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Serum creatinine to absolute lymphocyte count ratio effectively risk stratifies patients who require intensive care in hospitalized patients with coronavirus disease 2019

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Abstract

Patients with preexisting kidney disease or acute kidney injury had poorer outcomes in coronavirus disease 2019 (COVID-19) illness. Lymphopenia was associated with more severe illness. Risk stratification with simple laboratory tests may help appropriate site patients in a cost-effective manner and ease the burden on healthcare systems. We examined a ratio of serum creatinine level to absolute lymphocyte count at presentation (creatinine-lymphocyte ratio, CLR) in predicting outcomes in hospitalized patients with COVID-19. We analyzed 553 consecutive polymerase chain reaction-positive SARS-COV-2 hospitalized patients. Patients with end-stage kidney disease were excluded. Serum creatinine and full blood count (FBC) examination were obtained within the first day of admission. We examined the utility of CLR in predicting adverse clinical outcomes (requiring intensive care, mechanical ventilation, acute kidney injury requiring renal replacement therapy or death). An optimized cutoff of CLR > 77 was derived for predicting adverse outcomes (72.2% sensitivity, and 83.9% specificity). Ninety-seven patients (17.5%) fell within this cut off. These patients were older and more likely to have chronic medical conditions. A higher proportion of these patients had adverse outcomes (13.4% vs 1.1%, $P < .001$). On receiver operating curve analyses, CLR predicted patients who had adverse outcomes well (area under curve [AUC] = 0.82, 95%CI 0.72–0.92), which was comparable to other laboratory tests like serum ferritin, C-reactive protein and lactate dehydrogenase. Elevated CLR on admission, which may be determined by relatively simple laboratory tests, was able to reasonably discriminate patients who had experienced adverse outcomes during their hospital stay. This may be a simple and cost-effective means of risk stratification and triage.

Abbreviations: AKI = acute kidney injury, AUC = area under curve, CLR = creatinine-to-lymphocyte ratio, COVID-19 = coronavirus disease 2019, FBC = full blood count, ROC = receiver operating characteristic, SARS-CoV-2 = severe acute respiratory distress syndrome coronavirus 2.

Keywords: acute kidney injury, COVID-19, creatinine, lymphopenia, outcomes, Singapore

1. Introduction

Although initially thought to predominantly affecting the lung and respiratory system, SARS-CoV-2 has now been shown to have deleterious effects on multiple organ systems.[1–3] The effect of the SARS-COV-2 on the kidneys remain to be fully understood, but kidney injury as a consequence of coronavirus disease 2019 (COVID-19) has been widely reported.[4,5] Because of heterogeneity in cohorts, the reported prevalence of acute kidney injury (AKI) has varied widely, from 5% to 29% depending on the center and countries studied.[6,7]

In fact, in several countries hardest hit by COVID-19, nephrology services have been overwhelmed in coping with the significant increased load of patients (by up to 18-fold) requiring renal replacement therapy as a result of the infection.[8] Of note, beyond the acute injury that could arise in the context of COVID-19 illness, patients with preexisting kidney disease were also found to be at increased risk of mortality and complications.[9,10]

In Singapore, the COVID-19 outbreak began with returning travelers that imported the disease. These included travelers returning from Europe, China and Hong Kong. Despite containment and isolation measures, several clusters of cases developed within the local population.[11,12] Finally, there were large outbreaks of cases within the migrant worker dormitories. These migrant workers were male laborers who were young and fit, from predominantly Indian or Bangladeshi descent and had relatively few medical comorbidities.[13,14]

Early in the pandemic, all tertiary hospitals were used to quarantine patients with COVID-19 to limit its spread. This was before the construction and implementation of purpose-built community isolation facilities. This approach was different from other countries, were hospital admissions had been limited to patients with moderate to severe COVID-19 illness. Because the vast majority of our cohort had been young migrant workers with few medical comorbidities and relatively mild COVID-19 illness, we were able to study and gain insight into the full spectrum of COVID-19 illness, from mild disease to severe disease requiring intensive care.[15]

