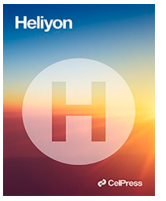
Heliyon 10 (2024) e39980

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

High inflammatory indices are significant predictors of disease severity in maintenance hemodialysis patients with COVID-19: A cross-sectional study

Sujuan Feng [b], Han Li [a,*], Shixiang Wang [a]

[a] Institute of Uro-Nephrology, Beijing Chao-Yang Hospital, Capital Medical University, Beijing, 100020, China
[b] Department of Urology, Beijing Chao-Yang Hospital, Capital Medical University, Beijing, 100020, China

ARTICLE INFO

Keywords:
Maintenance hemodialysis
Platelet/lymphocyte ratio
Neutrophil/lymphocyte ratio
COVID-19
Inflammation

ABSTRACT

Background: The patients with kidney failure who undergo maintenance hemodialysis (MHD) at high risk of morbidity and mortality from COVID-19. Previous studies showed that inflammation plays an important role in the progression of COVID-19. This study aimed to evaluate the prognostic value of the inflammatory indices in MHD patients with COVID-19.
Methods: We included 141 patients receive MHD in this single-center. SARS-CoV-2 infection was confirmed by a positive result in RT-PCR analysis of nasal and pharyngeal swab samples, and the demographic, clinical, and laboratory data from December 1, 2022, to January 31, 2023 were reviewed. Inflammatory indices including PLR, NLR and SII were calculated. Binary logistics regression was used to examine the association between inflammatory indices and SARS-CoV-2 infection in MHD patients. The ROC curves were used to detect the sensitivity and specificity of these inflammatory indices in prediction of SARS-CoV-2 infection status in MHD patients.
Results: SARS-CoV-2 infection was detected in 76.43 % of the 141 MHD patients. Lymphocyte (LY), aspartate transaminase (AST), blood urea nitrogen (BUN), uric acid (UA), PLR, NLR and SII were significant predictors of no SARS-CoV-2 infection and symptomatic SARS-CoV-2 infection. In addition, LY, serum ferritin (SF), AST, BUN, UA, PLR and NLR were significant predictors of asymptomatic SARS-CoV-2 infection and symptomatic SARS-CoV-2 infection. The ROC curves showed the best sensitivity and specificity of PLR (66.7 % sensitivity; 68.8 % specificity) and NLR (51.9 % sensitivity; 86.3 % specificity) in predicting symptomatic SARS-CoV-2 infection.
Conclusion: PLR and NLR can be used as simple and inexpensive biomarkers in predicting the prognosis of COVID-19 in MHD patients.

1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and has profound adverse effects on the patients with kidney failure who receive maintenance hemodialysis (MHD). Studies from different country have confirmed patients requiring hemodialysis are at an increased risk of SARS-CoV-2 infection and poor outcomes when compared with general population, due to the impaired immunity and multiple uremia-induced complications including cardiovascular disease, diabetes, and cerebrovascular disease [1–3].

* Corresponding author.
E-mail address: hanli@ccmu.edu.cn (H. Li).

https://doi.org/10.1016/j.heliyon.2024.e39980
Received 3 March 2024; Received in revised form 30 July 2024; Accepted 29 October 2024
Available online 8 November 2024

Inflammation plays a crucial role in the pathophysiological process of chronic kidney disease (CKD), especially end stage renal disease (ESRD). Multiple factors, such as reduced clearance of inflammatory mediators, oxidative stress, frequent infections, intestinal dysbiosis, metabolic acidosis, and technical factors relating to dialysis, contribute to chronic inflammation state in MHD patients [4–6], and further increased susceptibility to SARS-CoV-2 infection [7].

In recent years, plenty of evidence showed that the ratios of different blood cell components, including platelet/lymphocyte ratio (PLR), neutrophil/lymphocyte ratio (NLR) and platelet × neutrophil/lymphocyte ratio (SII), can effectively reflect the inflammatory state of MHD patients and have good predictive value in the outcome of ESRD [8]. Yaprak M et al. suggested that although both NLR and PLR were associated with all-cause mortality in hemodialysis patients, only PLR could independently predict all-cause mortality in these populations [9]. Another study demonstrated that SII was an independent risk factor for all-cause, cardiovascular, and cancer mortality among CKD patients [10].

In the COVID-19, changes in PLR, NLR and SII were also observed. Recent studies found a significant increase of PLR in patients with positive SARS-CoV-2 compared to healthy individuals [11]. Furthermore, NLR was a prognostic factor for endotracheal intubation upon hospital admission and independent predictor for risk of mortality in COVID-19 patients [12]. One study suggested that the SII was a potential new diagnosed biomarker in severe-patients with COVID-19 [13]. Accordingly, this study aims to verify the relationship between these inflammatory indices and the prognosis among MHD patients with SARS-CoV-2 infection.

2. Materials and methods

2.1. Study design and participants

The study was a single-center retrospective study performed on SARS-CoV-2 infected patients with MHD, which was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Beijing Chao-Yang Hospital, Capital Medical University, and the approval number of the ethics committee is 2021-KE-166. Written informed consents were obtained from all participants.

