

Neutrophil Lymphocyte Ratio As An Early Biomarker Of Surgical Site Infection In Patients Who Underwent Spine Surgery Treated At H. Adam Malik Hospital Medan

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Abstract

Introduction: Surgical wound infection is one of the most common nosocomial infections after surgery. The incidence rate of SSI in the surgical stage is relatively high, especially in orthopedic surgery; the incidence can be up to 71%. Surgical site infection after spine surgery usually occurs through direct inoculation during the surgical procedure. Using blood and wound culture as the gold standard also has several obstacles. Due to the above constraints, an alternative marker is needed to diagnose early SSI events. One marker that can be used is the neutrophil-lymphocyte ratio. The use of the neutrophil-lymphocyte balance is relevant and consistent with the pathogenesis of SSI.

Methods: This research is an observational study with a retrospective data collection method. This study took blood samples from patients who had undergone spinal surgery, as many as 60. The sample was checked for NLR on postoperative day 5. Analyze the sensitivity, specificity, and cut-off values of NLR as an early biomarker of SSI in patients who have undergone spinal surgery

Results: This study was attended by 60 spinal post-op patients treated at H. Adam Malik General Hospital Medan from November 2021 - January 2022. The number of male patients was 29 (48%), and female patients, a total of 31 people (51%). The mean age of the subjects was 52 years. The Spearman correlation test shows a significant relationship between NLR and SSI with sufficient correlation strength. A value of $r > 0.497$ obtains the average NLR of 10.10 with a standard deviation of 5.27 with a value of $p < 0.0005$.

Conclusions: There is a significant relationship between NLR and SSI. Further research is needed involving more subjects; NLR relates to other imaging tests, such as MRI, to strengthen the early detection of SSI or with culture.

Keywords: SSI, Spinal Surgery, NLR.

I. INTRODUCTION

Surgical wound infection is one of the most common nosocomial infections after surgery. Besides urinary tract infections, pneumonia, and infections in the bloodstream, the incidence is estimated at 2-11% in all surgical interventions. The high incidence of surgical wound infections causes increased mortality, morbidity, and length of stay, becoming an economic burden on hospital resources. Based on previous studies, the incidence of SSI in the surgical stage is relatively high, especially in orthopedic surgery; the incidence can be up to 71%. Seeing the high incidence rate, surgical wound infection in orthopedic surgery will cause harmful complications for patients. One of the most common operations performed is spinal surgery. SSI significantly affects patients after spinal surgery, which leads to high morbidity and mortality.¹

One of the critical roles in efforts to reduce SSI is to prevent risk factors from occurring. The risk factors for SSI after orthopedic surgery are patient and environmental. Patient factors that increase the risk include gender, age, comorbidities, poor nutritional status, smokers, ASA scores, and steroid use. For environmental factors such as the cleanliness of the operating room, operating equipment, and antibiotics used

Spine surgery has the highest SSI rate, reporting a prevalence rate of 9.4%. Minimally invasive spine surgery has a lower infection rate than open surgery procedures. The study by Smith et al. concluded the overall infection rate depends on the site of spinal surgery. The highest SSI rate was for thoracic (2.1%) surgical procedures, followed by lumbar (1.6%).³ Surgical site infection after

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spinal surgery usually occurs through direct inoculation during the surgical procedure, hematogenous spread, and early postoperative contamination. Microbiological confirmation of the cause of SSI after spinal surgery is significant as the gold standard for diagnosing SSI and guides antibiotic therapy. Blood cultures and surgical wound cultures are recommended in patients with suspected SSI. *Staphylococcus aureus* remains the primary causative agent of SSI, which is responsible for approximately 50% of cases

The most common symptom of SSI following spinal surgery is back pain, usually 1 month after the procedure, with a range of 2 days to more than 3 months post-intervention. The pain is characteristically localized, continuous, and not relieved by pain medication. It can spread to the hips, legs, scrotum, groin, abdomen, and perineum.⁵