Therefore, with many healthcare systems overwhelmed, it was important to derive a simple and cost-effective means of risk stratification of hospitalized patients with COVID-19 for appropriating siting of care. For example, hospital beds may be limited during a surge of COVID-19 cases. Therefore, risk stratification for individual patients becomes particularly important to help clinicians decide which patients are at risk of deterioration and requiring further hospitalization, while identifying other patients who are lower risk and may safely recover in an outpatient setting. With this background, we aimed to investigate the relationship between baseline measurements of serum creatinine and lymphopenia in relation to clinical outcomes in patients with COVID-19. When compared with other biomarkers that had been studied in the prognostication of patients with COVID-19, such as the C-reactive protein, serum lactate dehydrogenase or ferritin levels, the full blood count (FBC) and serum creatinine are laboratory tests that are readily available, with a quick turnaround time, and are relatively cost-effective. This would thus potentially make it an effective risk stratification tool, even if resource-poor settings.

Of note, elevated serum creatinine at presentation would be seen in significant acute kidney injury or in patients with advanced chronic kidney disease, both of which reflect a susceptible host to severe illness. Lymphopenia (as defined by a low absolute lymphocyte count) would have reflected more severe disease. Therefore, we hypothesized that an index or ratio examining serum creatinine to absolute lymphocyte count may effectively discriminate patients with poor clinical outcomes in hospitalized patients with COVID-19.

2. Methods

The first 554 consecutive hospitalized patients who had positive polymerase chain reaction positive SARS-CoV-2 infection from a nasopharyngeal swab were studied. These patients had been admitted to a single tertiary healthcare institution from February to April 2020. We excluded patients with end-stage renal disease on renal replacement therapy (1 patient was excluded, and the remaining 553 patients were included for analysis). We followed all patients for clinical progress and outcomes during their hospital stay and none of the patients had been lost to follow-up. The electronic medical records of each patient were accessed retrospectively to collect data on the demographic background, prior medical conditions, and clinical presentation. We computed the day of illness at presentation based on the number of days from symptom onset to the day of presentation at the hospital. This study was conducted in accordance with the Declaration of Helsinki, and had been approved by the hospital's institutional review board (National Healthcare Group Domain Specific Review Board 2020/00545) prior to the conduct of the study. Data collected was anonymized and a waiver of informed consent had been obtained from the institutional review board.

All patients examined had baseline laboratory tests including serum creatinine (measured in µmol/L, isotope-dilution mass spectrometry standardized) and FBC examination within the first 24 hour of admission. Chest X-rays were also performed to identify patients with radiological evidence of pneumonia. We followed these patients for clinical outcomes during the hospital admission, including patients who required supplemental oxygenation, required intensive care or mechanical ventilation and experienced adverse clinical events such as myocarditis/myocardial injury or death. Composite adverse clinical events were defined by patients who required intensive care, required mechanical ventilation, had severe acute kidney injury requiring renal replacement therapy, or death.

The estimated glomerular filtration rate was calculated by the chronic kidney disease epidemiology collaboration formula, taking into account the serum creatinine, age, gender and ethnicity of the patient.[16] The serum creatinine to absolute lymphocyte count ratio (CLR) was calculated by dividing the serum creatinine at presentation (in µmol/L) by the absolute lymphocyte count ($\times 10^9$/L) based on the FBC at presentation. Area under receiver operating characteristic curve (ROC) was calculated to evaluate the performance of CLR in predicting composite adverse clinical outcomes. An optimized cutoff for CLR was derived by Youden index. CLR was also evaluated for its performance in predicting patients who developed radiological evidence of pneumonia. Performance of other biomarkers in predicting adverse clinical outcomes such as C-reactive protein, serum ferritin and lactate dehydrogenase were also tabulated using ROC curves. The population was divided into those with elevated CLR and those without, and their baseline clinical characteristics were compared.

