Orjinal Araştırma **Van Sağ. Bil. Derg.** *2024; 17(2): 69-75.*
Original Research *https://doi.org/10.52976/vansaglik.1354802*

Nephrological Problems in COVID19 Patients:A Retrospective Single Centre Study

COVID-19 Hastalarında Nefrolojik Problemler: Retrospektif Tek Merkezli Çalışma

Ergin Karadaş[1], Mehmet Erdem[*2]*

[1]Department of Internal Medicine, Ozalp State Hospital, Van, Türkiye

[2]Department of Internal Medicine, Van Yuzuncu Yil University, Van, Türkiye

Cited: Karadaş E, Erdem M (2024). Nephrological problems in COVID19 patients: A retrospective single centre study. *Van Sağlık Bilimleri Dergisi*, 17(2),69-75.

ABSTRACT

Objective: The SARS CoV-2 virus that emerged in 2019 and the emerging pandemic are full of journeys. The nephrological effects of the pandemic have been a matter of curiosity. In this study, nephrological problems were investigated in COVID-19 positive patients hospitalized in clinical and intensive care units.

Material and Method: The research is an observational cross-sectional retrospective study. Between November 2020 and November 2021, blood and urine analyzes sent from patients aged 18-90 who were followed up in the COVID-19 Intensive Care Unit and COVID-19 clinics were examined. 79 patients were included in the study. The diagnosis of COVID-19 was made by considering reverse-transcriptase polymerase chain reaction test, thorax computed tomography and clinical situation. These 79 patients were compared in terms of acute kidney injury, electrolyte imbalance and complete urinalysis disorders.

Results: Acute kidney injury was detected in 32.9% of patients. 42.3% of patients with acute kidney injury were female, 57.7% were male. 73.1% of the patients with acute kidney injury were hospitalized in the intensive care unit. Hematuria and proteinuria were detected in 65% and 27%, respectively. In the examinations performed, 65% hematuria, 27% proteinuria, 44% hyponatremia, 4% hypernatremia, 13% hypokalemia, 11% hyperkalemia, 11% hypophosphatemia, 6% hyperphosphatemia, 9% hypomagnesemia, 3% hypermagnesemia, 24% hypocalcemia and 65% hypoalbuminemia were detected.

Conclusion: Acute kidney injury, hematuria and proteinuria were statistically significant in patients diagnosed with COVID-19 and hospitalized and followed up. There are also electrolyte imbalances and hypoalbuminemia in patients. Follow-up of patients with COVID-19 should be carefully monitored in terms of nephrology.

Keywords: *COVID-19, Acute kidney injury, Hematuria, Proteinuria, Electrolyte Imbalance*

ÖZET

Giriş: 2019 yılında ortaya çıkan SARS CoV-2 virüsü ve meydana getirdiği pandemi tüm dünyayı etkisi altına almıştır. Pandeminin nefrolojik etkileri merak konusu olmuştur. Bu çalışmada klinik ve yoğun bakımda yatan COVID-19 pozitif hastalarda nefrolojik problemler araştırıldı.

Materyalve Metot: Araştırma gözlemsel kesitsel retrospektif bir çalışmadır. Kasım 2020 –Kasım 2021 tarihleri arasında COVID-19 Yoğun Bakım Ünitesi ve COVID-19 kliniklerinde takip edilen 18-90 yaş arası hastalardan gönderilen kan ve idrar tahlilleri incelendi. Çalışmaya 79 hasta dahil edildi. COVID-19 tanısı, revers-transkriptaz polimeraz zincir reaksiyonu testi, toraks bilgisayarlı tomografi ve klinik durum gözetilerek konuldu. Bu 79 hastanın akut böbrek hasarı, elektrolit imbalansı ve tam idrar tetkiki bozuklukları açısından karşılaştırılması yapıldı. Ayrıca COVID-19 tanılı grupta hastaların yaş, cinsiyet bilgileri ve yattığı klinik açısından da karşılaştırması yapıldı.

