

# Elevated Delta Neutrophil Index (DNI) as a Predictor of Systemic Inflammatory Response Syndrome (SIRS) In Patients with Generalized Peritonitis at Prof Dr. I.G.N.G. Ngoerah Hospital, Denpasar

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## ABSTRACT

**Background:** Generalized peritonitis is an emergency case in the field of surgery. Which includes an inflammatory process in the peritoneum. Systemic inflammatory response syndrome (SIRS) is a defense response to a stressor. Delta Neutrophil Index (DNI) is a parameter that reflects the ratio of infection and inflammation. This study examines the role of DNI as a predictor of SIRS in generalized peritonitis patients at Prof. Dr. IGNG Ngoerah General Hospital. **Method:** Cross-sectional analytic observational research. Data collection was from July 2022 to October 2022. Patients diagnosed with generalized peritonitis were taken for blood samples. The DNI examination was carried out at the Surya Husadha Hospital Laboratory. Samples were excluded if they suffered from immunodeficiency diseases, autoimmune diseases and refused to participate. The DNI value is determined by the cut-off point on the ROC curve. Bivariate analysis using Chi square test and multivariate analysis using logistic regression test. The p value <0.05 indicates a significant result. **Result:** This study involved 55 respondents with 41 positive SIRS respondents and 14 negative SIRS respondents. ROC curve analysis showed the DNI value with a cut-off point of 8.9 (sensitivity 85.4% and specificity 85.7%). Bivariate analysis of the DNI 8.9 with the incidence of SIRS obtained RR 3 (p = 0.000; 95% CI 1.11- 6.90). Multivariate analysis of DNI values with the incidence of SIRS showed a significant relationship (p = 0.000). **Conclusion:** DNI value of 8.9 is an excellent predictor of SIRS in patients with generalized peritonitis.

**Keywords:** generalized peritonitis; SIRS; DNI

## INTRODUCTION

Generalized peritonitis is an emergency case that often occurs in the surgical field. The incidence of mortality is still reported to be quite high, which requires attention for surgeons in its management with the aim of reducing the incidence of mortality in cases of generalized peritonitis.

Generalized peritonitis is a potentially life-threatening intra-abdominal disorder [1]. Generalized peritonitis is a major contributor to non-traumatic emergency mortality and the second leading cause of sepsis. [2]. Generalized peritonitis increases the risk of perioperative morbidity and mortality and imposes a high economic burden on patients, families and the healthcare system as a whole.

Despite tremendous advances in laboratory tests, ancillary tests, perioperative resuscitation, surgical techniques and intensive care, the management of generalized peritonitis is still very complex [3].

The main causes of peritonitis cases found in the African region are perforated gastroduodenal ulcer, perforated appendicitis and typhoid ileal perforation. Postoperative mortality rates vary between 8.4% and 34%. [2-4]. Generalized peritonitis also causes postoperative complications such as surgical site infection, chest infection, postoperative intestinal obstruction peritonitis, thromboembolic disease, incisional hernia, wound dehiscence, enterocutaneous fistula, reoperation and prolonged hospital stay [2,5].

An investigation in 68 health institutions in Europe for more than 6 months found 2,152 patients with abdominal infectious complications with a mortality rate of 7.5%. A survey conducted by the World Society of Emergency Surgery stated that 88% of infectious episodes were intra-abdominal nosocomial infections. Generalized peritonitis was found to be 43% while localized peritonitis or abscess peritonitis was 57% with a mortality rate of 10% [6].

The epidemiology of generalized peritonitis in Indonesia has not been widely reported but some studies show the prevalence of peritonitis in patients with appendicitis is 62.8%. [7]. The prevalence of generalized peritonitis in men (68.4%) was higher than in women (31.6%). The most common age group was 10-19 years (24.5%). Generalized secondary peritonitis due to appendiceal perforation was the most common type of peritonitis (53.1%). Most peritonitis patients received surgical management in the form of exploratory laparotomy and appendectomy (64.3%) [8].

Indonesia has a high incidence of peritonitis, which is a form of complicated intra-abdominal infection, as much as 9% of the total population of Indonesia, or around 179,000 people [9]. Puspitadewi analyzed the factors that influence mortality in patients with complicated abdominal infections based on the Mannheim Peritonitis Index (IPM) score, and found that the variables of duration and organ failure have a significant relationship with mortality [10].