Statistical analyses to compare the abovementioned groups involved Student t tests for continuous parameters, with the data presented in as means (±standard deviation). Categorical parameters were examined by Chi-squared tests (or Fisher exact test where appropriate), with the data being presented as frequencies and percentages. Significant parameters identified on univariate analyses that were not collinear were entered into multivariable logistic regression analysis to identify parameters independently associated with patients who had adverse clinical outcomes. A P value of <.05 was considered significant. All data analysis was done on SPSS version 20.0 (SPSS, Inc., Chicago, Illinois).

3. Results

CLR performed reasonably well in identifying patients who had pneumonia (Fig. 1A, AUC 0.62, 95%CI 0.53–0.70), and composite adverse clinical outcomes (Fig. 1B, AUC 0.82,
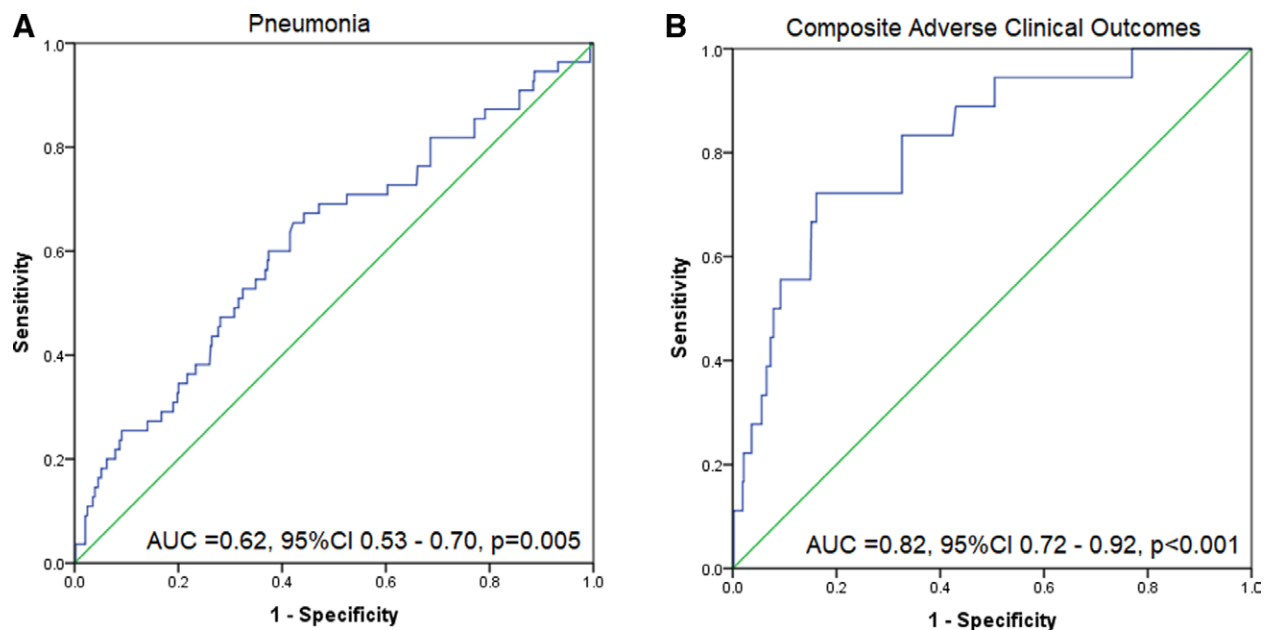
Figure 1. The performance of the Creatinine-to-lymphocyte ratio in (CLR) predicting patients who have (A) radiological evidence of pneumonia, and (B) composite adverse clinical outcomes (acute kidney injury requiring renal replacement therapy, mechanical ventilation, requiring intensive care) in hospitalized patients with COVID-19. COVID-19 = coronavirus disease 2019.

95%CI 0.72–0.92). An optimized cutoff of CLR > 77 was determined by Youden index (sensitivity 72.2% and specificity 83.9%). Of the 553 patients examined, 97 patients (17.5%) had an elevated CLR. These patients with elevated CLR tended to be older (42 ± 14 vs 36 ± 11 years, $P < .001$), but were similar in terms of gender (82.4% vs 87.3% male, $P = .534$). These patients were also more likely to have prior medical conditions such as hypertension (29.8% vs 7.7%, $P = .002$), hyperlipidemia (29.8% vs 3.5%, $P < .001$), and diabetes mellitus (7.2% vs 2.9%, $P = .022$) (Table 1). Two patients had chronic kidney disease prior to admission, both of which had an elevated CLR.