Bulgular: Hastaların %32,9 unda akut böbrek hasarı tespit edildi. Akut böbrek hasarı olan hastaların %42,3'ü kadın, %57,7'si erkek idi. Akut böbrek hasarı olan hastaların %73,1'i yoğun bakımda yatan hastalar idi. Yapılan tetkiklerde %65 hematüri, %27 proteinüri %44'ünde hiponatremi, %4'ünde hipernatremi, %13'ünde hipokalemi, %11 hiperkalemi, %11 hipofosfatemi, %6 hiperfosfatemi, %9 hipomagnezemi, %3 hipermagnezemi, %24 hipokalsemi ve %65 hipoalbuminemi tespit edildi.

Sonuç: COVID-19 tanısı alan ve yatırılıp takip ve tedavisi yapılan hastalarda akut böbrek hasarı, hematüri ve proteinüri istatistiksel olarak anlamlı sonuç verdi. Ayrıca hastalarda elektrolit imbalansı ve hipoalbuminemi de mevcuttur. C0VİD-19 hastalarının takipleri nefrolojik açıdan dikkatle izlenmelidir.

***Anahtar kelimeler*:** *COVID-19, Akut böbrek hasarı, Hematüri, Proteinüri, Elektrolit İmbalansı*

**Corresponding author: Mehmet Erdem. E-mail:* dr.mehmet_erdem65@hotmail.com.
ORCIDS: Ergin Karataş: 0009-0007-9195-1299, *Mehmet Erdem*: 0000-0001-5439-9473

Received: 04.09.2023, Accepted: 13.06.2024 and Publeshed: 30.08.2024

INTRODUCTION

The outbreak of SARS-CoV-2 infection was officially declared a pandemic by the World Health Organization (WHO) on March 11, 2020 and designated "Coronavirus Disease 2019 (COVID-19)" (Park, 2020). COVID-19 is a respiratory disease that was first identified in Wuhan, China, in December 2019 (Lai et al., 2020). The first case was reported in Turkey on March 10, 2020 (Yeşilbağ and Aytoğu, 2020).

Coronaviruses are medium-sized, enveloped, positive-sense single-stranded RNA viruses with a crown-like appearance (Nakagawa and Miyazawa, 2020). While some types of coronaviruses cause mild symptoms similar to the common cold in humans, others lead to severe respiratory illness and even death (Chan et al., 2020). SARS-CoV-2 spreads primarily through droplets (Rothan and Byrareddy, 2020). Cough, muscle pain, and headache are the most commonly reported symptoms in COVID-19 patients (Table 1). In addition, symptoms such as diarrhea, sore throat, and abnormalities in smell or taste have been well-defined (Huang et al., 2020). The importance of laboratory findings is noteworthy, as they play a crucial role in determining the severity of the disease and assessing the risk of potential complications such as acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC), and multiorgan failure. It has been observed that COVID-19 primarily affects the kidneys, after the lungs in infected patients (Cheng et al., 2020).

The etiopathogenesis of acute kidney injury (AKI) associated with COVID-19 is thought to be primarily due to a cytokine storm. A cytokine storm is a severe hyperreaction of the immune system characterized by the rapid and excessive release of cytokines into systemic circulation. Dehydration, nephrotoxic agents, mechanical ventilation, direct immune-mediated renal cell injury, fever, and other multifactorial interactions are involved (Stasi et al., 2020). The detection of live SARS-CoV-2 in the urine of COVID-19 patients suggests a direct effect of the virus on renal tubules. SARS-CoV-2 is thought to induce acute tubular necrosis through direct cytopathic effects. Su et al. demonstrated the presence of virus particles in tubular cells and podocytes in renal biopsy analyses (Su et al., 2020). Clinical signs of AKI include oliguria or anuria. Laboratory findings in AKI include hyperkalemia, acidemia, hypocalcemia, hyperphosphatemia, and hypermagnesemia (Kellum et al., 2012). Life-threatening complications of AKI may include pulmonary edema, severe acidosis, and hyperkalemia, all of which require immediate evaluation and treatment (Fortenberry et al., 2013). Treatment of AKI should be based on three main principles: ensuring optimal intravascular volume, providing symptomatic supportive care (including appropriate nutritional support, discontinuation of nephrotoxic drugs, treatment of hyperkalemia, hyperphosphatemia, hypocalcemia, acidosis, and hypertension), and targeted therapies for etiology (Spasovski et al., 2014).