A total of 141 ESRD patients undergoing MHD who were admitted to the Department of Blood Purification, Beijing Chao-Yang Hospital, Capital Medical University were recruited from December 1, 2022, to January 31, 2023. The dialysis treatment was performed as previously described [30]. All patients underwent hemodialysis three times a week for 4 h per session. Sugar-free bicarbonate dialysates and heparin anticoagulants were applied during hemodialysis. Dialysate flow was 500 mL/min, and blood flow was 200–350 mL/min. Dialysate ingredients were 138–140 mmol/L sodium, 2.0–2.5 mmol/L potassium, 1.25–1.5 mmol/L calcium, and 0.5 mmol/L magnesium.

The inclusion criteria were as follows: (1) aged >18 years, (2) hemodialysis duration of > 3 months, (3) in a stable condition, and (4) SARS-CoV-2 confirmed by a positive result in real-time reverse transcriptase-polymerase chain reaction (RT-PCR) analysis of nasal and pharyngeal swab samples, and all patients with symptoms had complete medical records. Exclusion criteria were as follows: (1) acute renal failure, (2) infectious diseases within 1 month, (3) severe cardiovascular or cerebrovascular diseases within 1 month, (4) active liver diseases or cancer, (5) active systemic autoimmune diseases, (6) primary immune deficiencies, (7) idiopathic pulmonary fibrosis, (8) chronic obstructive pulmonary disease, (9) smoking habit. None of these ESRD patients had been vaccinated against COVID-19. All patients were divided into three groups according to their RT-PCR results and medical records: (1) No SARS-CoV-2 infection, (2) asymptomatic SARS-CoV-2 infection, and (3) symptomatic SARS-CoV-2 infection. Patients in No SARS-CoV-2 infection group were those MHD patients with neither SARS-CoV-2 infection nor COVID-19 symptoms. Patients with asymptomatic SARS-COV-2 infection were defined as those who have only positive RT-PCR results but no clinical symptoms. Patients with symptomatic SARS-CoV-2 infection should meet all the following criteria: fever and clinical signs of acute respiratory infection, such as cough, headache, muscle or body aches, sore throat, diarrhea etc, but no hospitalization and not to be admitted to intensive care unit (ICU).

2.2. Data collection

The demographic data of MHD patients including age, gender, body mass index (BMI), dialysis duration, history of hypertension, diabetic mellitus, kidney transplantation, and use of immunosuppressive drugs was obtained from medical records. Fasting blood samples were collected before hemodialysis during the mid-week session, and the laboratory parameters were detected using an automatic hemocyte analyzer (SYSMEX XN-10, Japan) and automatic biochemical analyzer (Simens Advia 2400, USA).

The following systemic inflammatory indices were calculated: PLR (platelet/lymphocyte ratio), NLR (neutrophil/lymphocyte ratio), and SII (platelet × neutrophil/lymphocyte).

2.3. Statistical analysis

SPSS 27.0 (Version 27.0, IBM Corp, Armonk, NY, USA) was used to analyze the data. Shapiro test was used to assess the normality hypothesis, and normally distributed Numeric variables were reported as mean ± standard deviation. T-test or One-way analyses was used to compare these variables between each groups. Non-normally distributed data are expressed as median (interquartile range), and the Mann–Whitney *U* test was used to analyzed these variables between groups. Categorical variables are expressed as frequencies (%), and ratios were compared between groups using a chi-square test. The risk factors for SARS-CoV-2 infection in MHD patients were further identified by a binary logistics regression with a forward stepwise method. A p-value <0.05 was considered statistically significant. The area under the receiver operating characteristic curve (AUC-ROC) was used to detect the sensitivity and specificity of

these inflammatory indices in prediction of MHD patients SARS-CoV-2 infection. The cut off value was calculated based on the maximum Youden index (sensitivity + specificity-1).

3. Results

3.1. Demographic and biochemical parameters of MHD patients with and without SARS-CoV-2 infection

A total of 141 MHD patients were enrolled, including 73 males (51.77 %) and 68 females (48.23 %). The mean age of these patients was 57.52 ± 11.498. The median duration of dialysis was 95.00 (38.50–146.50) months. 107 (76.43 %) patients were detected to SARS-CoV-2 infection. As shown in Table 1, the lymphocyte (LY), serum ferritin (SF), aspartate transaminase (AST), blood urea nitrogen (BUN), uric acid (UA), PLR, NLR and SII levels were significantly changed, and no significant differences were observed between the other parameters.

To confirm the differences of these parameters in three groups, we further pairwise compared each indicator. Table 2 showed that lymphocytes, BUN and UA levels in MHD patients with no SARS-CoV-2 infection and asymptomatic SARS-CoV-2 infection were higher than those of MHD patients in symptomatic SARS-CoV-2 infection group. PLR, NLR and SII levels were significantly higher in the symptomatic SARS-CoV-2 infection than that in the no SARS-CoV-2 infection and asymptomatic SARS-CoV-2 infection groups. AST and ferritin levels only increased in symptomatic SARS-CoV-2 infection group than that in the asymptomatic SARS-CoV-2 infection group.