Patients with elevated CLR also tended to have a longer duration of fever (2.0 ± 2.0 vs 1.0 ± 2.4 days, $P < .001$), with more grossly elevated markers of inflammation, such as an elevated serum C-reactive protein level (25.1 ± 36.5 vs 11.8 ± 24.5 ng/dL, $P < .001$), serum ferritin level (261.0 ± 402.3 vs 163.0 ± 152.0 ng/mL, $P < .001$). Patients when elevated CLR were more likely to have pneumonia (19.6% vs 8.7%, $P = .022$), require supplement oxygen (17.5% vs 4.8%, $P < .001$), and experience composite adverse clinical outcomes (13.4% vs 1.1%, $P < .001$).

In our study cohort, 18 patients (3.3%) required intensive care. These patients were older and more likely to have chronic medical conditions. Markers of inflammation such as C-reactive protein (84.1 ± 53.4 ng/dL vs 11.9 ± 23.3 ng/dL, $P < .001$) and serum ferritin (668.7 ± 451.2 vs 166.7 ± 192.5 ng/mL, $P < .001$) were markedly elevated in those who required intensive care. The creatinine-to-lymphocyte ratio (CLR) was also significantly elevated in patients who required intensive care (121.0 ± 106.0 vs 58.3 ± 119.1, $P = .028$) (Table 2). On multivariable logistic regression, after adjusting for age and prior medication conditions, elevated CLR (>77) remained independently associated with severe disease with adverse clinical outcomes (adjusted odds ratio 6.94, 95%CI 2.16–22.2, $P < .001$) (Table 3).

Serum creatinine alone predicted the need for intensive care with an AUC of 0.67 (95%CI 0.52–0.83, $P = .010$), while the presence of lymphopenia alone predicted adverse clinical outcomes with an AUC of 0.77 (95%CI 0.65–0.89, $P < .001$) on

ROC curve analyses. As a combined ratio, CLR was able to reasonably predict patients who experienced adverse composite clinical outcomes (AUC = 0.82, 95%CI 0.72–0.92, $P < .001$). This was similar to other established biomarkers such as lactate dehydrogenase, C-reactive protein and serum ferritin (Table 4).

4. Discussion

We studied a population with relatively mild disease with only 10.1% (n = 56) of the cohort having radiological evidence of pneumonia and 3.3% (n = 18) requiring intensive care. Even so, we demonstrated the elevated CLR (based on simple laboratory tests obtained on admission) may reasonably discriminate patients with adverse clinical outcomes in the form of requiring intensive care, mechanical ventilation or acute kidney injury requiring renal replacement therapy during their hospitalization.

CLR reflects the presence of kidney disease (both acute kidney injury and chronic kidney disease), and thus when indexed against the absolute lymphocyte count, was able to provide added discrimination to identify patients at high risk of clinical deterioration from COVID-19. In COVID-19, the role of the absolute lymphocyte count has been extensively studied, and it has been shown that more significant lymphopenia was associated with more severe disease. Although our study was not designed to evaluate the etiology and mechanisms for kidney injury in COVID-19 illness, prior studies have proposed several possibilities. Elevated serum creatinine appeared to predict deterioration in COVID-19. In our context, the most predominant reason for this may be "pre-renal" kidney. In the context of systemic illness, increased insensible losses from prolonged fever as well as reduced oral intake result in volume contraction and a consequent elevation in serum creatinine and reduction in the estimated glomerular filtration rate.[17,18] This notion was supported by our data as well, given that the elevation in serum creatinine was often mild, and quickly reversible after intravenous hydration on repeat measurement prior to discharge. Furthermore, patients with prolonged duration of fever were also more likely to elevated CLR.

Table 1

Differences in demographics and clinical profile of patients with or without elevated creatinine:lymphocyte ratio (CLR).