MATERIAL and METHOD

This retrospective and single-center study was conducted in the Covid-19 3rd Level Intensive Care Unit and Covid-19 Clinics of Dursun Odabaş Medical Center, Van Yüzüncü Yıl University Faculty of Medicine.

The study involved COVID-19 patients aged 18 years and older who were hospitalized in the Covid-19 Intensive Care Unit and Clinics of Dursun Odabaş Medical Center between November 2020 and November 2021. The diagnosis of COVID-19 was confirmed by RT-PCR tests, thoracic CT scans, and clinical assessments.

Only patients with a definite diagnosis of COVID-19 and aged 18 to 90 years were included in the study. Individuals with an inconclusive diagnosis of COVID-19, pregnant patients, and individuals younger than 18 years were excluded from the study.

Statistical Analysis: The data collected during the study were analyzed with the statistical software package, IBM SPSS with a confidence level of 95% (p=0.05). Frequency and percentage distributions of the groups were generated. Pairwise group comparisons were performed using the chi-square test, and results for Pearson's chi-square, Fisher's exact test, and odds ratios were reported.

RESULTS

A total of 79 patients, were enrolled in our study, of whom 44 (56%) were female and 35 (44%) were male, all of whom were treated in the intensive care unit and clinic with a diagnosis of COVID-19. Among these 79 patients, 26 (32.9%) were diagnosed with AKI. The mean age of females was 64.9 ± 17.36 years, whereas the mean age of males was 59.7 ± 18.36 years. AKI was present in 11 (42.3%) of females and 15 (57.7%) of males.

Of the 79 patients, 36 (46%) were admitted to the intensive care unit, and 43 (54%) were followed up in the regular clinic setting. Of the patients with AKI, 19 (73.1%) were in the intensive care unit, while 7 (26.9%) were among those treated in the clinic. The location of hospitalization significantly influenced renal injury. Specifically, the likelihood that a patient was in the intensive care unit increased the risk of AKI by 5.8-fold (Table 2).

Hematuria was observed in 51 patients (65%), 21 of whom had AKI. The presence of AKI was associated with hematuria in 84% of cases, while 58.8% of patients without AKI also had positive hematuria findings. Statistical analysis revealed a significant association between hematuria and renal impairment ($p<0.05$), meaning that the likelihood of AKI increased 3.7-fold in the presence of hematuria (Table 2).

Proteinuria was detected in 21 patients (27%). Of these, 7 had trace proteinuria, 9 had 1+ proteinuria, and 5 had 2+ proteinuria. Of the patients with AKI, 13 (52%) had proteinuria. The association between proteinuria and renal injury was statistically significant ($p<0.05$), showing a 5.6-fold increased likelihood of AKI in the presence of proteinuria (Table 2).Regarding electrolyte imbalance, 35 patients (44%) had hyponatremia, while hypernatremia was observed in 3 patients (4%). Of the patients with AKI, 11 (42.3%) had hyponatremia. In addition, 10 patients (13%) had hypokalemia, and 9 (11%) had hyperkalemia. Among the patients with AKI, 6 (66.7%) had hyperkalemia. Furthermore, 19 patients (24%) had hypocalcemia, 6 (8%) had hyperphosphatemia, and 11 (14%) had hypophosphatemia. Finally, 9 patients (11%) had hypomagnesemia (Table 3)

Table 1. Common symptoms of COVID-19

50% cough
43% fever (subjective or >100.4°F/38°C)
36% myalgia
34% headache
29% shortness of berath
20% throat pain
19% diarrhea
12% nausea and vomiting
Each of the following symptoms was observed in less than 10% of the patients: loss of smell or taste, abdominal pain, and runny nose.

Table 2. Relationship between AKI and gender, clinical service, hematuria, and proteinuria

	Acute Kidney Injury				
	Positive n (%)	**Negative n (%)**	**Total n (%)**	***p***	**OR (%95CI)**
Render					
Female	11 (42.3)	33 (62.3)	44 (56)	0.147	
Male	15 (57.7)	20 (37.7)	35 (44)		
Clinical Service					
Intensive Care	19 (73.1)	17 (32.1)	36 (46)	0.001	5.8 (2-16.3)
Clinic	7 (26.9)	36 (67.9)	43 (54)		
Hematuria					
Positive	21 (84)	30 (58.8)	51 (65)	0.038	3.7 (1.1-12.3)
Negative	4 (16)	21 (41.2)	25 (32)		
Proteinuria					
Positive	13 (52)	8 (16.3)	21 (27)	0.02	5.6 (1.9-16.5)
Negative	12 (48)	41 (83.7)	53 (67)		

Ki-SquareTesttableandOddsratio-%95ConfidenceIntervalvalues.

