and a lengthy hospital stay.[2,6-8]

The Neutrophil-Lymphocyte Ratio (NLR) has been recognized as a critical sign in assessing systemic inflammation associated with various medical disorders. Many studies have also shown that the NLR is a better measure of inflammation than the total leukocyte count, neutrophil count, or lymphocyte count because it is less affected by physiological factors such as dehydration or physical exertion. This test is more straightforward and less expensive to perform. Currently, several ideal sepsis markers exist, such as procalcitonin and C-Reactive Protein. They are, however, still limited, especially in developing countries, due to the examination's high cost.[9-11]

Cho *et al*. published a previous study in 2018 showing that the NLR might predict the severity of acute pancreatitis and the development of complications. In 2017, Kumar *et al*. stated that procalcitonin might be used as an accomplished and simple-to-use single marker rather than a multi-scoring system, which is complex and challenging to manage. This study aimed to examine the usefulness of NLR in predicting acute pancreatitis severity and compare its diagnostic value with that of Procalcitonin to predict disease severity.[4,12]

METHODS

This is a cross-sectional study using secondary data from subjects in the medical record installation of Dr. Wahidin Sudirohusodo Hospital, Makassar, in

July 2019. The clinical, laboratory and radiological data of patients diagnosed with acute pancreatitis admitted to Dr. Wahidin Sudirohusodo Hospital from January 2014 to May 2019 were retrospectively analyzed.

Thirty-five out of the 42 subjects reviewed met the inclusion and exclusion criteria. Inclusion criteria included subjects who were hospitalized and had complete data of blood count and procalcitonin test results. Exclusion criteria included incomplete clinical or laboratory data, chronic pancreatitis, patients with known renal and liver disease or malignancy findings, and subjects who already had severe infection episodes during the previous month. To create an identical subject group, subjects who had symptoms over 48 hours before hospital admission were also excluded. The differential leukocyte counts were determined using the hematology analyzer with the absolute value and computed by multiplying the number of leukocytes by the percentage of each type of leukocyte needed for the analysis. An electrochemiluminescence immunoassay has been used to determine the procalcitonin level. The 2012 revised Atlanta Classification was used to assess the disease severity. The statistical analysis in this study included descriptive calculations, frequency distribution and Kruskal-Wallis tests, a Post-Hoc test, and a Pearson correlation test. The p-value less than 0.05 was stated as significant.

The Health Research Ethics Commission of Faculty of Medicine of Hasanuddin University and Dr. Wahidin Sudirohusodo Hospital approved the ethical eligibility with the following Number: 350/UN4.6.4.5.31/PP36/2019.

RESULTS AND DISCUSSIONS

This study involved 35 subjects who met the inclusion criteria. All characteristics of the subjects were categorized based on their gender, age, laboratory data, etiology, severity, and clinical outcome (Table 1).

According to Table 1, the percentage of males and females in this study was equal. The mean age was 44.17±12.9 years in this study. The most common cause of the disease was Gallstones (77.1%), the most common severity was mild (54.2%), and the highest

Table 1. Characteristics of subjects

Variable	n	%	Mean±SD
Gender			
Male	17	48.6	
Female	18	51.4	
Age (years)			44.17±12.91
< 25	3	8.6	
26-45	12	34.3	
46-65	18	51.4	
> 65	2	5.7	
Laboratory data			
NLR			9.93±11.19
Procalcitonin (ng/mL)			8.13±11.25
Etiology			
Alcohol	2	5.7	
Gallstones	27	77.1	
Idiopathic	3	8.6	
Drug (Acetaminophen)	1	2.9	
Post-ERCP	2	5.7	
Severity			
Mild	19	54.2	
Moderate	8	22.9	
Severe	8	22.9	
Outcome			
Survive	27	77.1	
Death	8	22.9	

Note: SD: Standard Deviation
ERCP: Endoscopic Retrograde Cholangiopancreatography

outcome was survival (77.1%).