Parameter	Overall (n = 553)	CLR > 77* (n = 97)	CLR ≤ 77 (n = 456)	P value
Age (yr)	37 (±11)	42 (±14)	36 (±11)	<.001
Gender (male)	478 (86.1%)	80 (82.4%)	398 (87.3%)	.534
Medical co-morbidities				
Hypertension	52 (9.4%)	17 (29.8%)	35 (7.7%)	.002
Hyperlipidemia	33 (5.9%)	17 (29.8%)	16 (3.5%)	<.001
Diabetes mellitus	20 (3.6%)	7 (7.2%)	13 (2.9%)	.022
Asthma	6 (1.1%)	0 (0.0%)	6 (1.3%)	.283
Ischemic heart disease	4 (0.7%)	2 (2.1%)	2 (0.4%)	.067
Chronic kidney disease	2 (0.4%)	2 (2.1%)	0 (0.0%)	.001
No previous medical conditions	491 (88.8%)	23 (23.7%)	39 (8.6%)	<.001
Clinical profile				
Day of illness at presentation	3 (±5)	4 (±8)	3 (±4)	.712
Length of days with fever	1.2 (±2.4)	2.0 (±2.0)	1.0 (±2.4)	<.001
Admission temperature (°C)	37.5 (±0.8)	38.0 (±0.8)	37.4 (±0.8)	<.001
Systolic blood pressure (mm Hg)	130 (±17)	128 (±18)	131 (±17)	.207
Diastolic blood pressure (mm Hg)	81 (±12)	78 (±12)	82 (±12)	.003
Oxygen saturation (%)	98 (±3)	97 (±5)	98 (±1)	<.001
Pulse rate (per min)	94 (±19)	101 (±21)	93 (±18)	<.001
Respiratory rate (per min)	19 (±6)	20 (±3)	19 (±6)	.391
Laboratory investigations				
Total white cell count (×10⁹/L)	6.5 (±2.2)	6.2 (±2.9)	6.5 (±2.0)	.228
Absolute lymphocyte count (×10⁹/L)	1.9 (±2.0)	0.9 (±0.2)	2.1 (±2.2)	<.001
Hemoglobin (g/dL)	14.9 (±1.6)	14.4 (±1.8)	15.0 (±1.6)	.001
Platelet count (×10⁹/L)	228 (±60)	199 (±43)	235 (±62)	<.001
Sodium (mmol/L)	138 (±3)	137 (±3)	139 (±2)	<.001
Potassium (mmol/L)	4.0 (±2.8)	3.8 (±0.4)	4.1 (3.0)	.392
Urea (mmol/L)	3.9 (±2.6)	4.6 (±2.9)	3.7 (±2.5)	.003
Creatinine (µmol/L)	79.4 (±19.6)	94.6 (±31.3)	74.8 (±13.8)	<.001
eGFR (mL/min)	105.5 (±18.1)	89.4 (±23.2)	109.0 (±14.6)	<.001
AST (U/L)	37.9 (±48.8)	49.7 (±109.1)	35.4 (±19.5)	.013
ALT (U/L)	45.7 (±44.2)	44.6 (±65.9)	46.0 (±38.2)	.796
LDH (U/L)	433.7 (±419.9)	512.6 (±598.0)	417.5 (±371.9)	.053
C-reactive protein (ng/dL)	13.9 (±27.2)	25.1 (±36.5)	11.8 (±24.5)	<.001
Ferritin (ng/mL)	178.8 (±215.7)	261.0 (±402.3)	163.0 (±152.0)	<.001
Troponin I (ng/mL)	118.5	444.0 (±1136.4)	10.0 (±23.2)	.030
Clinical progress and outcomes				
Pneumonia	56 (10.1%)	16 (19.6%)	40 (8.7%)	.022
Requiring oxygen	16 (2.8%)	9 (9.3%)	7 (1.5%)	<.001
Persistent fever >72 h	39 (7.1%)	17 (17.5%)	22 (4.8%)	<.001
Required intensive care monitoring	18 (3.3%)	13 (13.4%)	5 (1.1%)	<.001
Required mechanical ventilation	15 (2.7%)	11 (11.3%)	4 (0.9%)	<.001
Acute kidney injury requiring renal replacement therapy	5 (0.9%)	3 (3.1%)	2 (0.4%)	.008
Myocarditis/myocardial injury	3 (0.5%)	2 (2.1%)	1 (0.2%)	.070
Death	2 (0.4%)	0 (0.0%)	2 (0.4%)	.537
Composite adverse clinical outcomes (intensive care, mechanical ventilation, AKI requiring RRT, death)	18 (3.3%)	13 (13.4%)	5 (1.1%)	<.001
Creatinine/Lymphocyte ratio	62 (±127)	135 (±172)	56 (±121)	<.001