The pathophysiology of generalized peritonitis includes inflammatory processes in the peritoneum caused by infectious or chemical agents that irritate the peritoneal cavity and then hematogenous spread of infection from other parts of the body to the peritoneal cavity or by hollow intraabdominal perforation that causes the entry of bacteria into the peritoneal cavity [4,11]. A strong local inflammatory response can control the inflammation so that there is no spread, but if not treated properly, it will cause spread to the systemic circulation which can lead to bacteremia, systemic inflammation, septic shock, and multi-organ failure [3,12].

Systemic inflammatory response syndrome (SIRS) is the body's exaggerated defense response to a harmful stressor (infection, trauma, surgery, acute inflammation, ischemia or reperfusion, or malignancy,) to localize and then eliminate the source [13,14]. The resulting inflammation elicits a complex interplay of humoral and cellular immune responses, cytokines, and complement pathways such that a systemic inflammatory response syndrome occurs when an imbalance between proinflammatory and anti-inflammatory cascades occurs [13,15]. Systemic inflammatory response syndrome that occurs after surgery can be a potential early marker of postoperative complications and organ failure [16].

Infection is commonly assessed using several parameters, such as increased white blood cell counts and elevated markers of acute phase infection such as procalcitonin and C-reactive protein (CRP)

[16]. The use of markers is expected to be an option in determining disease prognosis. Several parameters have been used to diagnose, estimate, and monitor worsening in patients, one of which is neutrophils. Neutrophils are leukocytes with a considerable amount of blood as the first line in dealing with inflammation and infection. Microorganisms can stimulate an inflammatory response that causes neutrophils in circulation to enter the tissue. Neutrophils destroy microorganisms in several ways including phagocytosis, secreting antimicrobial substances, and formation of neutrophil extracellular traps (NETs). Neutrophil activation also induces the release of proteinases into surrounding tissues, resulting in damage to the host. Neutrophils are capable of producing many cytokines and chemokines that influence the inflammatory response as well as the immune response [17]. Neutrophils appear within two to four hours and dominate the cell types in the peritoneum from 48 to 72 hours. The destroyed bacteria release lipopolysaccharides and other cellular components that further stimulate a pro-inflammatory response [19].

Research by Sudiartha et al (2020) evaluated the neutrophil-lymphocyte ratio as a sepsis screening in patients with generalized peritonitis because it has better sensitivity and accuracy but is still confirmed by blood culture as a standard [18]. Serum procalcitonin can be used as an additional non-invasive biomarker in diagnosing bacterial peritonitis with a high degree of accuracy in cirrhotic patients but the addition of CRP does not seem to significantly improve the diagnostic accuracy of procalcitonin [21].

Delta Neutrophil Index (DNI) has been suggested as a marker of immature neutrophils as an indication of infection or sepsis [19]. Delta Neutrophil Index describes the difference between leukocytes counted in the myeloperoxidase (MPO) channel and those counted in the nuclear lobularity channel provided by an automated hematology counting device. Delta neutrophil index is a parameter that reflects the ratio of infection and inflammation associated with immature neutrophils to the total number of neutrophils. Delta Neutrophil Index has predictive value and prognostic value in several different infectious conditions such as acute appendicitis, bacterial peritonitis, and sepsis [20,21].

Delta Neutrophil Index reflects the ratio of immature neutrophils to total neutrophil count measured using myeloperoxidase channel and core lobularity automated hematology tools; which can be used to predict the prognosis of various infectious or inflammatory conditions. In fact, it indicates the number of immature neutrophils released into the circulation [22,23].

Delta Neutrophil Index correlates strongly with immature granulocyte count as an additional marker in infection and inflammatory reactions. Delta Neutrophil Index was also identified as a predictive factor of fungal infection in SIRS patients. Delta Neutrophil Index and patient clinical characteristics

are useful in determining the occurrence of fungal infection in SIRS patients [14].

The results of research by Lee et al (2017) involving 171 respondents found that the DNI cut-off point value of 4.3% was significantly associated with surgical intervention as much as 22.2%. Research by Soh & Lim (2019) found that patients with high DNI were associated with a high incidence of bacteremia and sepsis, longer hospitalization time, and higher postoperative complications, so it was concluded that DNI was practically very useful as a marker in predicting the prognosis of patients who needed abdominal surgery interventions [24].