The laboratory tests that surgeons use most frequently for the diagnosis of SSI in patients undergoing spinal surgery are white blood cell count (WBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). CRP and ESR numbers are susceptible, but many obstacles exist in daily practice. One of the obstacles is that ESR and CRP increase postoperatively, but surgeons cannot differentiate between patients who are genuinely infected and not infected. ⁶ The use of blood culture and wound culture as gold standards also has several obstacles, namely the problematic, complicated culture technique and takes a long time, requires sophisticated and special tools, and generally, the patient has been given various kinds of antibiotics before being cultured,

Due to some of the above constraints, an alternative marker is needed that can diagnose SSIs early. One marker that can be used is the neutrophil-lymphocyte ratio. The use of the neutrophil-lymphocyte balance is relevant and consistent with the pathogenesis of SSI. Where the characteristics of the early stages of SSI are an increase in the number of neutrophils and a decrease in the number of lymphocytes. So the neutrophil-lymphocyte ratio (NLR) was proposed as an alternative biomarker for detecting SSI. ^{9,10} The study of Inose et al., 2020 conducted a retrospective study of 254 patients undergoing spinal decompression surgery. The results of their study showed that NLR at 7 days postoperatively was a valuable marker for detecting surgical wound infection. ¹¹ So on that basis, researchers are interested in assessing the role of NLR, which can be used as an early biomarker of SSI in patients who have undergone spinal surgery who are treated at RSUP. H. Adam Malik, Medan.

Methods

This research is an observational study with cross-sectional data collection methods to determine whether NLR can be an early biomarker of SSI in patients who have undergone spinal surgery and are treated at RSUP. H. Adam Malik, Medan. The study was conducted at the Department of Orthopedics and Traumatology FK USU / H. Adam Malik General Hospital in collaboration with the Department of Clinical Pathology FK USU / H. Adam Malik General Hospital from November 2021 - January 2022. The reachable population for this study was all patients who had undergone spinal surgery at H. Adam Malik General Hospital Medan from November 2021 - January 2022. The research sample is a portion of the population that meets the inclusion and exclusion criteria. Sampling was done by the non-probability selection, using a consecutive technique for all affordable populations that meet the research criteria. The inclusion criteria for this study were all patients who underwent spinal surgery and were willing to participate. The exclusion criteria of this study were patients with spondylitis, uncontrolled type 2 DM patients, obese patients, and patients with other sources of infection (e.g., sepsis).

The flow began with research conducted at the Haji Adam Malik General Hospital in Medan. Samples were selected consecutively and met the inclusion criteria. The research subjects were explained the purpose of the research and the benefits of the study; then, the research subjects were given a reason to fill out a letter of consent to participate in the research or informed consent. An NLR examination is carried out, and the samples needed for this examination are the patient's blood and blood serum. The patient's blood was sampled on the 5th day after spinal surgery. Blood sampling to obtain serum is done. Data analysis was performed using Statistik software. Data were analyzed descriptively to analyze the frequency distribution of research subjects based on their characteristics and risk factors.

Results

Table 1 presents the distribution of frequencies based on gender, with 29 men (48.3%) and 31 women (51.7%). In the sample characteristics based on age, the average age is obtained 52.71 ± 11.12 with an average body weight of approx 69.41 ± 12.38 . Based on the KGD levels, there were 41 (68.3%) people with KGD levels > 200 with KGD levels < 200 19 (31.7%). The duration of surgery was obtained at most > 3 hours 41 (68.3%) with an average length of stay > 6 days by 33 (55%) with a length of stay of at least > 2 days and > 7 days 1 person (1.7%). The sample distribution based on ethnicity found that the most Batak tribe was 36 people (60%), Javanese 10 people (16.7%), Padang 8 people (13.3), Karo 3 people (5%), Mandaling 2 people (3, 3%) and at least 1 Malay (1.7%).

