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Original Article

Acute kidney injury in hospitalized patients with COVID-19: A single center experience

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ABSTRACT

Objectives: The aim of this study was to evaluate the clinical features and outcomes of patients with coronavirus disease 2019 (COVID-19) who experienced acute kidney injury (AKI) during intensive care unit (ICU) hospitalization.

Materials and methods: Between March 01, 2020 and June 30, 2020, a total of 49 patients (28 males, 21 females; mean age: 75.5±12.5 years; range, 21 to 92 years) with COVID-19 PCR positive who were hospitalized with COVID-19 pneumonia in the ICU and developed AKI were evaluated with demographics, laboratory data, treatment, and outcome. The prognostic nutritional index (PNI), which is calculated using the serum albumin concentration and the total lymphocytic count was also evaluated. All patients were treated with favipiravir+low molecular weight heparin; laboratory tests were recorded before and after favipiravir treatment.

Results: Nine (18.4%) patients survived to hospital discharge. The mean PNI of the patients who survived was higher than in non-survivors. Lactate dehydrogenase (LDH), procalcitonin, ferritin, and C-reactive protein (CRP) results were higher in non-survivors. When we compare the PNI results, the mean PNI was lower after the favipiravir treatment. Leucocyte, neutrophil count, and neutrophil-lymphocyte ratio results were higher after the treatment. Creatinine, LDH, procalcitonin, ferritin, and CRP results were higher after the treatment in non-survivors.

Conclusion: Acute kidney injury was related to a significant mortality rate in COVID-19 hospitalized patients. Prognostic nutritional index may be a valuable clinical marker for predicting survival in COVID-19 patients.

Keywords: Acute kidney injury, COVID-19, neutrophil lymphocyte ratio, prognostic nutritional index.

Preliminary reports indicate that acute kidney injury (AKI) seems to be associated with coronavirus disease 2019 (COVID-19) severity and outcomes.[1] Although the reported incidence of AKI among hospitalized patients with COVID-19 varies widely, AKI among hospitalized patients is associated with poor prognosis.[1-4] The aim of this study was to evaluate the clinical characteristics and outcomes in our COVID-19 patients who developed AKI during intensive care unit (ICU) hospitalization.

MATERIALS AND METHODS

This retrospective observational study was conducted at the Giresun University Hospital Department of Internal Medicine, Nephrology clinic between March 01, 2020 and June 30, 2020. A total of 49 patients (28 males, 21 females; mean age: 75.5±12.5 years; range, 21 to 92 years) with COVID-19 PCR positive who were hospitalized with COVID-19 pneumonia in the ICU and developed AKI were included in the study. Patients under the age of 18 were excluded from the study.

Acute kidney injury was defined according to the Kidney Disease: Improving Global

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Outcomes (KDIGO) criteria. The prognostic nutritional index (PNI) which is calculated using the serum albumin concentration and the total lymphocytic count was also evaluated [PNI=10 × serum albumin (g/dL)+0.005 × total lymphocyte count]. All patients were treated with favipiravir+low molecular weight heparin; laboratory tests were recorded before and after favipiravir treatment.

Statistical analysis

Statistical analyzes were performed with Number Cruncher Statistical System 2004 (NCSS, Utah, USA) and GraphPad Prism version 9.0.1 (GraphPad Software, LLC, USA). After investigating the conformity of continuous variables to a normal distribution with the Kolmogorov-Smirnov test, variables with Gaussian distribution were shown as mean±SD, while variables with non-gaussian distribution were shown as median (25^{th}-75^{th} percentile). Student's t-test or Mann-Whitney U test was used for independent group comparisons. Pearson's chi-square test or Yates' correction was used to compare group frequencies. Statistical significance was evaluated at the $p<0.05$ (two-tailed) level.

RESULTS

Demographic and clinical features

Nine (18.4%) patients survived to hospital discharge. Favipiravir, the recommended drug by the Turkish Ministry of Health, was uniformly supplied to all patients. Favipiravir treatment was initiated with two loading doses of 1600 mg each on day one, followed by 600 mg twice daily for 5-10 days. Low-molecular-weight heparin was administered to all patients. Laboratory tests were recorded before and after treatment.