AKI = acute kidney injury, ALT = alanine transaminase, AST = aspartate transaminase, LDH = lactate dehydrogenase, RRT = renal replacement therapy.

*At optimized cutoff by Youden index, CLR > 77 predicted composite adverse outcomes (ICU stay, AKI requiring RRT and/or mechanical ventilation) with 72.2% sensitivity and 83.9% specificity.

There may be other mechanisms to account for why elevated serum creatinine identified patients who would have more severe COVID-19 illness. The presence of raised serum creatinine at presentation (whether from acute kidney injury or preexisting chronic kidney disease) also represents patients who were more likely to require renal replacement therapy. Furthermore, may also be unique pathways where direct viral tropism for the angiotensin converting enzyme 2 receptors (ACE-2) of the nephron (specifically the proximal tubules and podocytes) may lead to direct renal injury.[19] In some cases, glomerulonephritis in the form of collapsing focal segmental glomerulosis has been described in postmortem studies.[20] However, the majority of the postmortem studied supported the notion that kidney injury was a result of systemic inflammation and its deleterious effects on hypoxia and hemodynamic instability, which consequently led to acute tubular injury.[20]

Prognosis of hospitalized patients with AKI had been significantly worse that the general population of patients with COVID-19. In some studies, those with AKI had mortality in excess of 70%.[21,22] In our cohort of hospitalized patients, those with milder disease had also been included, and the vast majority of our population consisted of migrant workers who were young. Nevertheless, even in this spectrum of disease, we demonstrated that elevated CLR was associated with higher rates of intensive care admissions for COVID-19. Long-term sequelae of this kidney injury have not been well-described, as follow-up for prior studies had often been limited to the during of the hospitalization.[23,24] Reassuringly, in our cohort of patients with milder disease, the majority of patients showed good renal recovery. The 5 patients with acute kidney injury requiring renal replacement therapy did not require long-term dialysis.

Lymphopenia (or a reduced absolute lymphocyte count) has been described as a establish marker of severe COVID-19 illness.[25] True enough, with taken as a ratio, we demonstrated that elevated CLR could reasonably discriminate patients with severe COVID-19 illness that required intensive care. The CLR

Table 2

Characteristics of hospitalized patients with COVID-19 with composite adverse clinical outcomes compared with those with milder disease.

Parameter	Composite adverse outcomes (n = 18)	No composite adverse outcomes (n = 535)	*P* value
Age (yr)	57 (±13)	36 (±11)	<.001
Gender (Male)	9 (50.0%)	469 (88.3%)	<.001
Hypertension	11 (61.1%)	41 (7.6%)	<.001
Hyperlipidemia	9 (50.0%)	24 (4.5%)	<.001
Diabetes mellitus	4 (22.2%)	16 (3.0%)	<.001
Total white cell count (×10⁹/L)	7.2 (±4.3)	6.5 (±2.1)	.168
Absolute neutrophil count (×10⁹/L)	5.7 (±4.2)	4.1 (±8.0)	.422
Absolute lymphocyte count (×10⁹/L)	1.0 (±0.4)	1.9 (±2.0)	.061
Creatinine (umol/L)	99.7 (±49.8)	77.6 (±17.4)	<.001
eGFR (mL/min)	68.7 (±20.5)	106.7 (±16.7)	<.001
C-reactive protein (ng/dL)	84.1 (±53.4)	11.9 (±23.3)	<.001
Ferritin (ng/mL)	668.7 (±451.2)	166.7 (±192.1)	<.001
LDH (U/L)	949.1 (±1320.0)	418.3 (±353.1)	<.001
Pneumonia on chest X-ray at presentation	12 (66.7%)	44 (8.2%)	<.001
Acute kidney injury requiring renal replacement therapy	5 (45.5%)	0 (0.0%)	<.001
Required mechanical ventilation	15 (83.3%)	0 (0.0%)	<.001
Death	2 (11.1%)	0 (0.0%)	<.001
Creatinine/lymphocyte ratio	121.0 (±106.0)	58.3 (±119.1)	.028