In the comorbid section, the most comorbid patients were diabetes accompanied by hypertension in 20 patients (33%), followed by the absence of comorbidities in 19 patients (31.7%). There were 7 people with diabetes and hypercholesterolemia (11.7), and there was 1 person each for diabetes accompanied by hypercholesterolemia and alcohol; diabetes with hypercholesterolemia and smoking; diabetes with hypertension and alcohol; hypertension accompanied by smoking; hypertension with hypercholesterolemia and alcohol; and for a history of type 2 diabetes mellitus.

Table 1. Characteristics of the Research Sample

Variable	Amount (%)
Gender	
Woman	31 (51.7)

Man	29 (48.3)
Age (years)	
Median	53
Mean \pm SB	52.7167 \pm 11.12196
range	21- 68
Weight (kg)	
Median	74
Mean \pm SB	69.4167 \pm 12.38410
range	49 - 89
Blood Sugar Levels	
<200	19 (31.7)
>200	41 (68.3)
Length of Treatment	
< 6 days	19 (31.7)
> 2 days	1 (1.7)
> 4 days	2 (3.3)
> 5 days	4 (6.7)
> 6 days	33 (55%)
> 7 days	1 (1.7)
Operation Length	
< 3 hours	19 (31.7)
> 3 hours	41 (68.3)
Operation Class	
Clean	19 (31.7)
Clean Contaminated	41 (68.3)
Body mass index	
<25	19 (31.7)
>25	41 (68.3)
Ethnic group	
Batak	36 (60)
Java	10 (16.7)
Karo	3 (5.0)
mandailing	2 (3.3)
Malay	1 (1.7)
Padang	8 (13.3)
Comorbid	
DM + Hypercholesterol	7 (11.7)
DM + Hypercholesterol + Alcohol	1 (1.7)
DM + Hypercholesterol + Smoking	1 (1.7)
DM type 2	1 (1.7)
DM + Hypertension	20 (33.3)
DM + Hypertension + Alcohol + Smoking	2 (3.3)
DM + Hypertension + Alcohol	1 (1.7)
DM + Hypertension + Smoking	3 (5.0)
Hypertension + Smoking	1 (1.7)
Hypertension + Hypercholesterol	3 (5.0)
Hypertension + Hypercholesterol + Alcohol	1 (1.7)
There aren't any	19 (31.7)

a) Categorical data is displayed in amount (percentage)

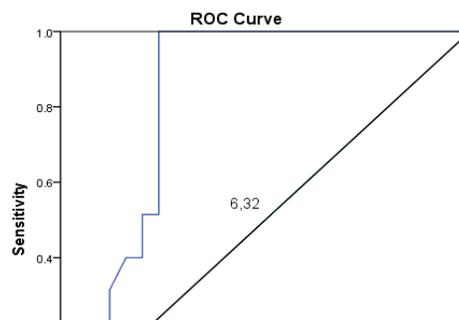
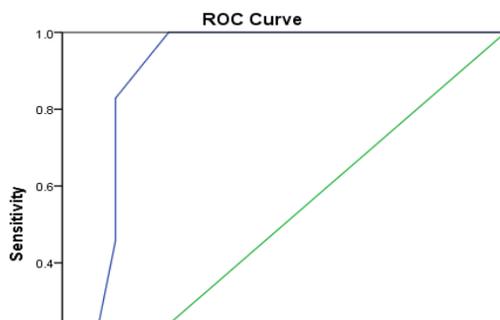


Figure 1. ROC NLRs

Table 2. Sensitivity, specificity, and AUC of NLR levels

	Sensitivity	specificity	AUC
NLR	82 %	88 %	0.89

Table 2 shows a diagnostic test found NLR to have sensitivity 82%, 88% specificity, and 89% accuracy with a cut-off of 12.93; this is the same as the PCT that obtained insensitivity 74%, 76% specificity, and 81% accuracy with a cut-off value of 6.32.