A study in Indonesia states that under stress or infection, immature neutrophils are released into circulation. Delta Neutrophil Index may reflect the number of immature neutrophils in circulation [25]. Delta Neutrophil Index also has better diagnostic accuracy as a marker of sepsis severity.

Delta Neutrophil Index may serve as a prognostic factor for sepsis [26]. Research on the use of DNI as a predictor of SIRS in generalized peritonitis has not been found, therefore researchers want to conduct research on DNI in its role as a predictor of SIRS in generalized peritonitis patients.

## METHODS

This study is an analytical observational study with a prospective cross-sectional design with the aim of knowing the ability of DNI as a predictor of SIRS in patients with generalized peritonitis. The study began with identifying patients with generalized peritonitis who came for treatment to Prof. Dr. I G.N.G. Ngoerah Hospital, then management was carried out in accordance with standard operating procedures and complete blood laboratory tests and DNI examinations were carried out. Furthermore, patients are followed whether SIRS occur or not.

The inclusion criteria in this study were as follows: 1) All patients diagnosed with generalized peritonitis; 2) Patients aged over 18 years to 60 years; 3) Patients were willing to participate in the study and signed informed consent. The exclusion criteria in this study are as follows: 1) Patients are suffering from immunodeficiency diseases that can cause a decrease in the number of B lymphocytes, T lymphocytes, and macrophages such as leukemia, lymphoma, acute renal failure, HIV infection, sarcoidosis, splenectomy; 2) Patients are suffering from autoimmune diseases such as Systemic Lupus Erythematosus (SLE), hepatic cirrhosis, rheumatoid arthritis, insulin-dependent diabetes mellitus; 3) Patient refuses to participate in research. The dropout criteria in terms of laboratory examination is if the volume of samples received by the laboratory is not appropriate (< 2 mL).

Data analysis using the help of SPSS version 26 which includes descriptive and bivariate analysis. The ability of DNI to predict the occurrence of mortality in patients with Generalized Peritonitis used the ROC (Receiver Operating Characteristic) curve. ROC curve assessment based on the area under the ROC curve is stated when  $\geq 70\%$ . Then find the best cut-off point of DNI to predict the occurrence of SIRS by determining the farthest coordinate point of the ROC curve. Furthermore, bivariate tests were carried out to determine the relationship of each independent variable with the dependent variable with Chi-square so that the RR value was known. Determine the cutoff point and AUC (Area Under Curve) and calculate the RR value of the DNI value with a 2x2 table.

## RESULTS

This study involved 55 patient respondents with generalized peritonitis. The characteristics of respondents were described based on age, gender, diagnosis, surgery. The data is presented in Table 1.

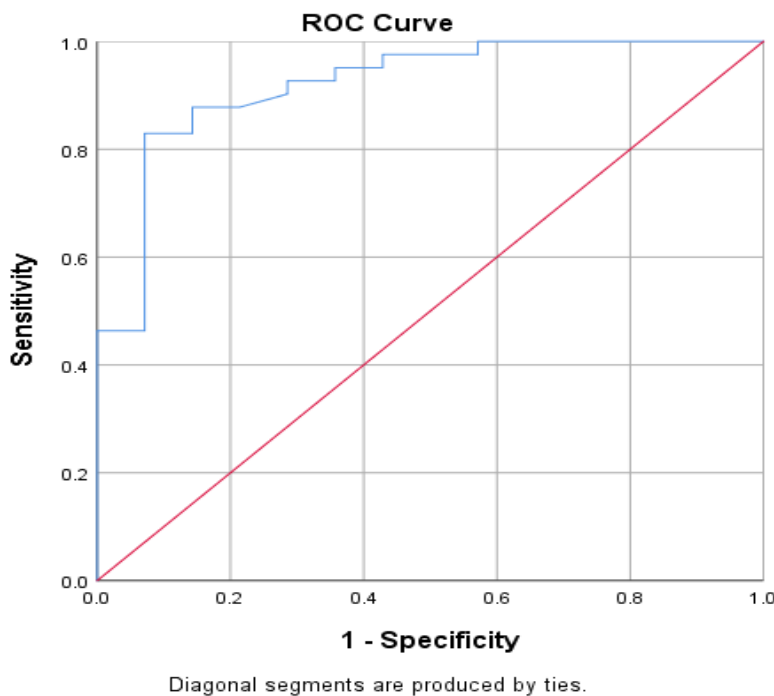
**TABLE 1:** Respondent characteristics.