Shah *et al.* reported in 2018 that the risk of severe pancreatitis increased with age in both males and females; however, females over the age of 60 had a higher risk. Obesity is more frequent in females, and it can cause gallstones. Alcohol-induced acute pancreatitis in this etiology, consumption of >100 g of alcohol in 24 hours, and low fat intake are significant risk factors. Alcohol origin is seen in 30% of pancreatitis. It is present in males predominantly; most of them are young adults.[6,13]

The updated 2012 Atlanta criteria classify acute pancreatitis as mild, moderate, or severe. The condition is often mild, self-limiting, and curable with conservative treatments in most patients. Crockett et al. reported that most cases with acute pancreatitis are minor, with mere pancreatic interstitial abnormalities but no local or systemic complications. Transient organ failure is defined as the failure of an organ that recovers within 48 hours, whereas chronic organ failure does not resolve. Severe acute pancreatitis is characterized by persistent organ failure and one or more local complications. Mild acute pancreatitis results in organ failure in the absence of local or systemic complications.[14,15]

In patients with acute pancreatitis, the mean value of NLR was higher, as seen in Table 2. However, it was discovered that procalcitonin outperformed NLR to predict acute pancreatitis severity. A previous study by Kokulu *et al.* in Turkey showed that the NLR could predict the severity of acute pancreatitis. The neutrophil to lymphocyte ratio, which is derived from a differential leukocyte count, serves as a quick indicator of the severity of the inflammatory disease. Immunocompetent white blood cell populations are critical for the systemic explosive response to infection. Neutrophil predominance is also observed in leukocytotic bacterial infections. Since neutrophil predominance is a sign of bacterial infection, it may precursor severe disease. Bacterial infection is a significant predictor of organ failure in acute pancreatitis patients.[10,16]

Procalcitonin is a 116-amino acid propeptide of calcitonin with a molecular weight of 13 kDa that acts as an early indicator of systemic bacterial infection, sepsis, and multiorgan failure. Procalcitonin is synthesized in the thyroid gland's C-cells as the intracellular prohormone of calcitonin and is detected at picogram levels in the plasma (0.05 ng/mL). Secretion begins four hours after stimulation and reaches a maximum level eight hours later.[5,12]

Table 3 shows that the NLR had no significant difference among all the categories of disease severity. Contrastingly, the follow-up test results for procalcitonin showed significant disparities in all clinical degrees. The NLR gives more advantages due to its sensitivity to detect disease severity, ability to be assessed early, reproducibility, accessibility, and relatively inexpensive cost. However, the NLR is not specific for acute pancreatitis. This study found that

Table 2. Analysis of the NLR and procalcitonin based on disease severity

Variable	Severity	n	Mean±SD	p*
NLR	Mild	19	6.72±5.57	
	Moderate	8	10.01±5.28	0.011
	Severe	8	17.48±20.18	
Procalcitonin	Mild	19	1.02±0.74	
	Moderate	8	7.81±4.39	0.001
	Severe	8	25.31±10.96	

*Kruskal-Wallis test

Table 3. Analysis of NLR and procalcitonin based on the classification of disease severity

Variable	Severity	Mean Difference	95% CI		p*
			Min	Max	
NLR	Mild-moderate	0.113	- 0.134	- 0.239	0.078
	Mild-severe	0.188	0.615	0.314	0.005
	Moderate-severe	0.749	- 0.752	0.225	0.317
Procalcitonin	Mild-moderate	0.762	0.491	1.033	0.001
	Mild-severe	0.916	0.645	1.187	0.001
	Moderate-severe	0.154	- 0.167	0.476	0.001

*Post-Hoc Test

NLR may be evaluated as part of the regular laboratory test for individuals with acute pancreatitis without any extra expenditures. It was also proposed that continuous NLR monitoring on each admission day offered a dynamic representation of the varied course of acute pancreatitis. Continuous monitoring of procalcitonin in patients with acute pancreatitis is a routine procedure. Because procalcitonin is a better predictor of acute pancreatitis severity, one might wonder if NLR monitoring adds any value as procalcitonin's predictive value rises in the days

Table 4. The correlation between the NLR and procalcitonin based on disease severity

Variable	n	r	p*
NLR	35	0.528	0.001
Procalcitonin	35	0.897	0.001

*Pearson correlation test, p < 0.05

The NLR had a significant correlation with the severity of disease, as shown in Table 4. Procalcitonin, on the other side, has a significant link to the severity of the condition. Both have a positive relationship; therefore, more significance in the NLR or procalcitonin score represents the severity of the illness in acute pancreatitis.

According to Kumar *et al.*, procalcitonin might be used as a single potential marker instead of a multifactorial scoring system, which is thought to be complex and challenging to apply. The NLR cut-off value of >7.13 showed 87.5% sensitivity and 69.5% specificity compared with procalcitonin was more accurate than the NLR in predicting disease severity. The best cut-off value for serum procalcitonin to predict severe acute pancreatitis was 0.5-1.2 ng/mL, which showed a sensitivity of 92.6% and specificity of 80.3%. However, this marker cannot be used because of its high cost and limited availability.[12,16,17]

The number of subjects involved in this study was too few. As this is a single-center study, the results should be validated in other settings. Due to improper medical records documentation, some subjects ought to be eliminated to obtain all necessary data. In addition, this study did not report NLR and procalcitonin data in the next days following patient admission.

