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Correlation between Neutrophil-to-Lymphocyte Ratio with Disease Severity in Diabetic Patients with COVID-19 at Tertiary Referral Hospital in Indonesia

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Abstract: Coronavirus disease 2019 (COVID-19) is highly transmissible and spreads quickly with the clinical presentation varies from asymptomatic to severe respiratory symptoms, even leading to death. Diabetes mellitus is one of the main comorbidities contributing to worsening the COVID-19 cases. Increased Neutrophil-to-Lymphocyte Ratio (NLR) is considered as an early warning of COVID-19 severity. This study evaluated the correlation between NLR with disease severity at admission in diabetic patients with COVID-19 at a tertiary referral hospital in Indonesia. The authors performed a retrospective study using secondary data from medical records of diabetic inpatients with COVID-19 from May to September 2020. The demographic data were collected from the medical record and the hematologic parameter from the laboratory. NLR was calculated by dividing the absolute neutrophils counts by the absolute lymphocyte counts. The data was analyzed with a significance level of $p < 0.05$. Study subjects consisted of 100 non-severe cases and 128 severe cases. The median NLR of severe and non-severe groups was 9.7 vs. 5.22 ($p < 0.001$). The correlation coefficients of NLR with disease severity were 0.52 ($p < 0.001$). The calculated Area Under the Curve (AUC) of the ROC analysis for the NLR was 0.803 (cut-off: > 6.15; $p < 0.001$) with sensitivity 91%, specificity 64%, negative predictive value 16%, and positive predictive value 75.82%. NLR had a significant positive correlation with disease severity at admission in diabetic patients with COVID-19. As simple, rapid, and cost-effective biomarkers, NLR can help clinicians identify potentially severe cases early, conduct early triage, and initiate effective management in time so the progress of disease severity should be possibly prevented.

Keywords: COVID-19, diabetic patients, disease severity, neutrophil-to-lymphocyte ratio.

三级转诊医院糖尿病患者中性粒细胞与淋巴细胞比率 与中性粒细胞与淋巴细胞比率疾病轻重程度的相关性分析在印度尼西亚

提要: 2019 年冠状病毒病 (新冠肺炎) 具有高度传染性并迅速传播，临床表现从无症状到严重的呼吸道症状不等，甚至导致死亡。糖尿病是导致 新冠肺炎 病例恶化的主要合并症之一。中性粒细胞与淋巴细胞比率 的增加被认为是 新冠肺炎 严重性的早期预警。本研究旨在评估印度尼西亚三级转诊医院 新冠肺炎 糖尿病患者入院时 中性粒細胞轉淋巴細胞 与疾病严重程度之间的相关性。我们使用 2020 年 5 月至 9 月 新冠肺炎 糖尿病住院患者病历的二手数据进行了一项回顾性研究。人口统计学数据来自病历和实验室的血液学参数。中性粒細胞轉淋巴細胞 是通过将绝对中性粒细胞计数除以绝对淋巴细胞计数来计算的。以磷<0.05 的显着性

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水平分析数据. 研究对象由 100 名非重症病例和 128 名重症病例组成。重度和非重度组的中位 中性粒細胞與淋巴細胞的比率 分别为 9.7 和 5.22（磷<0.001)。中性粒細胞與淋巴細胞的比率 与疾病严重程度的相关系数为 0.52 (磷<0.001). 中性粒細胞與淋巴細胞的比率 的 接收器操作特性 分析的计算曲线下面积 为 0.803（临界值：>6.15；磷<0.001），灵敏度为 91%，特异性为 64%，阴性预测值为 16%，阳性预测值为 75.82%. 中性粒細胞轉淋巴細胞 与 新冠肺炎 糖尿病患者入院时的疾病严重程度呈显着正相关。中性粒細胞轉淋巴細胞 作为简单、快速且具有成本效益的生物标志物，可以帮助临床医生及早识别潜在的严重病例，进行早期分类，并及时启动有效管理，从而可能阻止疾病严重程度的进展。