Table 1
Demographic and biochemical parameters of MHD patients.

Item	Total	No COVID-19 infection	asymptomatic COVID-19 infection	symptomatic COVID-19 infection	F/Z/χ^2	p value
Male, n (%)	73 (51.77 %)	19 (55.88 %)	38 (47.50 %)	16 (59.26 %)	1.421	0.491
Age (years)	57.52 ± 11.498	54.26 ± 12.580	58.36 ± 10.956	59.15 ± 11.289	1.871	0.158
Dialysis Duration (months)	95.00(38.50–146.50)	124.500 (38.750–175.250)	92.500(40.250–142.000)	104.000 (30.000–140.000)	1.537	0.464
Kidney transplantation (%)	26 (18.44 %)	7 (20.59 %)	12 (15.00 %)	7 (25.93 %)	1.740	0.419
Diabetic Mellitus (%)	32 (22.70 %)	5 (14.71 %)	21 (26.25 %)	6 (22.22 %)	1.817	0.403
Hypertension (%)	138(97.87 %)	32 (94.12 %)	79 (98.75 %)	27 (100 %)	3.185	0.203
WBC ($\times 10^9$/L)	6.336 ± 1.794	6.054 ± 1.668	6.536 ± 1.817	6.098 ± 1.864	1.159	0.317
NEUT ($\times 10^9$/L)	4.260(3.430–5.425)	4.035(3.043–4.755)	4.370(3.470–5.375)	4.650(3.480–5.910)	3.355	0.187
LY ($\times 10^9$/L)	1.030(0.780–1.405)	1.075(0.803–1.598)	1.085(0.880–1.525)	0.700(0.440–1.030)	8.447	<0.001[a]
PLT ($\times 10^9$/L)	176.00(142.00–227.50)	171.50(131.25–228.75)	180.00(147.00–247.25)	169.00(142.00–200.00)	1.539	0.344
HGB (g/L)	111.26 ± 16.146	113.44 ± 21.153	111.09 ± 12.457	109.00 ± 18.778	0.576	0.564
RDW (%)	13.800(13.100–15.000)	13.800(13.200–15.000)	13.900(13.025–15.275)	13.800(13.100–14.400)	0.156	0.925
Alb (g/L)	41.300 (38.850–43.1000)	41.800(38.900–43.325)	41.450(38.925–42.975)	40.500(38.000–43.500)	0.622	0.733
SF (ng/mL)	102.100 (42.400–237.200)	95.850 (42.275–277.750)	76.650(35.275–167.175)	156.200 (83.500–308.500)	7.513	0.023[a]
ALT (U/L)	12.000(8.000–16.500)	11.000(9.000–15.500)	11.000(8.000–15.750)	15.000(9.000–19.000)	2.975	0.226
AST (U/L)	14.000(12.000–18.500)	14.000(11.750–18.000)	13.000(11.000–18.000)	17.000(13.000–24.000)	6.990	0.030[a]
BUN (mmol/L)	21.543 ± 6.634	22.679 ± 6.136	22.119 ± 6.179	18.403 ± 7.761	3.998	0.021[a]
Scr (μmol/L)	807.572 ± 254.049	861.579 ± 249.695	814.696 ± 231.997	718.456 ± 304.369	2.514	0.085
UA (μmol/L)	391.000 (315.500–434.000)	395.50(355.50–446.75)	400.500 (318.500–435.250)	303.00(201.00–403.00)	3.370	0.011[a]
TG (mmol/L)	1.790(1.210–2.435)	1.720(1.198–3.230)	1.900(1.245–2.383)	1.590(1.090–2.430)	0.308	0.857
CHO(mmol/L)	4.007 ± 0.931	3.960 ± 0.828	4.025 ± 0.907	4.015 ± 1.136	0.057	0.944
Fe (μmol/L)	11.000(8.800–14.450)	12.700(8.800–14.400)	10.750(8.300–14.500)	11.300(9.000–14.500)	0.725	0.696
TIBC (μmol/L)	45.848 ± 11.736	44.250 ± 10.563	46.388 ± 12.809	46.263 ± 9.852	0.413	0.662
TSAT	0.260(0.181-.0240)	0.280(0.204–0.377)	0.258(0.175–0.348)	0.240(0.190–0.299)	1.026	0.599
PLR	177.982 (126.179–243.902)	167.100 (118.646–229.236)	173.864 (120.823–233.734)	232.099 (177.778–378.571)	10.574	0.003[a]
NLR	3.982(3.110–5.907)	3.815(2.507–5.457)	3.748(2.926–5.378)	6.407(3.863–11.151)	10.683	<0.001[a]
SII	756.346 (524.069–1173.943)	706.328 (426.752–1072.590)	649.418 (515.329–1143.154)	1005.963 (693.657–1517.371)	9.059	0.006[a]