Laboratory data

Leucocyte, neutrophil count, and neutrophil-lymphocyte ratio (NLR) were higher in non-survivors. The mean PNI of the patients who survived was higher than in non-survivors. Lactate dehydrogenase (LDH), aspartate transferase (AST), procalcitonin, ferritin, D-dimer and C-reactive protein (CRP) results were higher in non-survivors. There was no statistically significant difference between the mean serum creatinine values of the patients. When we compare the PNI results, the mean PNI was lower after the favipiravir treatment. Leucocyte, neutrophil count, and NLR results were higher after the treatment in the non-

Table 1. Clinical and laboratory findings of patients after favipiravir treatment

	Discharged (n=9)				Dead (n=40)				
	n	Mean±SD	Median	Min-Max	n	Mean±SD	Median	Min-Max	*p*
Age (year)		78.3±6.6				74.8±13.4			0.451
Sex									1.000
Male	5				23				
Female	4				17				
Prognostic nutritional index		32.4±7.2				25.2±6.3			**0.049**
White blood cell		10.4±5.6				16.8±10.4			**0.017**
Neutrophil		8.3±5.8				14.3±9.2			**0.011**
Lymphocyte			1.26	0.55-1.80			0.64	0.40-1.33	0.159
Neutrophil-lymphocyte ratio			5.59	3.48-10.47			19.7	10.5-28	**0.025**
Hemoglobin (g/dL)		10.6±1.8				10.8±2.3			0.877
Creatinine		2.15±0.96				2.19±1.53			0.597
Lactate dehydrogenase			213	164-312			683	293-1379	**<0,001**
Aspartate transferase			16	12-34			43	26-87	**0.012**
Troponin T			0.042	0.024-0.078			0.109	0.056-0.0583	**0.050**
Procalcytonin			0.195	0.145-0.253			0.945	0.310-2.448	**0.070**
Ferritin			240	99-872			690	456-1238	**0.048**
D-dimer			604	425-1895			4083	1898-6376	**0.003**
C-reactive protein			19.3	14.2-35.7			142.0	85.6-259.3	**<0.001**

SD: Standard deviation.

Table 2. Laboratory findings of the non-survived patients before and after favipiravir treatment (n=40)

	Before treatment			After treatment			
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	*p*
Prognostic nutritional index	32.1±7.2			25.2±6.3			<0.0001
White blood cell	12.3±8.5			16.8±10.4			0.011
Neutrophil	10.1±7.7			14.3±9.2			0.012
Lymphocyte		0.80	0.51-1.41		0.64	0.40-1.33	0.973
Hemoglobin (g/dL)	11.4±2.47			10.8±2.3			0.008
Neutrophil-lymphocyte ratio		11.2	4.3-19.2		19.7	10.5-28	0.013
C-reactive protein (mg/dL)		110.5	35.8-147.9		142	85.6-259.3	0.009
Creatinine (mg/dL)	1.49±1.21			2.19±1.53			0.033
Lactate dehydrogenase		398	282-592		683	293-1379	0.011
Troponin T		0.057	0.021-0.234		0.109	0.056-0.583	0.004
Procalcitonin		0.275	0.140-2.220		0.945	0.310-2.448	0.327
Ferritin		514	239-1210		690	456-1238	0.026
D-dimer		2451	997-4955		4083	1898-6376	0.045

SD: Standard deviation.

survived patient group. Serum creatinine, LDH, Troponin T, ferritin, D-dimer, and CRP results were higher after the treatment in non-survivors. The clinical and laboratory parameters of patients are shown in Table 1 and Table 2.

DISCUSSION

Acute kidney injury is common among patients hospitalized with COVID-19 and is associated with high mortality.[5] Mortality was 50%-60.5% among patients in COVID-19-positive AKI patients.[1,6] In a study by Yan et al.[7] including 882 COVID-19 patients, the mean age of patients was 71, and patients with AKI had higher mortality than those without AKI (59.1% *vs.* 7.8%; p<0.001). In another study, Li et al.[8] found that patients with AKI had a significantly higher risk for in-hospital mortality than severely and critically ill patients without AKI. Similarly, in another study Xu et al.[9] reported that the risk of in-hospital mortality was highest in patients with COVID-19 and AKI [odds ratio (OR) 80.3, 95% confidence interval (CI) (27.3-235.6)], followed by COVID-19 without AKI [16.3 (6.28-42.4)]. Acute kidney injury is a common and serious complication of COVID-19. Older age and having severe COVID-19 were independent risk factors for AKI. A meta-analysis conducted in 2020 showed that the risk of in-hospital mortality was significantly increased in patients with COVID-19 complicated by AKI.[10] In a study by Ng et al.[11] of the 3,216 patients with AKI, a total of 1,491 (46.4%) died. Acute kidney injury in hospitalized patients with COVID-19 is associated with a significant risk of death. Mortality is higher in our patient group. The high mortality rate of our patients may be due to the fact that the patients are severely ill that they need intensive care follow-up and they are of advanced age.