关键词: 新冠肺炎，糖尿病患者，疾病严重程度，中性粒细胞与淋巴细胞的比率。

1. Introduction

The new coronavirus disease-19 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), emerged in late December 2019 in Wuhan, China, and World Health Organization, on January 30, 2020, called public health emergency [1]. It has spread worldwide rapidly and widely. Meanwhile, new cases in Indonesia are still increasing, with the total number of confirmed COVID-19 cases as of mid-September 2020 228,993 people with 9,100 deaths [2]. COVID-19 infection can be categorized as an asymptomatic, mild, moderate, severe, or critical disease [3, 4]. Clinically, supposed early warning of severe COVID-19 infection can be identified, so timely intervention and treatment may help reduce mortality, improve the cure rate, and shorten the hospital stay.

Diabetes mellitus (DM) is one of the most prevalent chronic conditions with devastating multi-systemic complications and was estimated to have inflicted 463 million people in 2019 [5]. Many reports show that diabetes is a frequent pre-existing condition associated with severe disease in COVID-19 patients, and it is an unholy situation wherein one disease entity compliments the other. How diabetes increases the severity of COVID-19 is unclear, though several factors may be responsible [6]. Diabetes is a chronic inflammatory condition, so a pro-inflammatory state could accentuate the cytokine storm, which is believed to be responsible for acute respiratory distress syndrome (ARDS) as well as multi-organ dysfunction in COVID-19. Poor glycemic control, event transient hyperglycemia may temporarily affect innate immune responses to infection. Immune defects named inappropriate T-cell action, impaired natural killer cell activity, and defects in complement action could reduce viral clearance.

Further, diabetes is associated with increased plasminogen levels, which have been postulated to increase the virulence of SARS CoV-2. Increased viral replication in diabetes may also be due to increased furin, a type-1-membrane-bound- protease involved in coronavirus entry into the cell. In addition, pre-existing comorbidities associated with diabetes like hypertension, coronary artery disease, chronic kidney disease, and obesity may further impair immunity and predispose to severe infection [7, 8, 9].

Neutrophil-to-Lymphocyte Ratio (NLR) is an easy-to-analyzed inflammation biomarker that is feasible in all hospital settings. Many studies denote elevated NLR as an excellent early warning factor to identify severe disease in COVID-19 [10-15]. However, a few studies analyzing the correlation between NLR with severity in special populations like diabetic patients. According to the background, this study aimed to analyze the correlation between NLR with disease severity at admission in diabetic patients with COVID-19.

2. Methods

2.1. Study Design, Participants, and Data Collection

This study was a retrospective, cross-sectional method, which was carried out by taking secondary data from May to September 2020 with patients who have diagnosed diabetes with COVID-19 in the medical records of Dr. Soetomo Hospital Surabaya, a major tertiary referral hospital in Indonesia and has been mainly responsible for the treatments of COVID-19 patients assigned by the government.

Diabetic patients were admitted to the wards with COVID-19 infection confirmed by real-time reverse transcription-polymerase chain reaction (RT-PCR). Inclusion criteria were as follows: (1) diabetic with COVID-19, (2) results of blood routine examination were obtained within 24 hours of admission. Patients were excluded using the following criteria: (1) patients with known hematological illnesses, with known HIV-positive status, those on chemotherapeutic drugs, long-term glucocorticoids, and pregnant women because these conditions affect the NLR, (2) patients with missing data.

The severity of the disease was classified into non-severe cases (mild and moderate symptoms) and severe cases (severe symptoms and critical illness) based on the severity of symptoms according to interim guidance of the World Health Organization. Severe cases were defined when one of the following criteria was present: (1) respiratory distress (respiratory rate over 30 breaths per minute), (2) oxygen saturation ≤ 93% on room air, and (3) arterial blood oxygen partial pressure (PaO2)/oxygen concentration (FiO2) ≤ 300 mmHg (l mmHg = 0.133 kPa).