| Characteristics                               | SIRS events     |                 | P        |
|---|-----------------|-----------------|----------|
|   | SIRS            | No SIRS         |          |
| Age (mean $\pm$ SD) years                     | 50,1 $\pm$ 22,7 | 51,7 $\pm$ 27,4 | 0,487**  |
| Gender  |                 |                 |          |
| Male  | 24 (43,6%)      | 8 (14,5%)       | 0,927*** |
| Female  | 17 (30,9%)      | 6 (10,9%)       |          |
| BMI (mean $\pm$ SD) kg/m <sup>2</sup>         | 21,2 $\pm$ 3,5  | 20,8 $\pm$ 4,2  | 0,549*   |
| WBC (mean $\pm$ SD) 10 / $\mu$ l <sup>3</sup> | 16 $\pm$ 9      | 18,1 $\pm$ 6,7  | 0,740*   |
| DNI (mean $\pm$ SD) (%)                       | 20,6 $\pm$ 16   | 6,8 $\pm$ 3     | 0,000**  |
| Causes of surgery                             |                 |                 |          |
| Appendiceal perforation                       | 12 (21,8%)      | 7 (12,7%)       | 0,841*** |
| Gaster Perforation                            | 9 (16,4%)       | 3 (5,5%)        |          |
| Perforated Ileum                              | 7 (12,7%)       | 2 (3,6%)        |          |
| Jejunum perforation                           | 3 (5,5%)        | 1 (1,8%)        |          |
| Caecum perforation                            | 2 (3,6%)        | 0 (0%)          |          |
| Sigmoid perforation                           | 2(3,6%)         | 0 (0%)          |          |
| Hepar   | 2 (3,6%)        | 1 (1,8%)        |          |
| Gynecology Perforation                        | 3 (5,5%)        | 0 (0%)          |          |
| Buli Rupture                                  | 1 (1,8%)        | 0 (0%)          |          |
| Length of hospital stay (mean $\pm$ SD) days  | 8,7 $\pm$ 6,5   | 7,4 $\pm$ 3,7   |          |

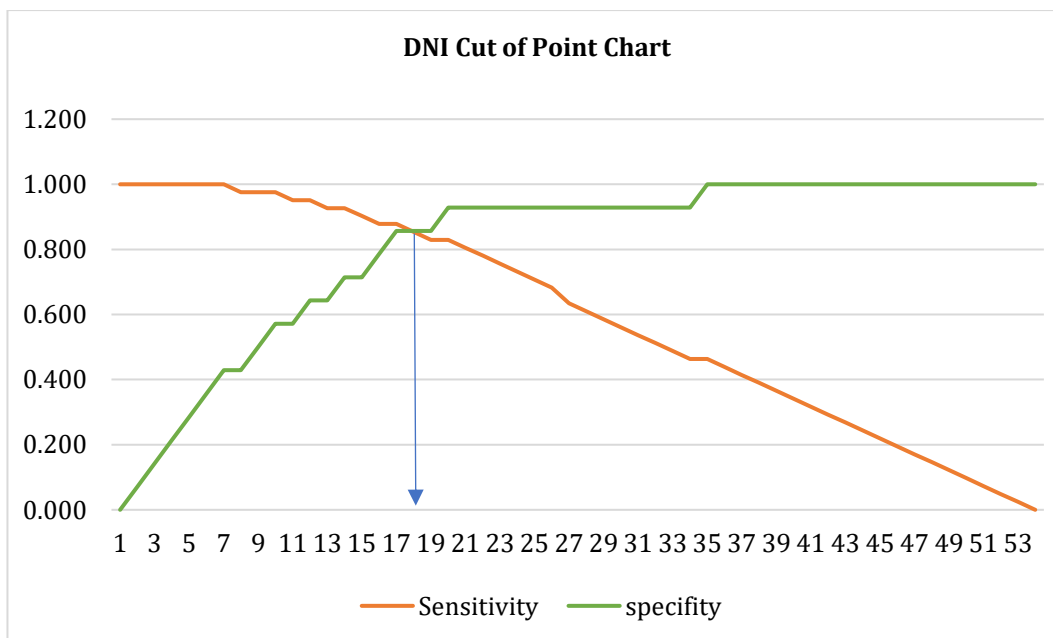
\*Independent t test, \*\* Mann Whitney U test, \*\*\* Chi Square