Regarding electrolyte imbalance, 35 patients (44%) had hyponatremia, while hypernatremia was observed in 3 patients (4%). Of the patients with AKI, 11 (42.3%) had hyponatremia. In addition, 10 patients (13%) had hypokalemia, and 9 (11%) had hyperkalemia. Among the patients with AKI, 6 (66.7%) had hyperkalemia. Furthermore, 19 patients (24%) had hypocalcemia, 6 (8%) had hyperphosphatemia, and 11 (14%) had hypophosphatemia. Finally, 9 patients (11%) had hypomagnesemia (Table 3)

Table 3. Comparison of patients regarding electrolyte imbalance

	Acute Kidney Injury		
	Positive n (%)	**Negative n (%)**	**Total n (%)**
Sodium (Na)			
Low	11 (42.3)	24 (45.3)	35 (44)
Normal	12 (46.2)	29 (54.7)	41 (52)
High	3 (11.5)	0	3 (4)
Potassium (K)			
Low	3 (30)	7 (70)	10 (13)
Normal	17 (28.3)	43 (71.7)	60 (76)
High	6 (66.7)	3 (33.3)	9 (11)
Calcium (Ca)			
Low	7 (36.8)	12 (63.2)	19 (24)
Normal	18 (31)	40 (69)	58 (73)
Phosphorus (P)			
Low	6 (54.5)	5 (45.5)	11 (14)
Normal	11 (28.9)	27 (71.1)	38 (48)
High	4 (66.7)	2 (33.3)	6 (8)
Magnesium (Mg)			
Low	5 (55.6)	4 (44.4)	9 (11)
Normal	16 (32.7)	33 (67.3)	49 (62)
High	1 (33.3)	2 (66.7)	3 (4)

Ki-SquareTesttable. The results were not statistically significant due to the limited sample sizes in some groups.

DISCUSSION

Patients with suspected or confirmed COVID-19 may have AKI as part of their overall illness (Yang et al., 2020). Two extensive observational studies conducted in a cohort of over 5000 COVID-19 hospitalized patients reported AKI incidence rates ranging from 32% to 37% (Bowe et al., 2021). Several independent predictors of AKI have been identified, including advanced age, male sex, African-American ethnicity, obesity, diabetes, hypertension, cardiovascular disease, low estimated glomerular filtration rate (e-GFR), elevated interleukin-6 levels, and the need for mechanical ventilation or vasopressor therapy (Chan et al., 2021). Among the various speculations about the pathogenesis of AKI in the course of COVID-19, one hypothesis suggests direct penetration of the virus into the renal tubules and glomeruli. This intriguing concept has led to autopsy studies that have indeed demonstrated the presence of viral particles and viral antigenic structures in various renal tissues, particularly in proximal tubules and podocytes (Su et al., 2020). Furthermore, it is worth noting that the hemodynamic changes associated with cytokine release syndrome in COVID-19 patients may also contribute to the development of acute tubular necrosis (ATN) (Martinez-Rojas et al., 2020). In our study, the prevalence of AKI in COVID-19 patients was 32.9%, which is consistent with the existing literature.

In COVID-19 patients, renal involvement may manifest as AKI, hematuria, or proteinuria, and is associated with a higher risk of mortality (Larsen et al., 2020). Hematuria and proteinuria, especially with predominant albuminuria, are the most common urinary findings before the full clinical development of AKI. In one study, proteinuria was found in 44% of cases, hematuria in 26.9%, and increased creatinine levels in 15.5% of patients on admission. In a small percentage (3.2%) of cases, AKI was detected in the first days of the study (Karras et al., 2021). Hong et al., who studied the incidence of early renal damage, demonstrated abnormalities of eGFR (66.7%), creatinine clearance (41.7%), and microalbuminuria (41.7%) in patients who did not have significant increases in BUN and creatinine levels (Hong et al., 2020). In our study, hematuria was observed in 65% and proteinuria in 27% of the patients. Moreover, 84% of patients had hematuria, and 13% had proteinuria, which is in good agreement with the existing literature.