Information on demographic data, symptoms, pre-existing comorbidities, and laboratory results were collected. The routine laboratory tests complete blood count (CBC), liver function tests (LFTs), renal function test (RFTs), serum electrolytes, C-reactive protein (CRP), Albumin serum, and blood glucose level. CBC was analyzed using the hospital laboratory system, Sysmex XS-800i. The NLR was calculated using the simple formula absolute number of neutrophils divided by an absolute number of lymphocytes. The time from the onset of illness to the hospital admission was also recorded. The assessment of disease severity and laboratory tests was performed on the day of the patient admission before treatment.

2.2. Statistical Analysis

The authors describe the categorical variables as number (n) and percentages (%), and continuous variables as mean standard deviation (SD) if they are typically distributed or median with interquartile ranges (IQR) if they are not. The Kolmogorov-Smirnov test was used to verify the normality of the distribution. Independent-group t-test was used to compare parametric continuous variables or Mann-Whitney U test for non-parametric continuous variables. The proportion for categorical variables was compared using the Chi-square test or Fisher's exact test. Correlation between variables was assessed using Spearman's correlation analysis.

Receiver operating characteristics (ROC) were used to study the accuracy of the various predictive test. All statistical analyses were performed using SPSS version 25.0 software. Two-sided P values of less than 0.05 were considered statistically significant.

2.3. Ethical Approval

Health Research Ethics Committee of Dr. Soetomo Hospital (Surabaya, Indonesia) approved this study protocol.

3. Results

Two hundred twenty-eight diabetic patients who were confirmed positive for COVID-19 were included in this study. 100 (43.86%) were non-severe cases, and 128 (56.14%) were severe cases. The demographic and clinical characteristics of all patients were shown in Table 1.

There were many significant differences in the parameters of baseline characteristics between the severe group and the non-severe group. Patients with the severe group had older age ≥60 years (36.7% vs. 23%, P = 0.037), more likely to had underlying comorbidities hypertension (43% vs. 29, P = 0.03) and chronic kidney disease (2.2% vs. 0%, P = 0.046), had symptoms dyspnea (74.2% vs. 52%, P = 0.001) and sore throat (16.4% vs. 5%, P = 0.007) compared to patients with the non-severe group. While in the non-severe group had symptoms anosmia (7% vs. 1.6%, P = 0.037), fatigue (30% vs. 18%, P = 0.033), and myalgia (8% vs. 1.6%, P = 0.018) compared to patients with severe group. There were no significant differences in sex, hospital admission, the onset of diabetes, use of diabetes medication, cardiovascular disease, cerebrovascular disease, the onset of symptoms to hospital admission, and symptoms such as dry cough, fever, anorexia, diarrhea, and runny nose.

Table 2 present the laboratory findings in the non-severe and severe group on the day of hospital admission in diabetic patients with COVID-19. There were many significant differences in the parameters of laboratory findings between non-severe and severe groups. Severe cases had higher white blood cell (9.93 vs 7.93, P = *0*.001); higher neutrophil count (8.26 vs 5.61, P < 0.001); higher neutrophil-to-lymphocyte ratio (NLR) (9.7 vs 5.22, P < 0.001); higher platelet-to-lymphocyte ratio (PLR) (304.1 vs 197.78, P < 0.001), higher-level aspartate aminotransferase (AST) (59 vs 46, P = 0.002), and higher-level C-reactive protein (CRP) (11.6 vs 7.4, P = 0.013), lower lymphocyte count (0.835 vs 1.29, P < 0.001) and lower albumin (3.1 vs 3.25, P = 0.018) compared to patients with the non-severe group. There were no significant differences in hemoglobin level, platelet count, plasma glucose level, sodium level, potassium level, creatinine level, blood urea nitrogen level, alanine aminotransferase level, activated partial thromboplastin time, and prothrombin time.