Figure 1 shows that the AUC value is 92.1%, meaning that if DNI is used to diagnose the occurrence of SIRS in 55 respondents, the correct conclusion is obtained in 51 patients.

Clinically, the AUC value of DNI is very satisfying because it is greater than the minimum AUC value expected by researchers which is 70%. and significance <0.05 (IK: 0.83-1.00). Furthermore, the cutoff point was sought and a cutoff point value of 8.9 was obtained.



**FIGURE 1:** ROC curve of DNI on the occurrence of SIRS.



**FIGURE 2:** DNI Cut off point graph.

Figure 2 shows that the DNI cut-off point is 18 and when viewed in the table, cut-off point 18 shows a value of 8.9 with a sensitivity of 85.4% and a specificity of 85.7% (Appendix 3 pp 101-102).

The DNI cut off point results were then analyzed using a 2x2 table to determine the ability of DNI to predict SIRS, sepsis and mortality in patients with generalized peritonitis. The data is presented in Table 2.

**TABLE 2:** Relationship between DNI and SIRS incidence.

| Variables     | SIRS events |            | RR | 95% IK    | p     |
|---------------|-------------|------------|----|-----------|-------|
|               | SIRS        | No         |    |           |       |
| DNI           |             |            |    |           |       |
| Cut off ≥ 8.9 | 35 (63,6%)  | 1 (1,8%)   | 3  | 1,58-5,98 | 0,000 |
| Cut off < 8.9 | 6 (10,9%)   | 13 (23,6%) |    |           |       |

Table 2 shows DNI ≥ 8.9 with SIRS in as many as 35 respondents (63.6%) and not SIRS in as many as 1 respondent (1.8%) while DNI < 8.9 was found to occur in SIRS 6 respondents (10.9%) and not SIRS as many as 13 respondents (23.6%).

Based on the 2x2 table, the RR value = 3 and the p-value is 0.000, then DNI increases the risk of SIRS in generalized peritonitis patients so that DNI can be a predictor of SIRS in generalized peritonitis patients.

**TABLE 3:** Relationship between DNI and incidence of sepsis.

| Variables     | Incidence of Sepsis |            | RR  | 95% IK    | p     |
|---------------|---------------------|------------|-----|-----------|-------|
|               | Sepsis              | No         |     |           |       |
| DNI           |                     |            |     |           |       |
| Cut off ≥ 8.9 | 21 (38,2%)          | 15 (27,3%) | 2,7 | 1,11-6,90 | 0,008 |
| Cut off < 8.9 | 4 (7,3%)            | 15 (27,3%) |     |           |       |

Table 3 shows DNI ≥ 8.9 with sepsis in as many as 21 respondents (38.2%) and not sepsis in as many as 15 respondents (27.3%) while DNI < 8.9 obtained sepsis in 4 respondents (7.3%) and not sepsis as

many as 15 respondents (27.3%). Based on the 2x2 table, the RR value is 2.7 the p-value is 0.008, and RR > 1, then DNI ≥ 8.9 increases the risk of sepsis in patients with generalized peritonitis.

**TABLE 4:** Relationship between DNI and mortality.

| Variables     | Mortality |            | RR  | 95% IK    | p     |
|---------------|-----------|------------|-----|-----------|-------|
|               | Yes       | No         |     |           |       |
| DNI           |           |            |     |           |       |
| Cut off ≥ 8.9 | 8 (14,5%) | 28 (50,9%) | 0,4 | 0,21-1,01 | 0,055 |
| Cut off < 8.9 | 9 (16,4%) | 10 (18,2%) |     |           |       |

Table 4 shows DNI ≥ 8.9 with mortality of as many as 8 respondents (14.5%) and no mortality of as many as 28 respondents (50.9%) while DNI < 8.9 was found to occur in 9 respondents (16.4%) and no mortality as many as 10 respondents (18.2%). Based on the 2x2 table, the RR value is 0.4 and the p-value is 0.055, which means that DNI is not associated with the occurrence of mortality in patients with generalized peritonitis.