CONCLUSIONS AND SUGGESTIONS

The NLR increased along with the increased disease severity, although no significant difference was found in all categories of disease severity. Procalcitonin increased significantly along with the increased disease severity, and there was a significant difference in the severity in all groups. Therefore, Procalcitonin was considered to have a stronger correlation than NLR in predicting the severity of acute pancreatitis. A further study was needed by using primary data with a more proportional sample population and other variables.

REFERENCES

1. Kaplan M, Ates I, Oztas E, Yuksel M, Akpinar MY, Coskun O, Kayacetin E. A new marker to determine the prognosis of acute pancreatitis: PLR and NLR combination. Journal of Medical Biochemistry, 2018; 37(1): 21.
2. Jeon TJ, Park JY. Clinical significance of the neutrophil-lymphocyte ratio as an early predictive marker for adverse outcomes in patients with acute pancreatitis. World Journal of Gastroenterology, 2017; 23(21): 3883.
3. Bhanou NM, Balachandran G, Jain NB. Neutrophil to Lymphocyte Ratio (NLR) in acute pancreatitis as an early predictor of severity and outcome. International Surgery Journal, 2018; 5(11): 3545-8.
4. Cho SK, Jung S, Lee KJ, Kim JW. Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio can predict the severity of gallstone pancreatitis. BMC Gastroenterology, 2018; 18(1): 1-6.
5. Madhu CP, Reddy DV. Procalcitonin as an early predictor of severity in acute pancreatitis. IJSS Journal of Surgery, 2017; 3(1): 53-7.
6. Andrade AM, Collazos SS, Andrade LM, Ortiz G, Andrade AM, *et al.* Acute pancreatitis. Emergency Medicine: Open Access, 2015; 5: 4.
7. Greenberg JA, Hsu J, Bawazeer M, Marshall J, Friedrich JO, *et al.* Clinical practice guideline: Management of acute pancreatitis. Canadian Journal of Surgery, 2016; 59(2): 128.
8. Güldoğan CE, Kılıç MÖ, Balamir İ, Tez M, Turhan T. Correlation between ischemia-modified albumin and Ranson score in acute pancreatitis. Turkish Journal of Trauma and Emergency Surgery, 2017; 23(6): 472-6.
9. Zhang Y, Wu W, Dong L, Yang C, Fan P, Wu H. Neutrophil to lymphocyte ratio predicts persistent organ failure and in-hospital mortality in an Asian Chinese population of acute pancreatitis. Medicine, 2016; 95: 37.
10. Yilmaz EE, Bozdag Z, Turkoglu A, Ulger BV, Arikanoglu Z. Use of the neutrophil to lymphocyte ratio compare CRP for the early prediction of acute pancreatitis severity. Annals of Medical Research, 2018; 25(3): 450-4.
11. Luhulima D, Marwito M, Eva O. Neutrophil to lymphocyte count ratio in bacterial sepsis. Indonesian Journal of Clinical Pathology and Medical Laboratory, 2018; 23(3): 257-62.
12. Kumar S, Jalan A, Patoway BN, Bhandari U. To access the role of serum procalcitonin in predicting the severity of acute pancreatitis. Kathmandu Univ. Med. J.(KUMJ), 2017; 15: 19-24.

13. Shah AP, Mourad MM, Bramhall SR. Acute pancreatitis: Current perspectives on diagnosis and management. Journal of Inflammation Research, 2018; 11: 77.

14. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, Tsiotos GG, Vege SS. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. Gut, 2013; 62(1): 102-11.

15. Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN, *et al*. American Gastroenterological Association Institute guideline on initial management of acute pancreatitis. Gastroenterology, 2018; 154(4): 1096-101.

16. Kokulu K, Günaydı n YK, Akı llı NB, Köylü R, Sert ET, Köylü Ö, Cander B. Relationship between the neutrophil-to-lymphocyte ratio in acute pancreatitis and the severity and systemic complications of the disease. The Turkish Journal of Gastroenterology, 2018; 29(6): 684.

17. Shinde VS, Kakrani VA, Gokhale VS, Thombre SK, Landge JA. Comparison of neutrophil to lymphocyte count ratio, APACHE II score, and SOFA score as prognostic markers in the setting of emergency medicine. International Journal of Healthcare and Biomedical Research, 2016; 4(4): 46-5.