The prognostic nutritional index, which is calculated from the serum albumin concentration and total lymphocyte count in peripheral blood, is an index that reflects chronic inflammation, immune system, and nutritional status and indicates prognostic significance in different patients.[12] The prognostic nutritional index had been described as a simple and objective indicator of adverse outcomes not only in chronic conditions but also in acute illnesses, including acute coronary syndrome, acute heart failure, and stroke.[13] Although it did not reach statistical significance in our study, PNI values were found to be lower in the non-survivor group at the time of hospital admission (32.1±7.2 *vs.* 34.6±7.7; p=0.162). This may be due to the small number of our patient group. In our study after favipiravir treatment, the mean PNI of the patients who survived was higher than in

non-survivors (32.4±7.2 *vs.* 25.2±6.3; p=0.049). In a study with a larger number of COVID-19 patients (n=450); a comparison of baseline characteristics showed non-survivors had higher age (p<0.001) and lower PNI (p<0.001).[14] There is no study in the literature investigating the relationship between PNI and mortality in patients with COVID-19-positive AKI. A low prognostic nutritional index was significantly associated with postoperative complications and survival in patients undergoing cardiovascular surgery.[15] Similarly, in another study PNI values ≤34 were associated with a two-fold higher risk of overall mortality and a three-fold higher risk of in-hospital mortality in elderly patients hospitalized for acute heart failure.[16]

The neutrophil-lymphocyte ratio is a common and quick index of inflammation detection in laboratory examination. It is used in the diagnosis, treatment, and prognosis evaluation of pneumonia.[17] In addition, NLR constitutes a novel prognostic marker for oncologic, cardiovascular, and infectious diseases. Based on this, studies investigating the prognostic value of NLR in COVID-19 infection were conducted.[18-20] In our study; leucocyte, neutrophil count, and NLR were higher in non-survivors. Similarly, we found the ferritin, D-dimer, and CRP values to be statistically significantly higher in the non-survivor group. In the study of Wang et al.[21] they found that the patients with a high level of CRP, NLR, or D-dimer performed shorter overall survival time (all p<0.05). They reported that the combination of CRP, NLR, and D-dimer could be an effective predictor for aggravation and death in patients with COVID-19.

There are studies/reviews conducted on the treatment of COVID-19.[22-25] The efficacy of favipiravir treatment is still unclear. In our patient group, all patients were treated with favipiravir. It is not possible to evaluate the efficacy of favipiravir treatment due to the small number of our patients. The small sample size and retrospective nature are the major limitations of our study.

In conclusion, AKI in hospitalized patients with COVID-19 was associated with high mortality. The prognostic nutritional index may be a useful clinical marker that can be used for estimating survival in COVID-19 patients.

Ethics Committee Approval: The study protocol was approved by the Gumushane University Ethics Committee (date: 23.02.2022, no: 2022/1). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Chan L, Chaudhary K, Saha A, Chauhan K, Vaid A, Zhao S, et al. AKI in hospitalized patients with COVID-19. J Am Soc Nephrol 2021;32:151-60. doi: 10.1681/ASN.2020050615.
2. Hirsch JS, Ng JH, Ross DW, Sharma P, Shah HH, Barnett RL, et al. Acute kidney injury in patients hospitalized with COVID-19. Kidney Int 2020;98:209-18. doi: 10.1016/j.kint.2020.05.006.
3. Epic Health Research Network. Acute kidney injury in admitted COVID-19 patients. Epic Health Research Network. Published July 1, 2020. Available at: https: //www.ehrn.org/acute-kidney-injury-in-admitted-covid-19-patients/ [Accessed: July 11, 2020]
4. Ricci Z, Cruz D, Ronco C. The RIFLE criteria and mortality in acute kidney injury: A systematic review. Kidney Int 2008;73:538-46. doi: 10.1038/sj.ki.5002743.
5. Chand S, Kapoor S, Orsi D, Fazzari MJ, Tanner TG, Umeh GC, et al. COVID-19-associated critical illness-report of the first 300 patients admitted to intensive care units at a New York city medical center. J Intensive Care Med 2020;35:963-70. doi: 10.1177/0885066620946692.
6. Kolhe NV, Fluck RJ, Selby NM, Taal MW. Acute kidney injury associated with COVID-19: A retrospective cohort study. PLoS Med 2020;17:e1003406. doi: 10.1371/journal.pmed.1003406.
7. Yan Q, Zuo P, Cheng L, Li Y, Song K, Chen Y, et al. Acute kidney injury is associated with in-hospital mortality in older patients with COVID-19. J Gerontol A Biol Sci Med Sci 2021;76:456-62. doi: 10.1093/gerona/glaa181.