COVID-19 = coronavirus disease 2019, eGFR = estimated glomerular filtration rate.

Table 3

Multivariable analyses showing creatinine/lymphocyte ratio independently associated with severe COVID-19 illness with composite adverse clinical outcomes in hospitalized patients.

Parameter	Adjusted odds ratio (95% confidence interval)	*P* value
Age (yr)	1.06 (1.01–1.11)	.019
No prior medical conditions	0.15 (0.04–0.61)	.008
Elevated creatinine/lymphocyte ratio > 77	6.94 (2.16–22.2)	.001

COVID-19 = coronavirus disease 2019.

Table 4

Comparing the performance (area under receiver operating characteristic curve) of various laboratory parameters in predicting patients with composite adverse clinical outcomes (acute kidney injury requiring renal replacement therapy, mechanical ventilation, requiring intensive care, or death) amongst hospitalized patients with COVID-19.

Laboratory parameter	Area under curve (95% confidence interval)	*P* value
Absolute lymphocyte count	0.81 (0.73–0.90)	<.001
Serum creatinine	0.66 (0.50–0.82)	.023
Serum ferritin	0.83 (0.67–0.99)	<.001
C-reactive protein	0.97 (0.94–0.99)	<.001
Lactate dehydrogenase	0.86 (0.76–0.95)	<.001
Creatinine:lymphocyte ratio (CLR)	0.82 (0.72–0.92)	<.001

COVID-19 = coronavirus disease 2019.

identifies 97 (17.3%) high risk patients out of a cohort of 553 hospitalized patients with COVID-19. Of these, 13 out of 97 (13.4%) experienced adverse outcomes, while 5 out of 456 (1.1%) experienced adverse outcomes. The use of this ratio is still imperfect, and future prospective studies are warranted to validate the use of this ratio and examine its prognostic value in other COVID-19 cohorts. It may also be studied in conjunction with existing tools to increase its sensitivity and specificity and aid in risk stratification of patients.

Indeed, if validated, this may be a simple and cost-effective tool that can risk stratify patients from the point of admission, identifying those at risk of deterioration and adverse clinical outcomes during their hospital stay. Accurately identifying such patients may help subsequently with triage and appropriate siting of care, thereby easing the burden on already significantly overwhelmed healthcare systems around the world.

5. Limitations

We studied a relatively small, single-center cohort of patients who were hospitalized with COVID-19. In Singapore, most of the patients had been hospitalized for quarantine purposes (prior to the construction of purpose-built community isolation facilities), and hence had relatively mild disease. However, this allowed us to study trends in the entire spectrum of COVID-19 illness. The large outbreak of cases in the migrant worker dormitories also meant that the study population had disproportionate numbers of migrant workers who were young and fit with relatively few medical comorbidities.[15] Hence, only a minor of the patients studied had chronic kidney disease prior to presentation. We only followed the clinical progress of patients within the initial hospital admission, and were not able to longitudinally examine patients for longer-term sequelae. Our study population had relatively few adverse outcomes

(2 deaths [0.5%], and 18 patients requiring intensive care [3.3%]). Nevertheless, despite the relatively small study population, we demonstrated the potential utility of CLR in predicting adverse clinical outcomes. Future prospective study in larger, multinational and multicenter cohorts would be helpful to validate this as a clinical risk stratification tool for hospitalized patients with COVID-19.