Values are means ± standard deviations or medians (25th–75th percentiles), unless otherwise specified.
Abbreviations: WBC White blood cell, NEUT Neutrophil, LY Lymphocyte, PLT Platelets, HGB Hemoglobin, RDW Red cell distribution width, Alb Albumin, SF Serum ferritin, ALT Alanine aminotransferase, AST Aspartate transaminase, BUN Blood urea nitrogen, Scr Serum creatinine, UA Uric acid, TG Triglyceride, CHO Total cholesterol, TIBC Total iron binding capacity, TSAT Transferin saturation, PLR Platelet/lymphocyte ratio, NLR Neutrophil/lymphocyte ratio, SII Platelet × neutrophil/lymphocyte.
[a] Significant at $p < 0.05$.

Table 2
Pairwise comparison of biochemical parameters of MHD patients.

Item	LY		SF		AST		BUN		UA		PLR		NLR		SII	
	t/Z	*p*	t/Z	*p*	t/Z	*p*	t/Z	*p*	t/Z	*p*	t/Z	*p*	t/Z	*p*	t/Z	*p*
No COVID-19 infection *vs.* asymptomatic COVID-19 infection	−0.282	0.778	−1.109	0.268	−0.531	0.595	0.444	0.658	−0.570	0.569	−0.262	0.792	−0.121	0.904	−0.734	0.463
No COVID-19 infection *vs.* symptomatic COVID-19 infection	−3.115	0.002[a]	−1.256	0.209	−1.914	0.056	2.404	0.019[a]	−2.614	0.009[a]	−2.977	0.003[a]	−3.158	0.002[a]	−3.035	0.002[a]
asymptomatic COVID-19 infection *vs.* symptomatic COVID-19 infection	−4.096	<0.001[a]	−2.772	0.006[a]	−2.607	0.009[a]	2.527	0.013[a]	−2.747	0.006[a]	−3.192	0.001[a]	−3.844	<0.001[a]	−2.783	0.005[a]

Abbreviations: LY Lymphocyte, SF Serum ferritin, AST Aspartate transaminase, BUN Blood urea nitrogen, UA Uric acid, PLR Platelet/lymphocyte ratio, NLR Neutrophil/lymphocyte ratio, SII Platelet × neutrophil/lymphocyte.

[a] Significant at $p < 0.05$.

3.2. Binary logistics analysis between SARS-CoV-2 infection and biochemical parameters in MHD patients

The results of the binary logistics analysis in Table 3 demonstrated the predictors for SARS-CoV-2 infection status of MHD patients. When compared to no SARS-CoV-2 infection group, lymphocytes (OR: 0.089, 95 % CI: 0.018–0.441, p = 0.003), AST (OR: 1.102, 95 % CI: 1.006–1.206, p = 0.036), BUN (OR: 0.898, 95 % CI: 0.810–0.996, p = 0.042), UA (OR: 0.993, 95 % CI: 0.986–0.999, p = 0.032), PLR (OR: 1.015, 95 % CI: 1.005–1.025, p = 0.003), NLR (OR: 1.468, 95 % CI: 1.005–1.025, p = 0.005) and SII (OR: 1.002, 95 % CI: 1.001–1.003, p = 0.006) were independently associated with symptomatic SARS-CoV-2 infection, after adjusting for confounding factors.

In addition, lymphocytes (OR: 0.093, 95 % CI: 0.023–0.368, p < 0.001), ferritin (OR: 1.004, 95 % CI: 1.001–1.007, p = 0.008), AST (OR: 1.062, 95 % CI: 1.107–1.109, p = 0.006), BUN (OR: 0.891, 95 % CI: 0.821–0.966, p = 0.005), UA (OR: 0.990, 95 % CI: 0.984–0.996, p = 0.002), PLR (OR: 1.005, 95 % CI: 1.001–1.008, p = 0.011) and NLR (OR: 1.182, 95 % CI: 1.033–1.352, p = 0.015) were independently associated with symptomatic SARS-CoV-2 infection when compared with asymptomatic SARS-CoV-2 infection group, after adjusting for confounding factors.

3.3. Sensitivity and specificity of biochemical parameters in SARS-CoV-2 infection prediction by ROC analysis

Fig. 1 elucidated the receiver operating characteristic (ROC) curves analysis for the prediction of SARS-CoV-2 infection status by using those biochemical parameters above mentioned. Fig. 1A showed the NLR, PLR and SII had good sensitivity and specificity in predicting symptomatic SARS-CoV-2 infection when compared with no SARS-CoV-2 infection group. The cutoff value of PLR was 170.909 (area under the curve [AUC]: 0.723; 95 % CI: 0.595–0.851; 81.5 % sensitivity; 52.9 % specificity), the cutoff value of NLR was 6.191 (AUC: 0.737; 95 % CI: 0.613–0.861; 51.9 % sensitivity; 85.3 % specificity), and the cutoff value of SII was 828.935 (AUC: 0.728; 95 % CI: 0.602–0.854; 74.1 % sensitivity; 67.6 % specificity).