Table 3 presents the results of Spearman correlation analysis between NLR with the severity of COVID-19. NLR in diabetic patients with COVID-19 has a significant positive correlation with disease severity (P < 0.001) with a moderate correlation strength (R = 0.52). The ROC curve in Figure 1 showed that The Area under Curve (AUC) for NLR was 0.803 [95% CI (0.74-0.865), P < 0.001]. NLR's cut-off-value as the optimal threshold for predicting the disease severity in diabetic patients with COVID-19 at admission is > 6.15 with the sensitivity of 90.6%, specificity of 64%, the positive predictive value 75.82%, and negative predictive value 16%. In addition, the positive likelihood ratio was 0.906/1 - 0.64 = 2.52, and the negative likelihood ratio was 1 - 0.906/0.64 = 0.15.

Table 1 Characteristics of research subjects

Variable	Total = 228 No(%)	Non-severe (n = 100)	Severe (n = 128)	P-value
Age, Median (IQR), y	**55 (50-61)**	**53.5 (48-58.5)**	**56 (52-61)**	**0.019[a*]**
<60 years	158 (69.3%)	77 (77%)	81 (63.3%)	0.037[b*]
≥60 years	70 (30.7%)	23 (23%)	47 (36.7%)	
Sex				
Female	112(49.1%)	45 (45%)	67 (52.3%)	0.273 [b]
Male	116 (50.9%)	55 (55%)	61 (47.7%)	
Hospital admission				
Referred	68 (29.8%)	25 (25%)	43 (33.6%)	0.161 [b]
Directly	160 (70.2%)	75 (75%)	85 (66.4%)	
Onset of T2DM				
New Onset	45 (19.7%)	19 (19%)	26 (20.3%)	0.262[c]
<5 Years	127 (55.7%)	52 (52%)	75 (58.6%)	
5-10 Years	35 (15.4%)	17 (17%)	18 (14.1%)	
>10 Years	21 (9.2%)	12 (12%)	9 (7%)	
Use of diabetes medication				
None	46 (20.2%)	19 (19%)	27 (21.1%)	0.15 [c]
Routine	113 (49.6%)	56 (56%)	57 (44.5%)	
Not Routine	69 (30.3%)	25 (25%)	44 (34.4%)	
Comorbidities	**97 (42.54%)**	**32 (32.99%)**	**65 (67.01%)**	**0.009 [b*]**
Hypertension	84 (36.8%)	29 929%)	55 (43%)	0.03 [b*]
Cardiovascular Disease	11 (4.8%)	6 (6%)	5 (3.9%)	0.466 [b]
Chronic Kidney Disease	9 (3.9%)	0 (0%)	5 (2.2%)	0.046 [b*]
Cerebrovascular Disease	5 (2.2%)	3 (3%)	6 (4.7%)	0.518 [b]
Sign and symptoms				
Dry Cough	170 (74.6%)	71 (71%)	99 (77.3%)	0.277 [b]
Fever	153 (67.1%)	68 (68%)	85 (66.4%)	0.8 [b]
Dyspnea	147 (64.5%)	52 (52%)	95 (74.2%)	0.001 [b*]
Anorexia	88 (38.6%)	43 (43%)	45 (35.2%)	0.229 [b]
Anosmia	9 (3.9%)	7 (7%)	2 (1.6%)	0.037 [b*]
Fatigue	53 (23.2%)	30 (30%)	23 (18%)	0.033 [b*]
Sore throat	26 (11.4%)	5 (5%)	21 (16.4%)	0.007 [b*]
Diarrhea	24 (10.5%)	11 (11%)	13 (10.2%)	0.838 [b]
Runny nose	16 (7%)	6 (6%)	10 (7.8%)	0.599 [b]
Myalgia	10 (14.4%)	8 (8%)	2 (1.6%)	0.018 [b*]
Illness onset to hospital admission, Median (IQR), days	4 (3-7)	4 (3-7)	4.5 (3-7)	0.536 [a]

Note: P-values comparing severe and non-severe cases are divided from [a] Mann-Whitney U test, [b] Chi-square test, and [c] Fisher's exact test. P < 0.05 was considered statistically significant and marked by [*]