The multivariate analysis aims to determine the effect of DNI on the incidence of SIRS by testing together with the variables of age, gender, and BMI. The first step is to test each variable one by one on the occurrence of SIRS.

**TABLE 5:** Relationship between age gender BMI and DNI with the incidence of SIRS.

| Variables              | SIRS events |            | RR  | 95% IK    | p     |
|------------------------|-------------|------------|-----|-----------|-------|
|                        | SIRS        | No         |     |           |       |
| <b>Age (n, %)</b>      |             |            |     |           |       |
| ≥ 60 years             | 16 (29,1%)  | 7 (12,7%)  | 0,8 | 0,64-1,23 | 0,472 |
| < 60 years             | 25 (45,5%)  | 7 (12,7%)  |     |           |       |
| <b>Gender (n, %)</b>   |             |            |     |           |       |
| Male                   | 24 (43,6%)  | 8 (14,5%)  | 1   | 0,74-1,39 | 0,927 |
| Female                 | 17 (30,9%)  | 6 (10,9%)  |     |           |       |
| <b>BMI (n, %)</b>      |             |            |     |           |       |
| ≥ 25 kg/m <sup>2</sup> | 7 (12,7%)   | 3 (5,5%)   | 0,9 | 0,59-1,43 | 0,715 |
| < 25 kg/m <sup>2</sup> | 34 (61,8%)  | 11 (20%)   |     |           |       |
| <b>DNI (n, %)</b>      |             |            |     |           |       |
| Cut off ≥ 8.9          | 35 (63,6%)  | 1 (1,8%)   | 3   | 1,58-5,98 | 0,000 |
| Cut off < 8.9          | 6 (10,9%)   | 13 (23,6%) |     |           |       |

Table 5 shows that bivariate age in this study was found to be unrelated to the occurrence of SIRS. The highest incidence of SIRS in the age category < 60 years (45.5%). The RR value was 0.8, meaning that age was not associated with the occurrence of SIRS. In the gender category, it was found that SIRS occurred more in men than women but statistically, gender was not associated with the occurrence of SIRS. It was statistically found that BMI was not associated with SIRS.

Multivariate analysis of results was performed using logistic regression. All variables were included together. The omnibus test results obtained data p value 0.000 and the Hosmer and Lane show test results obtained p value of 0.709 means that this test model is fit for use. The final results of the variables in the equation (Table 6).

**TABLE 6:** Multivariate analysis results.

| Variables | B      | Adj OR | IK95%         | p     |
|-----------|--------|--------|---------------|-------|
| Age       | 1,541  | 4,6    | 0,44-49,50    | 0,201 |
| Gender    | 0,820  | 2,2    | 0,33-17,19    | 0,427 |
| IMT       | -0,495 | 0,6    | 0,05-6,39     | 0,680 |
| DNI       | 5,186  | 178,7  | 10,69-2989,29 | 0,000 |

## DISCUSSION

In this study, the mean age of the SIRS group was 50.1 years while the mean age of the non-SIRS group was 51.7 years. There was no difference in age between the SIRS and non-SIRS groups. Based on gender, males in the SIRS group were higher (43.6%) compared to females (30.9%) but there was no difference in gender between the SIRS and no SIRS groups. Different results were found in research [27] involving 108 elderly patients, forty-two patients were male (38.9%) and the overall mean age was 72 years. A different study involving patients with peritonitis was conducted by Lim et al (2014) involving 75 patients with the mean age of the patients studied was 59 years and 87.7% were male [28].

Based on BMI, there was no difference between the BMI of the SIRS group and the non-SIRS group with an average of 20.8 kg/m<sup>2</sup> and 21.2 kg/m<sup>2</sup>. The body mass index was found to be most in the normal category of SIRS compared to not SIRS and statistically found IMT was not associated with SIRS. Research Angeles et al (2021) mentioned 13 patients with postoperative gastric perforation, the average age was 65.4 years (lowest age 33.9-highest 80.2) with a median BMI of 27.1 kg/m<sup>2</sup> (range 20.2-53.3). These results are different because the characteristics of the research subjects used are different.

