

THE RELATIONSHIP OF THE NUMBER OF NEUTROFIL LYMPHOCYTE RATIO WITH THE PICTURE OF COLITIS**Agita Angela Br Tarigan¹, Nicolas Xavier Ongko², Edlin³**

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Abstract

Colitis is an acute or chronic inflammation of the colon. The gold standard for diagnosis and monitoring of disease activity in colitis patients is endoscopy combined with pathology biopsy. However, endoscopy has disadvantages related to invasiveness, cost, and feasibility of use for long-term follow-up. The neutrophil-lymphocyte ratio is a simple biomarker that can serve as a useful biomarker for diagnosing and predicting mucosal inflammation in colitis. This study aims to determine whether there is an influence between the number of neutrophil-lymphocyte ratios and the appearance of colitis. This research is a cross-sectional observational analytical research. In this study, 44 medical record data were used. A total of 44 colitis medical record data for the 2022-2023 period were collected. The largest age group is 61-70 years with 11 people (25%), based on the gender group the largest is male with 30 people (68.2%), and based on histopathology the largest is 25 (56.8%) patients. who suffers from chronic colitis. However, in the study, there was no relationship between the neutrophil-lymphocyte ratio and the appearance of colitis, $P = 0.22$ ($P \text{ value} > 0.05$) and the Prevalence Ratio 95% CI 1,436 (0,832-2,476). Based on the results of this study, the majority of patients are male, based on the patient's age, the majority is between 61-70 years, and based on the histopathology picture, the majority is chronic colitis. However, in the study, there was no relationship between the neutrophil-lymphocyte ratio and the appearance of colitis, $P = 0.22$ ($P \text{ value} > 0.05$), and the 95% Prevalence Ratio was 1,436 (0,832-2,476).

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Colitis is acute or chronic inflammation of the colon. In colitis, there is inflammation of the mucosa and submucosa in the large intestine (Nizam Oesman, 2014) . The causes of colitis are autoimmune, infection, ischemia and drugs. In diagnosing colitis, several types of examination are required which include history, physical examination, laboratory, radiology, endoscopy and histopathology biopsy examination (Nadya Wulandari Alshant et al., 2022) . The gold standard for diagnosis and monitoring of disease activity in colitis patients is endoscopy combined with pathology biopsy (Ma et al., 2021) . However, endoscopy has disadvantages related to invasiveness, cost and feasibility of use for long-term follow-up. Biomarkers widely used in the treatment of colitis include C-reactive protein , erythrocyte sedimentation rate, complete blood cell count, fecal calprotectin, and fecal lactoferrin. (Langley et al., 2021). Fecal calprotectin and lactoferrin are more specific and sensitive. However, both are expensive and not commonly used in clinical practice. This indicates the need for accessible, effective and cost-effective biomarkers for appropriate management of colitis (Okba et al., 2019) .

The neutrophil to lymphocyte ratio is a simpler and cheaper biomarker compared to fecal lactoferrin. The neutrophil lymphocyte ratio may serve as a useful biomarker for diagnosing and predicting mucosal inflammation in colitis (Jeong et al., 2021) . Assessment

can be easily obtained for all hospitalized patients by evaluating a complete blood count (Langley et al., 2021) . The neutrophil lymphocyte ratio can be calculated by dividing the absolute number of neutrophils by the number of lymphocytes in a complete blood count , to evaluate systemic inflammation (Yoon et al., 2018) .

Previous research analyse the neutrophil lymphocyte ratio in ulcerative colitis, there was a significant increase in the neutrophil lymphocyte ratio observed in the active ulcerative colitis group compared to inactive ulcerative colitis (Okba et al., 2019) . Another study assessing peripheral blood neutrophil lymphocyte ratio in inflammatory bowel disease and disease activity was found to be a valuable biomarker for predicting disease severity in inflammatory bowel disease patients (Fu et al., 2021). There is no research on the relationship between the neutrophil lymphocyte ratio level and the appearance of colitis in general, so this study is intended to analyse the relationship between the number of neutrophil ratios and the appearance of chronic and non-chronic colitis.