Table 3. Correlation of NLR to SSI

<u>Variabel</u>	<u>Rata-rata</u>	<u>SD</u>	<u>Koefisien korelasi (r)</u>	<u>Nilai-p</u>
NLR	10.10	5.27	0,497	<0.001

a) Uji analisis menggunakan Spearman-Rho

*) Bermakna bila $p < 0.05$

□

Table 3 shows that the average NLR is 10.10 with a standard deviation of 5.27, and the value of $r > 0.497$ is obtained with a value of $p < 0.0001$, where there is a significant correlation with sufficient correlation strength.

Discussion

This study was attended by 60 spinal post-op patients treated at H. Adam Malik General Hospital Medan from November 2021 - January 2022. The number of patients was male, 29 people (48%), and female patients totaling 31 people (51%). The mean age of the subjects was 52 years, in line with research conducted by Inose et al., 2022. They conducted a retrospective study of 254 patients who underwent spinal surgery procedures. Patients were divided into SSI and non-SSI groups based on diagnosis. Their study showed that the incidence of SSI was 7 out of 254 patients (2.8%), all male with a mean age of 66.7 years. At the same time, the rest were the non-SSI group, which consisted of 159 male patients and 88 female patients. The mean age at surgery was 65.8 years.11

Surgical wound infection is one of the most common nosocomial infections after surgery. Based on previous studies, the incidence of SSI in the surgical stage is relatively high, especially in orthopedic surgery; the incidence can be up to 71%. One of the most common operations performed is spinal surgery. SSI significantly affects patients after spinal surgery, which leads to high morbidity and mortality. 12 One of the critical roles in efforts to reduce SSI is to prevent the occurrence of risk factors. Age can affect the occurrence of surgical wound infections in each individual due to the immature form of the body's defense system or a decrease in the body's resistance to disease. Old age is associated with a reduction in the body's resistance to infection.

Old age causes atrophy of the thymus with decreased function so that all of the thymus tissue can be replaced by fatty tissue so that as you get older, you are at risk for surgical wound infections. As we get older, the thymus gland has changed, but the number of T and B cells has not changed, increasing the formation of autoantibodies. In addition, the response of macrophages to foreign bodies in mucosal cells and skin cells and the formation of acute phase proteins has decreased, thereby increasing the risk factors for infection. 14

In our study for the group of patients likely to get SSI, we found 41 patients (68.3 %)who underwent spinal surgery had blood glucose levels > 200 mg/dl. Thirty-three patients (55%) who underwent spinal surgery had a longer stay of more than 6 days. Forty-one patients (68%) underwent spinal surgery for over 3 hours. And it was found that 20 patients (33%) who underwent spinal surgery had comorbid hypertension and type 2 DM in line with a study conducted by Al-Gamdi et al. 2021. Researchers conducted a retrospective study of 201 patients about to undergo spinal surgery. Their research showed a significant relationship between comorbid diseases such as type 2 DM, hypertension, smoking, and surgical wound infections ($p < 0.001$). In addition, the study found that spinal surgery procedures were carried out for more than 227 minutes.

This is also in line with research conducted by Ojo et al., 2016. Researchers conducted a retrospective study of 201 patients about to undergo spinal surgery. The results of their research showed that there was a significant relationship between the length of stay

of patients undergoing spinal surgery and the incidence of SSI. This study shows that patients with SSI have a length of stay of more than 5 days

uSpearman's correlation test shows a significant relationship between NLR and SSI with sufficient correlation strength. NLR average of 10.10 with a standard deviation of 5.27 obtained a value of $r > 0.497$ with a value of $p < 0.0001$. In line with the study conducted by Inose et al., 2020. We conducted a retrospective observational study of patients undergoing spinal decompression surgery. Two hundred fifty-four patients were divided into SSI groups and non-SSI groups based on the presence of SSI. We evaluated the results of NLR, which differed significantly between groups. Their results showed significant differences in the percentage of neutrophils and lymphocytes and NLR at 3-4 days postoperatively and NLR at 6-7 days postoperatively between the SSI and non-SSI groups. Among these markers, the lymphocyte percentage and NLR cut-off values at 3-4 days postoperatively to predict SSI were $< 15.1\%$ and > 4.91 , respectively. It was concluded that lymphocyte percentage and NLR at 3-4 and postoperatively are useful markers for early prediction of SSI in patients who have undergone spinal surgery. This parameter can help identify patients at higher risk of SSI after spinal surgery