Fig. 1B showed the NLR and PLR had good sensitivity and specificity in predicting symptomatic SARS-CoV-2 infection when compared with asymptomatic SARS-CoV-2 infection group. The cutoff value of PLR was 193.305 (area under the curve [AUC]: 0.706; 95 % CI: 0.593–0.819; 66.7 % sensitivity; 68.8 % specificity), the cutoff value of NLR was 6.274 (AUC: 0.748; 95 % CI: 0.644–0.852; 51.9 % sensitivity; 86.3 % specificity).

We further analyzed the combined predictive power of PLR, NLR and SII, the ROC curve showed the AUC of combined PLR, NLR and SII was 0.753 in predicting symptomatic SARS-CoV-2 infection when compared with no SARS-CoV-2 infection group (95 % CI: 0.631–0.874), and the AUC of combined PLR and NLR in predicting symptomatic SARS-CoV-2 infection from asymptomatic SARS-CoV-2 infection group was 0.751 (95 % CI: 0.646–0.856). This result suggested that the combination of inflammatory indices did not show better predictive value in symptomatic SARS-CoV-2 infection.

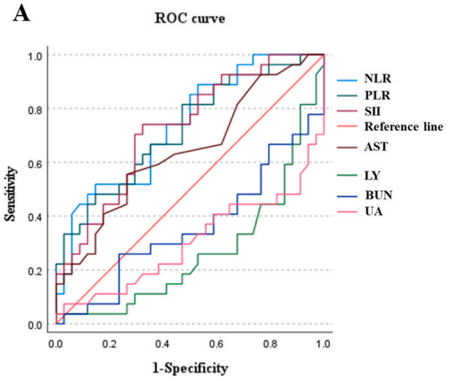
4. Discussion

The molecular pathogenesis of COVID-19 is still poorly understood. Aging, sex, cigarette smoke, obesity, and immune system dysregulation were reported to influence the development of COVID-19 [14]. It is well-documented that immune response is closely related to inflammatory reactions, and the inflammatory mechanisms play principal roles in COVID-19 patients. PLR, NLR and SII are systemic inflammatory indicators calculated from the complete blood count including neutrophils, lymphocytes and platelets. These indicators have recently been considered as diagnostics and predictive biomarkers in many diseases, such as cardiovascular diseases, systemic diseases and cancer [15,16]. Previous studies investigated the role of these systemic inflammatory indicators in other infectious diseases and demonstrated their ability on patients risk stratification [17]. Since the beginning of the pandemic, more and more studies have examined the role of these inflammatory indicators in COVID-19 prognostication and its utility as a biomarker of

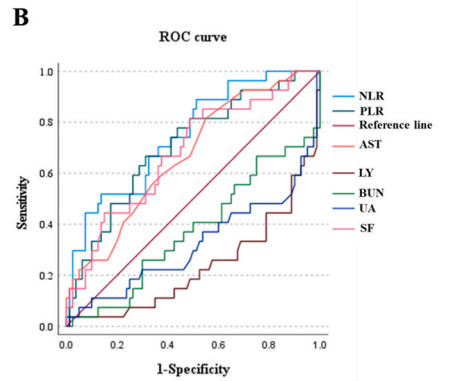
Table 3
Binary logistics analysis between COVID-19 infection and biochemical parameters in MHD patients.

	No COVID-19 infection *vs.* symptomatic COVID-19 infection				asymptomatic COVID-19 infection *vs.* symptomatic COVID-19 infection			
	Model 1		Model 2		Model 1		Model 2	
	OR(95%CI)	*p*	OR(95%CI)	*p*	OR(95%CI)	*p*	OR(95%CI)	*p*
LY	0.159(0.004–0.591)	0.006[a]	0.089(0.018–0.441)	0.003[a]	0.078(0.023–0.330)	<0.01[a]	0.093(0.023–0.368)	<0.01[a]
SF	1.001(0.998–1.003)	0.507	1.001(0.998–1.004)	0.438	1.004(1.001–1.007)	0.008[a]	1.004(1.001–1.007)	0.008[a]
AST	1.064(0.999–1.134)	0.054	1.102(1.006–1.206)	0.036[a]	1.060(1.013–1.109)	0.012[a]	1.062(1.107–1.109)	0.006[a]
BUN	0.910(0.838–0.989)	0.026[a]	0.898(0.810–0.996)	0.042[a]	0.914(0.850–0.983)	0.016[a]	0.891(0.821–0.966)	0.005[a]
UA	0.993(0.987–0.998)	0.013[a]	0.993(0.986–0.999)	0.032[a]	0.993(0.988–0.998)	0.008[a]	0.990(0.984–0.996)	0.002[a]
PLR	1.009(1.003–1.015)	0.006[a]	1.015(1.005–1.025)	0.003[a]	1.005(1.001–1.008)	0.007[a]	1.005(1.001–1.008)	0.011[a]
NLR	1.301(1.080–1.568)	0.006[a]	1.468(1.124–1.917)	0.005[a]	1.178(1.035–1.341)	0.013[a]	1.182(1.033–1.352)	0.015[a]
SII	1.002(1.000–1.003)	0.011[a]	1.002(1.001–1.003)	0.006[a]	1.000(1.000–1.001)	0.047[a]	1.001(1.000–1.001)	0.057