6. Conclusions

In Singapore, we report that the CLR at presentation may be useful way of risk stratifying hospitalized patients with COVID-19, identifying those with severe COVID-19 illness that may necessitate intensive care and closer monitoring.

Author contributions

JNN, TSL, MYS, NWSC, CHS were involved in the conception, data collection, analysis and writing of the manuscript. TYWL, SMT, ZYC, ZYL were involved in the data collection, analysis and review of the manuscript. HRC, PAT, AS, GBC, PAT were involved in the conception, data analysis and review of the manuscript.

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Correction

Horng Ruey Chua's name was incorrectly spelt as Horny Ruey Chua. This has been corrected.

References

[1] Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ. 2020;368:m606.

[2] Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. Lancet Gastroenterol Hepatol. 2020;5:428–30.

[3] Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323:1061–9.

[4] Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382:1708–20.

[5] Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395:507–13.

[6] Kolhe NV, Fluck RJ, Selby NM, et al. Acute kidney injury associated with COVID-19: a retrospective cohort study. PLoS Med. 2020;17:e1003406.

[7] Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. 2020;368:m1091.

[8] Fisher M, Prudhvi K, Brogan M, et al. Providing care to patients with AKI and COVID-19 infection: experience of front line nephrologists in New York. Kidney360. 2020;1:544–8.

[9] Cheng Y, Luo R, Wang K, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int. 2020;97:829–38.

[10] Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395:1054–62.

[11] Lim RJ, Lee TH, Lye DCB. From SARS to COVID-19: the Singapore journey. Med J Aust. 2012;212:497–502.

[12] Ngiam JN, Tham SM, Vasoo S, et al. COVID-19: local lessons from a global pandemic. Singapore Med J. 2020;61:341–2.

[13] Koh D. Migrant workers and COVID-19. Occup Environ Med. 2002;77:634–6.

[14] Bagdasarian N, Fisher D. Heterogenous COVID-19 transmission dynamics within Singapore: a clearer picture of future national responses. BMC Med. 2020;18:166.

[15] Ngiam JN, Chew N, Tham SM, et al. Demographic shift in COVID-19 patients in Singapore from an aged, at-risk population to young migrant workers with reduced risk of severe disease. Int J Infect Dis. 2021;103:329–35.

[16] Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150:604–12.

[17] Rudnick MR, Hilburg R. Acute kidney injury in COVID-19: another challenge for nephrology. Am J Nephrol. 2020;51:761–3.

[18] Farouk SS, Fiaccadori E, Cravedi P, et al. COVID-19 and the kidney: what we think we know so far and what we don't. J Nephrol. 2020;1:6.

[19] Battle D, Soler MJ, Sparks MA, et al. Acute kidney injury in COVID-19: emerging evidence of a distinct pathophysiology. J Am Soc Nephrol. 2020;31:1380–3.

[20] Kudose S, Batal I, Santoriello D, et al. Kidney biopsy findings in patients with COVID-19. J Am Soc Nephrol. 2020;31:1959–68.

[21] Hirsch JS, Ng JH, Ross DW, et al. Acute kidney injury in patients hospitalized with COVID-19. Kidney Int. 2020;98:209–18.

[22] Zahid U, Ramachandran P, Spitalewitz S, et al. Acute kidney injury in COVID-19 patients: an inner city hospital experience and policy implications. Am J Nephrol. 2020;51:786–96.

[23] Mohamed MMB, Lukitsch I, Torres-Ortiz AE, et al. Acute kidney injury associated with coronavirus disease 2019 in urban New Orleans. Kidney360. 2020;1:614–22.

[24] Suleyman G, Fadel RA, Malette KM, et al. Clinical characteristics and morbidity associated with coronavirus disease 2019 in a series of patients in metropolitan detroit. JAMA Netw Open. 2020;3:e2012270.

[25] Zhao Q, Meng M, Kumar R, et al. Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a systematic review and meta-analysis. Int J Infect Dis. 2020;96:131–5.