Surgical site infection after spinal surgery usually occurs through direct inoculation during the surgical procedure, hematogenous spread, and early postoperative contamination. Microbiological confirmation of the cause of SSI after spinal surgery is significant as a gold standard. Still, the culture technique is difficult, complicated, takes a long time, and requires sophisticated and special tools that take a long time, making it challenging to diagnose SSI early. Therefore, an alternative marker is needed that can diagnose SSIs early. One marker that can be used is the neutrophil-lymphocyte ratio.

In the hematological profile of patients with SSI, there is an increase in neutrophils and a decrease in lymphocytes, one of the body's defense responses against systemic infections. This parameter can be used as a determinant of the prognosis of SSI patients due to bacteria. The neutrophil-to-lymphocyte ratio can be obtained by dividing the absolute/or relative neutrophil count by the absolute/close lymphocyte count. All blood cells activated during systemic infection can significantly change the number, function, receptor expression, and secretion of various signaling molecules and humoral substances. A high NLR value is associated with systemic inflammation, stress, injury, trauma or major surgery, cancer, and a worsening prognosis concerning morbidity or mortality.

Table 2 shows using a diagnostic test found NLR to have a sensitivity of 82%, 88% specificity, and 89% accuracy with a cut-off of 12.93. Thus, using the NLR offers some initial diagnostic utility for predicting SSI occurrence after spinal surgery. The results of our ROC analysis can also show that NLR is for the early prediction of SSI after spinal decompression surgery because it has better specificity when used 3-4 days postoperatively. Based on our study, if the NLR is more than 12 at 3-4 postoperative days after spinal surgery, the surgeon should consider the possibility of SSI. Furthermore, if the patient has a fever, redness in or around the wound, or pus from the injury. Therefore diagnostic approaches such as exudate culture (pus from the wound), magnetic resonance imaging (MRI), and blood culture are recommended. After a definitive diagnosis of SSI,

Research conducted by Shen et al., 2019. They conducted a study of 293 patients undergoing posterior lumbar spine surgery enrolled in this study. Each patient's medical history was reviewed retrospectively, and patients were divided into the SSI group ($n = 13$) and the non-SSI group ($n = 280$). Laboratory data, including WBC total, neutrophil, and leukocyte count and percentage, NLR assessed at 4 and 7 days postoperatively, and CRP at 4 and 7 days postoperatively, were analyzed between the SSI and non-SSI groups. In addition, the predictive power and the NLR cut-off value for SSI are determined by the receiver operating characteristic (ROC) curve results. Their study results revealed that the median NLR increased markedly in the SSI group compared to the non-SSI group at 4 days ($p = 0.011$) and 7 days ($p = 0.047$) postoperatively. In addition, the percentage of neutrophils also increased dramatically in the SSI group at 4 and 7 days postoperatively ($p = 0.010$ and $p = 0.030$) compared to the non-SSI group. ROC results showed NLR at 4 days (cut-off > 5.19 ; sensitivity: 61.5%; specificity: 77.6%; AUC = 0.708) and 7 days (cut-off > 3.85 ; sensitivity: 69.2%; specificity: 62.7%; AUC = 0.663) postoperatively can significantly differentiate SSI and non-SSI groups. Logistic regression analysis showed that NLR at both postoperative time points (OR = 1.218; $p = 0.003$ and OR = 1.296; $p = 0.048$) could be a valuable predictor of SSI. NLR at 4 and 7 days postoperatively is a helpful laboratory predictor of SSI in posterior lumbar spine surgery patients.²⁰

Conclusion

Spearman's correlation test shows that there is a significant relationship between NLR and SSI with sufficient correlation strength. NLR average of 10.10 with a standard deviation of 5.27 obtained a value of $r > 0.497$ with a value of $p < 0.0001$.

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