There was no difference in WBC values between the SIRS and non-SIRS groups with a mean of  $16 \times 10^3 / \mu\text{l}$  and  $18 \times 10^3 / \mu\text{l}$ . Research Hyuk et al (2018) comparing the average WBC in patients with perforated gastric and not perforated gastric obtained that said most groups were perforated appendicitis there is a difference with an average of 9050 sell/ml - 11720 cells/ml. DNI laboratory results in the SIRS group with a mean of  $20.6 \pm 16$  and the non-SIRS group with a mean of  $6.8 \pm 3$ . There is a difference in DNI between the SIRS group and non-SIRS with a p-value <0.05. Research Bang et al (2020) found there was a significant difference in DNI with postoperative outcomes [30].

The most common surgical cause of generalized peritonitis in this study was appendicitis perforation in as many as 34 samples (34.5%) where SIRS occurred was 21.8%. This research is supported by Hyuk et al. (2018) which states that the largest group is perforated appendicitis. Research Karachentsev (2020) mentioned the main etiological factors of peritonitis, morbidity, and mortality are perforated peptic ulcer, acute appendicitis, pelvic inflammatory disease, small bowel perforation, and abdominal trauma.

The length of hospitalization in the SIRS group was found to be longer with a mean of 8.7 days compared to the non-SIRS group with a mean of 7.4 days, although statistically there was no difference in the length of hospitalization between the SIRS and non-SIRS groups. These results are in line with the research of Soh & Lim (2019) who found that patients with high DNI are associated with a high incidence of bacteremia and sepsis and longer hospitalization time.

The AUC value of DNI in this study was very satisfactory at 92.1% with a cutoff point value of 8.9. Different results were found in a study by Lee et al (2017) involving 171 respondents, where the DNI cut-off point value of 4.3% was significantly associated with surgical intervention by 22.2%. This is because the subjects involved in the study had different characteristics. Research by Soh & Lim (2019) found that patients with high DNI were associated with a higher incidence of bacteremia and sepsis, longer hospitalization time, and higher postoperative complications, so it was concluded that DNI was practically very useful as a marker in predicting the prognosis of patients who needed abdominal surgery interventions [27]. [24].

Research Hyuk et al (2018) found that DNI 1.4 was a reliable predictor of appendiceal perforation among elderly patients. Delta Neutrophil Index was significantly higher in the perforated appendicitis group than non-perforated, which could be explained

by the increased proportion of immature granulocytes in the circulation with disease progression due to bacterial infection of peri-appendiceal structures. In ROC curve analysis, DNI turned out to be a good predictor of appendiceal perforation (AUC 80.7%). Research Lim et al (2014) involving 75 patients found the median value of DNI at the time of diagnosis of peritonitis was 3.2% with a proportion of patients with SIRS of 82.7%.

In a meta-analysis J. W. Kim et al (2017) DNI was reported to have a prognostic impact on mortality in sepsis patients with an AUC value of 84%. Meta-analysis Ahn et al (2018) revealed the predictive accuracy of DNI for mortality in adult septic patients with an AUC of 82% with the best DNI threshold values in predicting mortality ranging from 1.3% to 7.6%. Research Bang et al (2020) found the AUC value of DNI was 88.7% cut-off point of 7.1% with a sensitivity of 85.7% and specificity of 84.4%.

The results showed that  $DNI \geq 8.9$  with the incidence of SIRS was more (63.6%) than not SIRS with an RR value of 3 and a p-value of 0.000, meaning that DNI increases the risk of SIRS in patients with generalized peritonitis so that DNI can be a predictor of SIRS in patients with generalized peritonitis. The results of this study are in line with the research Kim et al (2016) dan Uysal et al (2020) who mentioned that DNI has predictive value and prognostic value in several different infectious conditions such as acute appendicitis, bacterial peritonitis, and sepsis. Delta Neutrophil Index is considered a new predictor factor to distinguish infection from non-infection and predict the severity of sepsis. Delta Neutrophil Index was identified as a predictive factor of candida fungal infection in SIRS patients. Delta Neutrophil Index and clinical characteristics of patients are useful in determining the occurrence of candida fungal infection in SIRS patients [14].