Abbreviations: IQR - interquartile range

Table 2 Laboratory findings at admission in diabetic patients with COVID-19

	Median (IQR) Total (N = 228)	Non-severe (n = 100)	Severe (n = 128)	P value
Hemoglobin (g/L, normal range 11-15)	13.45 (12-14.6%)	13.7 (12-15.1)	13.35 (12-14.4)	0.091[a]
White blood cell count (x109/L, normal range 3.5-9.5)	8.96 (6.96-12.47)	7.93 (6.43-10.76)	9.94 (7.6-14.12)	0.001[b*]
Neutrophil count (x109/L, normal range 1.8-6.3)	7.4 (5.27-11.33)	5.61 (4.45-8.92)	8.26 (6.37-12.83)	0.000[b*]
Lymphocyte count (x109/L, normal range 1.1-3.2)	0.97 (0.75-13.47)	1.29 (0.91-1.61)	0.84 (0.64-10.88)	0.000[b*]
Platelet count (x109/L, normal range 125-350)	256.5 (206-337)	260.5 (193.75-349.75)	248.5 (208.5-328.25)	0.747[b]
The neutrophil-to-Lymphocyte ratio (NLR)	8.12 (5.48-12.35)	5.22 (2.99-8.2)	9.7 (7.4-14.34)	0.000[b*]
Platelet-to-Lymphocyte ratio (PLR)	265.97 (180.45-367.22)	197.78 (144.83-304.17)	304.1 (234.64-404.75)	0.000[b*]
Plasma glucose, mmol/L (normal range 140-180)	239 (160.5-312.25)	236 (166.75-288.75)	240.5 (14.25-336.25)	0.755[b]
Serum sodium, mmol/L (normal range 135-145)	135 (130.25-139)	134 (130-138)	135.5 (131-140)	0.128[b]
Serum potassium, mmol/L (normal range 3.5-5.5)	4.1 (3.5-4.7)	4.1 (3.5-4.6)	4.1 (3.5-4.7)	0.31[a]
Creatinine, mmol/L (normal range 0.4-1.2)	1.1 (0.8-1.6)	1 (0.8-1.48)	1.2 (0.8-1.88)	0.098[b]
BUN, mmol/L (normal range 25-67)	19 (12-30)	17 (11-26.75)	19 (13-31)	0.113[b]
Albumin, g/dL (normal range 3.4-5.4)	3.13 (2.9-3.35)	3.25 (2.9-3.5)	3.1 (2.9-3.3)	0.018[b*]
AST U/L (normal range 8-40)	52 (37-83)	46 (30-71.25)	59 (42-88.75)	0.002[b*]
ALT U/L (normal range 5-35)	46 (33-71.75)	44.5 (31-70)	46.5 (34-74.25)	0.347[b]
APTT, s (normal range 20-40)	26.35 (25.53-29.85)	26.35 (23.63-29.75)	26.35 (24.9-30.8)	0.15[b]
PT, s (normal range 9-14)	11.2 (10.2-13.5)	11 (10.13-13.15)	11.7 (10.33-13.6)	0.153[b]
CRP (normal range 0-8)	10.65 (4.76-16.6)	7.4 (3.83-14.4)	11.6 (6.22-17.73)	0.013[b*]

Note: P-values comparing severe and non-severe cases are divided from, at the test and [b] Mann-Whitney U-test. P<0.05 was considered statistically significant and marked by *

Abbreviations: IQR - interquartile range, BUN - blood urea nitrogen, AST - aspartate aminotransferase, ALT - alanine aminotransferase, APTT - activated partial thromboplastin, PT - prothrombin time, CRP - C-reactive protein, and COVID-19 - Coronavirus disease 2019.