RESEARCH METHODS

This research uses cross-sectional observational analytical methods. This study starts from August 2023 to September 2023 at RSU Royal Prima Medan. The measuring tool used in this research is medical records. Inclusion criteria for patients diagnosed with colitis were confirmed by examining anatomical histopathology biopsies and examining the neutrophil lymphocyte ratio. The exclusion criteria were patients who were not diagnosed with colitis and did not have their neutrophil lymphocyte ratio checked. The total population at RSU Royal Prima in 2022-2023 is 57 people. To determine the minimum sample size, GPower version 3.1.9.7 was used for Chi-square calculations. The type of power analysis used was a priori, with a medium effect size ($w=0.5$), $\alpha = 0.05$, Power = 0.8. So from the calculation results, a minimum sample size of 44 patients was obtained. The way to measure the neutrophil lymphocyte ratio is based on the complete blood count value, then the absolute neutrophil count divided by the absolute lymphocyte count. The results of measuring the neutrophil lymphocyte ratio were normal 1-2, increased >3 . Meanwhile, the way to measure colitis is based on histopathology biopsy images. After that, the measurement results were grouped into acute colitis and chronic colitis. The data will then be processed using the SPSS version 21 program, with a significance level of $p<0.05$.

RESULTS AND DISCUSSION

Table 1 Frequency Distribution of Patients Diagnosed with Colitis at RSU Royal Prima Medan 2022-2023 Based on Age

Patient Age	Frequency	Percentage (%)
11-20	1	2,3
21-30	8	18.2
31-40	6	13.6
41-50	5	11.4
51-60	6	13.6
61-70	11	25.0
71-80	5	11.4
81-90	2	4.5
Total	44	100

From table 1 based on age, it can be seen that of the 44 patients diagnosed with colitis, the majority were aged 61-70 years, 11 patients (25.0%). Patients experiencing colitis at the age of 60 years continue to increase, reaching (25%) of all colitis incidents. A cohort study in Sweden published in 2017 observed an incidence of inflammatory bowel disease (IBD) in the elderly of 35/100,000 people per year and around 24% of ulcerative colitis cases occurred in elderly individuals. In research conducted in China, the incidence of ulcerative colitis among the elderly is gradually increasing due to the influence of an unfavorable lifestyle (Zhang et al., 2023) .

In contrast to other research conducted by Okba et al (2019), it was found that the average age of developing colitis was 34 years. Different results were also obtained in research conducted at Ulin Regional Hospital, Banjarmasin. In 2020-2022, it was found that more people suffering from colitis were aged 46-55 years. This difference is caused by several things, firstly, there are still few studies on colitis and the available research is still limited, especially in Indonesia. And the second factor that needs to be considered is that the number of samples collected by researchers is still smaller than previous studies because of the limited number of samples obtained (Sunata et al., 2023) .

Table 2 Frequency Distribution of Patients Diagnosed with Colitis at RSU Royal Prima Medan 2022-2023 Based on Gender

Gender	Frequency	Percentage (%)
Man	30	68.2
Woman	14	31.8
Total	44	100.0

From table 2, based on gender, it can be seen that of the 44 patients who were diagnosed with colitis, the gender most frequently experienced colitis was male with a total of 30 people (68.2%). In line with research conducted by Demir et al (2015) There were 47 men (66.19%) who experienced ulcerative colitis. This equation is influenced by several factors, including: genetic factors, stress factors and especially environmental factors. Various environmental factors greatly contribute to the development of colitis and its complications affect the gender of the patient. Men are more susceptible to exposure to dangerous substances than women. Starting from consumption of drugs, work-related chemicals, sunlight, as well as lifestyle factors such as sleep and shift work (Sunata et al., 2023) .

Table 3 Frequency Distribution of Patients Diagnosed with Colitis at RSU Royal Prima Medan 2022-2023 Based on histopathology

Histopathology Features of Colitis	Frequency	Percentage
Non-Chronic Colitis	19	43.2
Chronic Colitis	25	56.8
Total	44	100.0

From table 3 based on histopathology images, it can be seen that of the 44 patients diagnosed with colitis, the highest number of patients diagnosed with chronic colitis was 25 patients (56.8%). In line with research conducted by Nadya Wulandari Alshant et al (2022) at RSUD Dr. Soetomo Surabaya, who researched the anatomical pathological picture of chronic colitis, showed that there are 113 patients diagnosed with chronic colitis . Risk factors for colitis include smoking, drugs, such as oral contraceptives, hormone replacement therapy, and non-steroidal anti-inflammatory drugs (Ungaro et al., 2017) . Another factor that needs to be considered is the delay in diagnosis, resulting in the need for surgical intervention at a later date (Blumenstein & Sonnenberg, 2023).