Multivariate analysis showed that DNI was the dominant predictor of SIRS with an OR of 178.7 (95% CI: 10.69-2989.29). This result is higher than the results of multiple regression analysis in the study of Hyuk et al (2018) with OR 9.38 (IK95%: 2.51- 35.0). Research Lim et al (2014) involving 172 patients with gram-negative bacteremia found a DNI of 7.6% was a predictor of early death with an OR of 305.1 (95% CI: 1.73-53983.52;  $p = 0.030$ ).

In this study, it was also found that DNI increases the risk of sepsis in patients with generalized peritonitis but DNI cannot be a predictor of mortality in patients with generalized peritonitis. DNI values have been studied in several different conditions including acute appendicitis, bacterial peritonitis, and sepsis and the results show a significant increase in complicated acute appendicitis, is a useful prognostic factor for the determination of 30-day mortality in spontaneous bacterial peritonitis, and is a useful marker for early diagnosis and prognostic assessment of patients with sepsis [20].

Systematic review and meta-analysis Ahn et al (2018) showed that DNI has prognostic value in

adults with sepsis. High DNI values tend to be associated with mortality in sepsis patients. Since sepsis is a rapidly progressive and unpredictable disease regardless of the provision of appropriate treatment DNI may be a new prognostic biomarker. A study in Indonesia mentioned that under stress or infection, immature neutrophils are released into circulation. Delta Neutrophil Index may reflect the number of immature neutrophils in circulation [25]. Delta Neutrophil Index also has better diagnostic accuracy as a marker of sepsis severity. Delta Neutrophil Index may serve as a prognostic factor for sepsis [26].

Delta Neutrophil Index is a measure that reflects the number of immature neutrophils in peripheral blood. Polymorphonuclear neutrophils are the first-line effectors of defense against bacteria. After a maturation period of 7-10 days, they migrate into the peripheral blood. The presence of immature neutrophils in the peripheral blood of adult patients indicates increased myeloid cell production generally accompanied by infection or severe inflammatory diseases. The automatic analyzer measures differential leukocyte count by two methods: cytochemical myeloperoxidase (MPO) reaction and light reflection of nuclear lobularity in white blood cells (leukocytes) [33].

Delta Neutrophil Index correlates strongly with immature neutrophils and has shown an association with disseminated intravascular coagulation score, positive blood culture rate, and mortality in patients with suspected sepsis. Delta Neutrophil Index reflects the fraction of circulating immature neutrophils. This index is identified by the automated blood cell analyzer as the difference between the leukocyte subfraction (determined by cytochemical myeloperoxidase reaction) and the leukocyte subfraction (determined using nuclear lobularity testing by reflected light). Delta Neutrophil Index was significantly associated with the diagnosis of bacteremia and sepsis severity and prognosis [33].

Research by Jeong et al (2020) showed that DNI performance is useful for the prediction of severity, surgical outcome, or mortality in patients with gastrointestinal diseases, given its high sensitivity, specificity, and AUC. Another finding of this study is that the timing of DNI measurement at the time of admission in the emergency department can be useful as a triage tool for patients with emerging gastrointestinal diseases. The diagnostic validity of high DNI is sufficient regardless of the type of gastrointestinal tract disease [23].

Delta Neutrophil Index correlates strongly with immature granulocyte counts as an additional marker in infections and inflammatory reactions [16]. Delta Neutrophil Index in the study of Soh & Lim (2019) is also known as a prognostic marker value in patients who enter the emergency room with complaints of acute abdominal pain. Patients with a DNI level of more than 0.9% who require surgery due to acute peritonitis should be monitored

with adequate treatment strategies. Delta Neutrophil Index can be used to select high-risk patients and treatment selection such as emergency surgery or intensive care [24]. Delta Neutrophil Index has the advantage of being a good predictor of appendiceal perforation and can be obtained quickly, DNI is particularly helpful in differentiating early perforating appendicitis from non-perforating appendicitis in elderly patients [27].

### CONCLUSION

The results of the study and discussion can conclude that DNI is an excellent predictor in predicting the occurrence of SIRS in patients with generalized peritonitis. This study also found the cutoff point value of DNI which is 8.9%. Multivariate results found that DNI was the dominant factor causing SIRS compared to other factors such as age, gender, and BMI.

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### DECLARATIONS

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