Table 3 Correlation NLR with severity COVID-19 in diabetic patients

	R-value	P-value
NLR	0.52	0.000

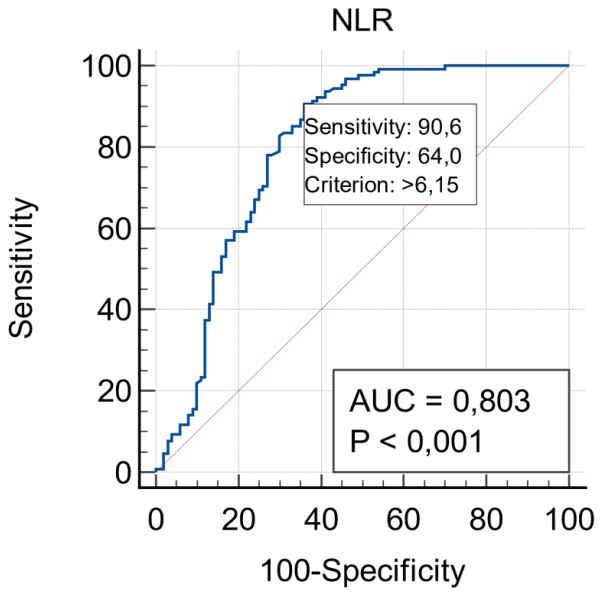

Fig. 1 The ROC curves of NLR in the predicting of severe COVID-19 in diabetic patients at admission

4. Discussion

This study was conducted at a tertiary referral hospital, where the patients who came were referred patients but in this study, more patients came directly than referred. This study showed significant differences between non-severe and severe median age (53.5 vs. 56 years; P=0.019). These conclusions are quite consistent with the previous studies [16]. Advanced chronological age is one of the main risk factors for the adverse outcomes of COVID-19, presumably due to immunological changes (immunoscence and inflammation) and other organ dysfunction [17, 18].

This study also found that the severe case of the diabetic patients with COVID-19 who had combined hypertension and chronic kidney disease were significantly higher than the non-severe cases group. This finding is supported by the results of a previous study [19-20]. The specific pathogenesis of hypertension that may lead to more severe COVID-19 remains to be studied. The imbalance of cytokines may be considered an explanation for the correlation between hypertension and severe COVID-19. Increasing clinical data have shown a relationship between the deterioration of COVID-19 and cytokine storms, such as elevated levels of interleukin-6, interleukin-7, granulocyte-macrophage-colony-stimulating-factor, and tumor necrosis factor-α [21]. Several lines of evidence suggested that CKD patients, especially those at advanced stages, are vulnerable to SARS-CoV-2 infection.

Moreover, a higher baseline serum creatinine level was an independent risk factor for in-hospital death in COVID-19 [22]. The basis for such vulnerability is likely multifactorial, and both environmental factors and medical factors such as old age, immune cell dysfunction, cardiovascular and pulmonary comorbidities need to be considered [23]. In conclusion, elderly or older people and a higher frequency of comorbidities in diabetic COVID-19 patients are more susceptible to severe or critical conditions.

Symptoms of COVID-19 may appear anytime from 2 to 14 days after exposure. Therefore, 14-day quarantine is recommended [24, 25]. This study showed no difference in onset of symptoms to hospital admission in patients with the severe and non-severe groups. The severe cases mostly had a cough, dyspnea, fever, and anorexia but significantly higher in dyspnea and sore throat than non-severe cases. The non-severe cases had significantly higher anosmia, fatigue, and myalgia than severe cases. This study was in line with a study in China that the most common symptoms observed from the onset include fever, cough, and fatigue [26]. A meta-analysis from 55 studies explained that clinical manifestations such as fever, cough, fatigue, anorexia, dyspnea, chest tightness, hemoptysis, diarrhea, and abdominal pain were significantly associated with the severity of cases. However, it was not for myalgia, pharyngalgia, nausea, vomiting, headache, dizziness, and sore throat [27]. Therefore, sore throat and dyspnea can be used as an early warning towards critical illness in diabetic patients with COVID-19.