Table 4 Correlation of Neutrophil Lymphocyte Ratio with Colitis Features

Neutrophil Lymphocyte Ratio	Colit				PR 95% CI	P value
	Non Chronic		Chronic			
	F	%	F	%		
Normal	10	55.6	8	34.6	0.424 (0.124-1.451)	0.22
Increase	9	44.4	17	65.4		
Total	19	100.0	25	100.0		

The neutrophil-to-lymphocyte ratio is an indicator of systemic inflammation based on complete blood count values (Huang et al., 2020). The neutrophil lymphocyte ratio consists of 2 main components. The first component is neutrophils, neutrophils are an

important component in adaptive immunity and the main effector cells during systemic inflammatory responses. Neutrophils are responsible for the first-line immune response against invading pathogens, through different mechanisms, including chemotaxis, phagocytosis, release of reactive oxygen species (ROS), granular proteins, and production and release of cytokines (Buonacera et al., 2022). In general, blood neutrophil counts increase with the development of inflammatory diseases (Huang et al., 2020). The second component of the neutrophil lymphocyte ratio is lymphocytes, lymphocytes are the main defense cells in the body and can reflect the ability of the immune system to respond to inflammation (Ma et al., 2021).

An increase in the neutrophil lymphocyte ratio occurs due to an increase in the number of neutrophils and a decrease in the number of lymphocytes. The neutrophil lymphocyte ratio can reflect the degree of systemic inflammation, because the neutrophil lymphocyte ratio contains 2 subtypes of leukocytes (Citra et al., 2022).

The way to measure the neutrophil lymphocyte ratio is based on the complete blood count value, then the absolute neutrophil count divided by the absolute lymphocyte count. The results of measuring the neutrophil lymphocyte ratio were normal 1-2, increased >3 . The appearance of colitis was assessed based on histopathology biopsy images which were grouped into non-chronic colitis and chronic colitis. The histopathology criteria for acute colitis are: mild focal increase in mononuclear cells, acute inflammation predominantly limited to the mucosa, erosion, ulceration and neutrophil inflammatory cell infiltration of the crypt epithelium (cryptitis) (Van Eyken et al., 2014). The histopathology criteria for chronic colitis are: crypt distortion, basal lymphoplasmacytic, paneth cell metaplasia, pyloric gland metaplasia and increased chronic inflammatory cells in the lamina propria (Arnold et al., 2015).

The data will then be processed using the SPSS version 21 program, with a significance level of $p < 0.05$. Bivariate test research showed that, of the 44 patients, 9 (44.4%) patients diagnosed with non-chronic colitis had an increase in the neutrophil ratio, 10 (55.6%) patients diagnosed with non-chronic colitis did not experience an increase in the neutrophil ratio, 17 (65.4%) patients diagnosed with chronic colitis had an increased neutrophil lymphocyte ratio and 8 (34.6%) patients diagnosed with chronic colitis did not experience an increased neutrophil ratio. The Chi square test results show a p value = 0.22 (P value > 0.05), so there is no significant relationship between the number of neutrophil lymphocyte ratios and the appearance of colitis. The results of the Prevalence Ratio 95% CI calculation show that chronic colitis has an increased ratio of neutrophils 1,436 (0,832-2,476) times compared to non-chronic colitis. So there is no relationship between the number of neutrophil lymphocyte ratios and the appearance of colitis in colitis patients at RSU Royal Prima Medan in 2022-2023. In contrast to this study, previous research which analyzed the neutrophil lymphocyte ratio in ulcerative colitis, there was a significant increase in the neutrophil lymphocyte ratio observed in the active ulcerative colitis group compared to inactive ulcerative colitis (Okba et al., 2019). Another study assessing peripheral blood neutrophil lymphocyte ratio in inflammatory bowel disease and disease activity was found to be a valuable biomarker for predicting disease severity in inflammatory bowel disease patients (Fu et al., 2021). In this study there was no relationship due to several reasons, including: First, the problem with the limited sample size was the research. These two studies only looked at the relationship between the neutrophil ratio and the appearance of acute and non-chronic colitis in general, and did not specifically look at the relationship between the neutrophil lymphocyte ratio in active chronic colitis and inactive chronic colitis.

CONCLUSION

Based on the results of this study, the majority of patients are male, based on the patient's age the majority is between 61-70 years and based on the histopathology picture, the majority is chronic colitis. However, in the study there was no relationship between the neutrophil lymphocyte ratio and the appearance of colitis at RSU Royal Prima Medan in 2022-2023 $P = 0.22$ (P value > 0.05) and the Prevalence Ratio 95% CI 1,436 (0,832-2,476).

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