Model 1: Crude analysis.
Model 2: After adjusting for age, sex, dialysis duration, history of kidney transplantation, history of hypertension, and diabetic mellitus.
Abbreviations: LY Lymphocyte, SF Serum ferritin, AST Aspartate transaminase, BUN Blood urea nitrogen, UA Uric acid, PLR Platelet/lymphocyte ratio, NLR Neutrophil/lymphocyte ratio, SII Platelet × neutrophil/lymphocyte.
[a] Significant at $p < 0.05$.



Variables	AUC
NLR	0.737
PLR	0.723
SII	0.728
AST	0.643
LY	0.266
BUN	0.358
UA	0.304



Variables	AUC
NLR	0.748
PLR	0.706
AST	0.668
LY	0.236
BUN	0.375
UA	0.323
SF	0.679

Fig. 1. Receiver operating characteristic curves (ROC) for the prediction of symptomatic SARS-COV-2 infection using biochemical parameters. A. ROC curve of the LY (Lymphocyte), AST (Aspartate transaminase), BUN (Blood urea nitrogen), UA (Uric acid), PLR (Platelet/lymphocyte ratio), NLR (Neutrophil/lymphocyte ratio) and SII (Platelet × neutrophil/lymphocyte) for differentiating symptomatic SARS-COV-2 infection from no SARS-COV-2 infection groups. B. ROC curve of the LY, SF (Serum ferritin), AST, BUN, UA, PLR and NLR for differentiating symptomatic SARS-COV-2 infection from asymptomatic SARS-COV-2 infection groups.

disease progression.

Earlier studies showed a high PLR during COVID-19 treatment is associated with high degree of cytokine storm and resulted in a longer hospital stay [18,19]. The report by Gujar et al. indicated a relatively high diagnostic value of PLR in predicting the SARS-CoV-2 infection [20]. Meanwhile, some studies proposed the ability of higher levels of NLR on COVID-19 diagnosis [21]. The study by Maddani et al. demonstrated that NLR was an independent predictor of the requirement of admission in critical care units, which had an excellent predictive value of the NLR parameter as a predictor of COVID-19 severity [22]. In association with NLR, PLR could help in diagnosing SARS-CoV-2 infection. Higher PLR also correlated with an increased risk of the poor clinical outcome of COVID-19 [23]. Asperges E et al. confirmed that NLR and PLR were higher in severe COVID-19 and were able to distinguish severity grades and mortality at different time points during the course of COVID-19 [19].

SII is one of the new indicators for assessing systemic inflammation, which shows the balance between the immune system of the host and the inflammatory state. There are also dynamic changes in the course of COVID-19. Ozdemir A et al. concluded that SII was able to distinguish SARS-CoV-2 infected CKD patients of worse survival [24]. In the study of Usul et al., SII was found to be higher in COVID-19 patients compared to healthy controls [25].

Studies in general COVID-19 cohorts have demonstrated a significant association between these three systemic inflammatory indicators at the time of COVID-19 presentation and worse clinical outcomes. Study from Mayne KJ et al. found the NLR at the time of hemodialysis initiation was independently associated with all-cause mortality [8]. NLR and PLR could be a certain diagnostic value for frailty in MHD patients, and MHD patients with frailty have an unfavorable prognosis, as of those with high NLR and PLR levels [26]. SII also could be used to predict mortality and ICU need for hospitalized MHD patients with SARS-CoV-2 infection [27].

In this study, we explored the potential association between PLR, NLR and SII and the infection status of MHD patients. Among all hematological parameters, PLR and NLR seems to be the best biomarker of systemic inflammation in MHD patients with SARS-CoV-2 infection. PLR and NLR showed the best sensitivity and specificity in our study, it could recognize the symptomatic SARS-CoV-2 MHD patients effectively from the other patients with a good value of the area under the ROC curve. It is worth noting that about 56.73 % of MHD patients were asymptomatic in this study, which similar with previous lectures. Clarke C et al. showed that asymptomatic SARS-CoV-2 MHD populations were estimated to be between 40.3 % [28]. Whereas in another study, 18.4 % of MHD patients had an asymptomatic SARS-CoV-2 infection [29].

This study had some limitations. Firstly, this retrospective study was conducted from a single institution, and the data are collected

based on the electronic medical records of the hospital. Secondly, the findings presented in this study were obtained only from a limited number of patients in our department, and therefore the global accuracy of our ROC curve estimation could be reduced. Thirdly, some residual confounding such as body composition, other inflammatory disease, medication use and smoking were not performed.