This study found that plasma glucose at admission between non-severe and severe cases was not significantly different, but the median of plasma glucose was>200 mg/dL. It was explained based on SARS-CoV-2 mediated damage of the pancreatic β-cell as ACE-2 is also expressed on the pancreatic islets. It could partly explain the worsening glucose control in diabetic patients with some functional β-cell in reserve [28]. Infection also causes a stress response in the body by increasing certain hormones such as cortisol and adrenaline. These hormones work against the action of insulin and, as a result, the body's production of glucose increases, which results in high blood sugar levels [29].

Higher neutrophil and lower lymphocyte count in this study showed a significant difference in severe than non-severe cases. Neutrophil and lymphocyte are two key indexes affected by SARS CoV-2 infection and demonstrated significant differences in the severe and non-severe COVID-19 infection [11, 30, 31]. Neutrophils are one of the human body's vital immune cells. When pathogenic microorganisms invade the body, immune cells tend to rapidly chemotactically gather to the infection site and play the role of host defense and immune regulation. Lymphocytes are the primary effector cells of the human immune response. The number of lymphocytes in the body is closely related to the body's immunity and defense system

against pathogenic microorganisms and is negatively correlated with inflammation.

NLR reflects the balance of the body's neutrophil, lymphocyte count levels, and the degree of systemic inflammation. Therefore, a high NLR is an important marker that indicates an imbalance in the inflammatory response and marker of disease severity [4, 32]. It is in line with this study that higher NLR was found a significant difference in the severe cases than in the non-severe group (9.7 vs. 5.22, $P < 0.001$). The present study also indicated a significant positive correlation between NLR with disease severity of COVID-19 in diabetic patients ($R = 0.52$, $P < 0.001$).

The authors performed the ROC analysis to predict the disease severity in hospitalized diabetic patients with COVID-19 and determined the cut-off levels on-time admission. The cut-off value of NLR obtained in this study was > 6.15 to predict severe cases. The ROC analysis performed according to the NLR cut-off values were calculated as AUC 0.803 (95% CI: 0.74-0.865, $P < 0.001$) with sensitivity 90.6%, specificity 64%, positive predictive value 75.82%, and negative predictive value of 16%. In addition, it was shown that the positive likelihood ratio = 2.52 (fair) and the negative likelihood ratio = 0.15 (excellent), indicating that the cut-off for NLR of 6.15 will provide sufficient probability in predicting the severity of diabetic COVID-19 patients. This value is higher than many studies about NLR and disease severity of COVID-19 (NLR values ranging from 3.3 to 5.9 to predict the severity) because, in diabetic conditions, NLR levels were also increased due to chronic low-grade inflammation [10]. However, no NLR consensus cut-off values have been established to determine normal and elevated NLR values, especially for COVID-19 [13-14, 32-34].

This study also had other abnormal indicators that had significant differences between the severe and non-severe cases, such as higher white blood count, PLR, and albumin serum AST and CRP. These abnormalities suggested that SARS CoV-2 infection might be associated with myocardial injury, hepatic injury, and other related organ damage [35].

5. Conclusion

This single-center observational study revealed that some findings in this study might be consistent in severe cases with previous studies, including higher age (≥ 60 years), history of hypertension and chronic kidney disease, presence of symptoms of dyspnea and sore throat, decreasing lymphocyte and albumin, and increasing white blood count, neutrophil count, CRP level, and alanine aminotransferase level. Early identification of risk factors for severe patients is vital to afford appropriate supportive care or access to the intensive care unit (ICU) if necessary. At admission, neutrophil to Lymphocyte Ratio (NLR) had a significant positive correlation with disease severity in diabetic patients with COVID-19. NLR has known as a simple, rapid, and cost-effective biomarker. Evaluating NLR can help clinicians predict severe cases early, conduct early triage, and initiate effective management in time, reducing the overall mortality of diabetic patients with COVID-19.

However, this study had certain limitations, such as having a small sample size, use secondary data from the medical record, and being a single-center study. For more accurate and precise results, wider generalizability of the findings, and larger sample size, clinical studies are required to confirm the findings further.

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