8. Li Q, Zhang T, Li F, Mao Z, Kang H, Tao L, et al. Acute kidney injury can predict in-hospital mortality in elderly patients with COVID-19 in the ICU: A single-center study. Clin Interv Aging 2020;15:2095-107. doi: 10.2147/CIA.S273720.
9. Xu H, Garcia-Ptacek S, Annetorp M, Bruchfeld A, Cederholm T, Johnson P, et al. Acute kidney injury and mortality risk in older adults with COVID-19. J Nephrol 2021;34:295-304. doi: 10.1007/s40620-021-01022-0.
10. Lin L, Wang X, Ren J, Sun Y, Yu R, Li K, et al. Risk factors and prognosis for COVID-19-induced acute kidney injury: A meta-analysis. BMJ Open 2020;10:e042573. doi: 10.1136/bmjopen-2020-042573.
11. Ng JH, Hirsch JS, Hazzan A, Wanchoo R, Shah HH, Malieckal DA, et al. Outcomes among patients hospitalized with COVID-19 and acute kidney injury. Am J Kidney Dis 2021;77:204-15.e1. doi: 10.1053/j.ajkd.2020.09.002.
12. Hong X, Cui B, Wang M, Yang Z, Wang L, Xu Q. Systemic immune-inflammation index, based on platelet counts and neutrophil-lymphocyte ratio, is useful for predicting prognosis in small cell lung cancer. Tohoku J Exp Med 2015;236:297-304. doi: 10.1620/tjem.236.297.
13. Hu Y, Cao Q, Wang H, Yang Y, Xiong Y, Li X, et al. Prognostic nutritional index predicts acute kidney injury and mortality of patients in the coronary care unit. Exp Ther Med 2021;21:123. doi: 10.3892/etm.2020.9555.
14. Wang R, He M, Yin W, Liao X, Wang B, Jin X, et al. The prognostic nutritional index is associated with mortality of COVID-19 patients in Wuhan, China. J Clin Lab Anal 2020;34:e23566. doi: 10.1002/jcla.23566.
15. Hayashi J, Uchida T, Ri S, Hamasaki A, Kuroda Y, Yamashita A, et al. Clinical significance of the prognostic nutritional index in patients undergoing cardiovascular surgery. Gen Thorac Cardiovasc Surg 2020;68:774-9. doi: 10.1007/s11748-020-01300-x.
16. Candeloro M, Di Nisio M, Balducci M, Genova S, Valeriani E, Pierdomenico SD, et al. Prognostic nutritional index in elderly patients hospitalized for acute heart failure. ESC Heart Fail 2020;7:2479-84. doi: 10.1002/ehf2.12812.
17. Reddy KS, Lsymj M. Role of the neutrophil-lymphocyte count ratio in the differential diagnosis between pulmonary tuberculosis and bacterial community-acquired pneumonia. J Assoc Physicians India 2020;68:82.
18. Basbus L, Lapidus MI, Martingano I, Puga MC, Pollán J. Neutrophil to lymphocyte ratio as a prognostic marker in COVID-19. Medicina (B Aires) 2020;80 Suppl 3:31-6.
19. Ye W, Chen G, Li X, Lan X, Ji C, Hou M, et al. Dynamic changes of D-dimer and neutrophil-lymphocyte count ratio as prognostic biomarkers in COVID-19. Respir Res 2020;21:169. doi: 10.1186/s12931-020-01428-7.
20. Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. Int Immunopharmacol 2020;84:106504. doi: 10.1016/j.intimp.2020.106504.
21. Wang Q, Cheng J, Shang J, Wang Y, Wan J, Yan YQ, et al. Clinical value of laboratory indicators for predicting disease progression and death in patients with COVID-19: A retrospective cohort study. BMJ Open 2021;11:e043790. doi: 10.1136/bmjopen-2020-043790.
22. Joshi S, Parkar J, Ansari A, Vora A, Talwar D, Tiwaskar M, et al. Role of favipiravir in the treatment of COVID-19. Int J Infect Dis 2021;102:501-8. doi: 10.1016/j.ijid.2020.10.069.
23. Ghasemnejad-Berenji M, Pashapour S. Favipiravir and COVID-19: A simplified summary. Drug Res (Stuttg) 2021;71:166-70. doi: 10.1055/a-1296-7935.
24. Kaya B, Barutcu Atas D, Tukenmez Tigen E, Asicioglu E, Arikan H, Tuglular S, et al. Favipiravir use in kidney transplant recipients with COVID-19: A single-center experience. Exp Clin Transplant 2022;20:143-9. doi: 10.6002/ect.2021.0252.
25. Cismaru C, Elec AD, Muntean A, Moisoiu T, Lupşe M, Antal O, et al. Favipiravir in kidney transplant recipients with COVID-19: A Romanian case series. Transplant Proc 2022;54:1489-93. doi: 10.1016/j.transproceed.2021.12.011.