In conclusion, a significant decline in lymphocyte count and consequently, the elevated PLR, NLR and SII were detected in symptomatic SARS-CoV-2 infection group in our study of MHD patients. ROC curves further demonstrated that only the higher level of PLR and NLR have good sensitivity and specificity on identification of symptomatic SARS-CoV-2 infection. These results indicated the possibility of using these coefficients as auxiliary markers in prognosis of MHD patients' condition due to SARS-CoV-2 infection.

CRediT authorship contribution statement

Sujuan Feng: Writing – original draft, Formal analysis, Data curation. **Han Li:** Writing – review & editing, Validation, Project administration, Conceptualization. **Shixiang Wang:** Visualization, Supervision, Investigation.

Ethics approval and consent to participate

This study was approved by the ethics committee of Beijing Chao-Yang Hospital, Capital Medical University and was conducted in accordance with the Declaration of Helsinki. The approval number of the ethics committee is 2021-KE-166. Written informed consents were obtained from all participants.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Funding

No founding.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledge

Not applicable.

References

[1] F. Alberici, E. Delbarba, C. Manenti, L. Econimo, F. Valerio, A. Pola, C. Maffei, S. Possenti, B. Lucca, R. Cortinovis, et al., A report from the Brescia Renal COVID Task Force on the clinical characteristics and short-term outcome of hemodialysis patients with SARS-CoV-2 infection, Kidney Int. 98 (2020) 20–26.
[2] C.M. Hsu, D.E. Weiner, G. Aweh, D.C. Miskulin, H.J. Manley, C. Stewart, V. Ladik, J. Hosford, E.C. Lacson, D.S. Johnson, E. Lacson, COVID-19 among US dialysis patients: risk factors and outcomes from a National dialysis provider, Am. J. Kidney Dis. 77 (2021) 748–756.
[3] H. Tang, J.B. Tian, J.W. Dong, X.T. Tang, Z.Y. Yan, Y.Y. Zhao, F. Xiong, X. Sun, C.X. Song, C.G. Xiang, et al., Serologic detection of SARS-CoV-2 infections in hemodialysis centers: a multicenter retrospective study in Wuhan, China, Am. J. Kidney Dis. 76 (2020) 490–499.
[4] Y. Obi, H. Qader, C.P. Kovesdy, K. Kalantar-Zadeh, Latest consensus and update on protein-energy wasting in chronic kidney disease, Curr. Opin. Clin. Nutr. Metab. Care 18 (2015) 254–262.
[5] S.C. Hung, Y.S. Lai, K.L. Kuo, D.C. Tarng, Volume overload and adverse outcomes in chronic kidney disease: clinical observational and animal studies, J. Am. Heart Assoc. 4 (2015).
[6] M.J. Sarnak, Cardiovascular complications in chronic kidney disease, Am. J. Kidney Dis. 41 (2003) 11–17.
[7] L. D'Marco, M.J. Puchades, M. Romero-Parra, E. Gimenez-Civera, M.J. Soler, A. Ortiz, J.L. Gorriz, Coronavirus disease 2019 in chronic kidney disease, Clin Kidney J 13 (2020) 297–306.
[8] K.J. Mayne, J.S. Lees, E. Rutherford, P.C. Thomson, J.P. Traynor, V. Dey, N.N. Lang, P.B. Mark, Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios: associations with mortality in a haemodialysis cohort, Clin Kidney J 16 (2023) 512–520.
[9] M. Yaprak, M.N. Turan, R. Dayanan, S. Akin, E. Degirmen, M. Yildirim, F. Turgut, Platelet-to-lymphocyte ratio predicts mortality better than neutrophil-to-lymphocyte ratio in hemodialysis patients, Int. Urol. Nephrol. 48 (2016) 1343–1348.
[10] W. Lai, Y. Xie, X. Zhao, X. Xu, S. Yu, H. Lu, H. Huang, Q. Li, J.Y. Xu, J. Liu, et al., Elevated systemic immune inflammation level increases the risk of total and cause-specific mortality among patients with chronic kidney disease: a large multi-center longitudinal study, Inflamm. Res. 72 (2023) 149–158.
[11] M. Eslamijouybari, K. Heydari, I. Maleki, M. Moosazadeh, A. Hedayatizadeh-Omran, L. Vahedi, R. Ghasemian, A. Sharifpour, R. Alizadeh-Navaei, Neutrophil-to-Lymphocyte and platelet-to-lymphocyte ratios in COVID-19 patients and control group and relationship with disease prognosis, Caspian J Intern Med 11 (2020) 531–535.
[12] D. Tatum, S. Taghavi, A. Houghton, J. Stover, E. Toraih, J. Duchesne, Neutrophil-to-Lymphocyte ratio and outcomes in Louisiana COVID-19 patients, Shock 54 (2020) 652–658.
[13] W. Xia, Y. Tan, S. Hu, C. Li, T. Jiang, Predictive value of systemic immune-inflammation index and neutrophil-to-lymphocyte ratio in patients with severe COVID-19, Clin. Appl. Thromb. Hemost. 28 (2022) 10760296221111391.
[14] G. Scaramuzzo, F. Nucera, A. Asmundo, R. Messina, M. Mari, F. Montanaro, M.D. Johansen, F. Monaco, G. Fadda, G. Tuccari, et al., Cellular and molecular features of COVID-19 associated ARDS: therapeutic relevance, J. Inflamm. 20 (2023) 11.

