

ABSTRAK

Latar belakang: Saat ini, angka kejadian COVID-19 masih tinggi dan angka kematiannya cenderung meningkat. Di Indonesia sendiri, total terdapat lebih dari 6 juta kasus dan 160 ribu kematian akibat COVID-19. Penanganan yang terlambat akan semakin meningkatkan keparahan dari penyakit ini, yang bahkan bisa berujung kematian. Hal ini dapat disebabkan oleh semakin meluasnya proses inflamasi akibat virus SARS-CoV-2 yang menimbulkan berbagai kerusakan pada jaringan dalam organ serta menekan sistem pertahanan tubuh. Pada awal seseorang terpapar virus atau agen inflamasi lainnya, jumlah neutrofil akan meningkat untuk melawan virus tersebut dan memicu inflamasi. Inflamasi tersebut berpengaruh pada penurunan kadar limfosit. Oleh karena itu, semakin parah inflamasi yang terjadi, semakin tinggi kadar *neutrophil-to-lymphocyte ratio* (NLR) dan secara tidak langsung, hal tersebut dapat meningkatkan risiko mortalitas. Terdapat beberapa studi terkait NLR dan mortalitas pada pasien COVID-19. Akan tetapi, ukuran sampelnya masih terbatas sehingga *generalizability*-nya masih perlu dikembangkan lebih lanjut. Selain itu, kebaruannya masih dapat dikembangkan mengingat terdapat beberapa varian COVID-19 yang muncul beberapa bulan terakhir, seperti varian Omicron yang baru memuncak pada Desember 2021 kemarin.

Tujuan: Mengetahui asosiasi antara *neutrophil-to-lymphocyte ratio* dan mortalitas pasien rawat inap COVID-19 di Rumah Sakit Umum Pusat Dr. Sardjito, Yogyakarta.

Metode: Studi kohort retrospektif yang datannya diambil melalui rekam medis pasien terkonfirmasi positif COVID-19. Pasien menjalani rawat inap pada periode Maret 2020—Desember 2022 dan berusia ≥ 18 tahun. Demografis pasien akan diuji menggunakan analisis univariat, asosiasi NLR dengan mortalitas akan dianalisis secara bivariat, sedangkan penentuan NLR sebagai prediktor mortalitas utama akan diuji dengan analisis multivariat.

Luaran: Terdapat asosiasi signifikan antara NLR dan mortalitas pada pasien COVID-19 baik secara kategorik maupun numerik. Secara numerik, median NLR pasien meninggal adalah 6,99, lebih tinggi daripada pasien hidup (NLR 4,41, $p < 0,001$). NLR tinggi ($\geq 5,65$) juga menjadi faktor independen terhadap mortalitas, dengan aOR 2,24, HR 1,02, dan *median survival* 13 hari. Faktor independen lain yang juga berperan, yakni jenis kelamin (pria) (aOR 2,31, $p = 0,002$), gangguan ginjal kronis (aOR 2,61, $p = 0,026$) dan tingkat derajat keparahan. Terdapat *scoring system* berdasarkan faktor-faktor tersebut.

Kesimpulan: Terdapat hubungan bermakna antara nilai NLR dan mortalitas pasien COVID-19 RSUP Dr. Sardjito. *Cut-off* NLR dan *scoring system* diharapkan dapat menjadi parameter klinisi dalam menentukan tatalaksana bagi pasien.

Kata kunci: *neutrophil-to-lymphocyte ratio*, COVID-19, mortalitas, inflamasi, progresi

ABSTRACT

Background: The COVID-19 incidence remains high, and the mortality rate increases. Indonesia has so far recorded over six million cases of COVID-19 in total, with a mortality rate of 160 thousand people. Immediate treatment is necessary to hinder the progression of severity and reduce mortality. SARS-CoV-2 virus induces an inflammatory process that may cause massive internal organ damage, as well as impairing immune defense mechanisms within the body. The neutrophil amount in blood increases on being exposed to a virus or any inflammatory agents. Consequently, the lymphocyte levels get reduced through this inflammation process. This means that high neutrophil-to-lymphocyte ratio (NLR) indicates a more severe form of inflammation, which might increase likelihoods for mortality due to the virus. Nevertheless, earlier studies have investigated mortality rates from NLR in COVID-19 patients; however, the small sample sizes necessitate generalizability tests. Moreover, new variants, such as Omicron, also highlight further need for investigation.

Objective: This study aims to determine the association between neutrophil-to-lymphocyte ratio and mortality amidst inpatients diagnosed with COVID-19 at Dr. Sardjito General Hospital in Yogyakarta, Indonesia.

Method: A retrospective cohort study using medical records of COVID-19-positive patients hospitalized between March 2020 and December 2022, aged 18 year and above, was conducted. Univariate analysis was used to analyze patient demographics. Analysis of NLR's association with mortality was done using bivariate analysis. Multivariable analysis was used to evaluate whether NLR is a major determinant of mortality.

Result: There are considerable evidence showing strong and significant association between NLR and COVID-19-related mortality in both numeric and categorical terms. The median NLR among deceased patients is 6.99, which was significantly higher than that of survivors (NLR 4.41, $p < 0.001$). This indicates an adjusted odds ratio (aOR) of 2.24, a hazard ratio (HR) of 1.02, and a medium survival time of 13 days for an NLR value of ≥ 5.65 . Apart from NLR, the independent risk factors for mortality in this analysis, are male gender (aOR 2.31; $p = 0.002$), chronic kidney disease (aOR 2.61; $p = 0.026$), and severity level. All those factors can be used in developing the scoring system of mortality rate.

Conclusion: This study shows there is a significant association between the values of neutrophil-to-lymphocyte ratio (NLR) and mortality among COVID-19 cases in Dr. Sardjito General Hospital. The NLR cut-off and the scoring system hopefully can be a parameter for clinicians in deciding the patients' treatment.

Keywords: neutrophil-to-lymphocyte ratio (NLR), COVID-19, mortality, inflammation, progression