[15] C. Wang, W. He, Y. Yuan, Y. Zhang, K. Li, R. Zou, Y. Liao, W. Liu, Z. Yang, D. Zuo, et al., Comparison of the prognostic value of inflammation-based scores in early recurrent hepatocellular carcinoma after hepatectomy, Liver Int. 40 (2020) 229–239.
[16] M. Tang, Z. Jia, J. Zhang, The prognostic role of prognostic nutritional index in nasopharyngeal carcinoma: a systematic review and meta-analysis, Int. J. Clin. Oncol. 26 (2021) 66–77.
[17] C.D. Russell, A. Parajuli, H.J. Gale, N.S. Bulteel, P. Schuetz, C.P.C. de Jager, A.J.M. Loonen, G.I. Merekoulias, J.K. Baillie, The utility of peripheral blood leucocyte ratios as biomarkers in infectious diseases: a systematic review and meta-analysis, J. Infect. 78 (2019) 339–348.
[18] R. Qu, Y. Ling, Y.H. Zhang, L.Y. Wei, X. Chen, X.M. Li, X.Y. Liu, H.M. Liu, Z. Guo, H. Ren, Q. Wang, Platelet-to-lymphocyte ratio is associated with prognosis in patients with coronavirus disease-19, J. Med. Virol. 92 (2020) 1533–1541.
[19] E. Asperges, G. Albi, V. Zuccaro, M. Sambo, T.C. Pieri, M. Calia, M. Colaneri, L. Maiocchi, F. Melazzini, A. Lasagna, et al., Dynamic NLR and PLR in predicting COVID-19 severity: a retrospective cohort study, Infect. Dis. Ther. 12 (2023) 1625–1640.
[20] E. Acar, A. Demir, B. Yildirim, M.G. Kaya, K. Gokcek, The role of hemogram parameters and C-reactive protein in predicting mortality in COVID-19 infection, Int. J. Clin. Pract. 75 (2021) e14256.
[21] J. Peng, D. Qi, G. Yuan, X. Deng, Y. Mei, L. Feng, D. Wang, Diagnostic value of peripheral hematologic markers for coronavirus disease 2019 (COVID-19): a multicenter, cross-sectional study, J. Clin. Lab. Anal. 34 (2020) e23475.
[22] S.S. Maddani, N. Gupta, S. Umakanth, S. Joylin, K. Saravu, Neutrophil-lymphocyte ratio in patients with COVID-19 as a simple Tool to predict requirement of admission to a critical care unit, Indian J. Crit. Care Med. 25 (2021) 535–539.
[23] A. Noor, F. Akhtar, S. Tashfeen, N. Anwar, B. Saleem, S.A. Khan, Z. Akram, S. Shahid, Neutrophil-to-Lymphocyte Ratio, derived Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio and Lymphocyte-to-Monocyte Ratio as risk factors in critically ill COVID-19 patients, a single centered study, J. Ayub Med. Coll. Abbottabad 32 (Suppl 1) (2020) S595–S601.
[24] A. Ozdemir, S.Y. Kocak, S.N. Karabela, M. Yilmaz, Can systemic immune inflammation index at admission predict in-hospital mortality in chronic kidney disease patients with SARS-CoV-2 infection? Nefrologia 42 (2022) 549–558.
[25] E. Usul, I. San, B. Bekgoz, A. Sahin, Role of hematological parameters in COVID-19 patients in the emergency room, Biomark Med 14 (2020) 1207–1215.
[26] J. Wang, L. Huang, M. Xu, L. Yang, X. Deng, B. Li, Study on the clinical implications of NLR and PLR for diagnosing frailty in maintenance hemodialysis patients and their correlations with patient prognosis, J Healthc Eng 2022 (2022) 1267200.
[27] C. Sevinc, R. Demirci, O. Timur, Predicting hospital mortality in COVID-19 hemodialysis patients with developed scores, Semin. Dial. 34 (2021) 347–359.
[28] C. Clarke, M. Prendecki, A. Dhutia, M.A. Ali, H. Sajjad, O. Shivakumar, L. Lightstone, P. Kelleher, M.C. Pickering, D. Thomas, et al., High prevalence of asymptomatic COVID-19 infection in hemodialysis patients detected using serologic screening, J. Am. Soc. Nephrol. 31 (2020) 1969–1975.
[29] H. Ezzat, N.M. Teama, W.A. Bichari, Prevalence of asymptomatic COVID-19 infection in hemodialysis patients and the risk of hypercoagulability: should we consider routine screening? Indian J. Nephrol. 33 (2023) 101–107.
[30] J. Feng, L. Yu, H. Li, S. Wang, High serum beta2-microglobulin is a significant predictor of mortality in maintenance hemodialysis patients, Semin. Dial. 36 (2023) 247–254.