In a study conducted in Hubei, China, 1254 patients diagnosed with COVID-19 were included. Hyponatremia was found in 9.9% of them and hypernatremia in 2.4%. Regarding the etiology of hyponatremia, gastrointestinal sodium losses due to diarrhea or vomiting could explain this fluid-electrolyte disturbance only in a minority of patients (8.7% diarrhea, 3.3% vomiting). Hypernatremia was less common in COVID-19 patients compared with hyponatremia (Hu et al., 2021). In our study, hyponatremia was found in

44% of patients and hypernatremia in 4%. Hyponatremia was observed in 42.3% of patients with AKI. These findings add to the growing body of evidence of the various renal manifestations and electrolyte imbalances observed in COVID-19 patients.

The results of a study conducted in Wenzhou, China, involving 179 COVID-19 patients, showed that hypokalemia was a significant electrolyte abnormality affecting 55% of the patients (Chen et al., 2020). Based on these results, the authors suggested that the main cause of hypokalemia was a disruption of ACE-2 by binding SARS-CoV-2 (Chen et al., 2020). In our study, hypokalemia was found in 13% of patients and hyperkalemia in 11%.

Cappellini et al. performed a comparative analysis of the calcium profiles of 420 COVID-19-diagnosed patients and 165 non-COVID-19 patients and found that COVID-19 patients had considerably lower serum total calcium and ionized calcium levels compared to non-COVID-19 patients. However, it was not presented whether the two groups matched in terms of disease severity (Cappellini et al., 2020). The hypocalcemia observed in COVID-19 could be attributed to the direct effect of SARS-CoV-2 or an imbalance of parathyroid hormone and/or 25-hydroxyvitamin D (Nieto-Torres et al., 2014). In our study, hypocalcemia was found in 24% of patients.

Gastrointestinal and renal tissues may be damaged by a cytokine storm and an overactive immune-inflammatory response, resulting in impaired phosphate reabsorption. Consequently, the frequent intestinal dysfunction and AKI observed in COVID-19 patients may be additional risk factors for hypophosphatemia (Ghosn et al., 2021). In our study, hypophosphatemia was observed in 14% of patients and hyperphosphatemia in 8%. Therefore, it is crucial to monitor patients closely for hypophosphatemia.

It has been reported that magnesium supplementation might have positive effects on COVID-19-related complications such as pulmonary fibrosis and thrombosis (De Baaij et al., 2015). Additionally, COVID-19 may induce a cytokine storm, leading to ATP depletion and, consequently, the need for phosphate and magnesium. Therefore, it is important to provide magnesium to patients (van Kempen and Deixler, 2021). In our study, hypomagnesemia was observed in 11% of patients. Thus, the supply of magnesium is crucial to prevent potential complications associated with hypomagnesemia.

Conclusion

In this retrospective, single-center study, we assessed the prevalence of AKI, hematuria, proteinuria, and electrolyte imbalances in COVID-19 patients. The results highlight the importance of a multidisciplinary approach to the monitoring and effective management of these renal complications effectively. Timely interventions and appropriate electrolyte replacement strategies are critical for addressing the observed nephrological disorders in these patients.

Given the impact of these renal manifestations, it is crucial to emphasize the need for long-term follow-up for COVID-19 patients. Integrating comprehensive monitoring protocols and targeted interventions may contribute to better management of COVID-19-associated renal impairment.

Our study aimed to investigate the effects of COVID-19 on the kidneys, and the results are consistent with existing literature, which is supportive of COVID-19-induced renal complications. Nevertheless, further comprehensive studies are needed to fully comprehend the chronic effects of COVID-19 on renal function. Further research efforts will allow us to unravel the underlying mechanisms and develop tailored therapeutic approaches to effectively address the nephrological problems associated with COVID-19.

Conflict of Interest

The authors declare that there is no conflict of interest

Financial Support

None declared

Ethics Approval

The required approval for conducting the study was obtained from the Ethics Committee of the Faculty of Medicine, Van Yuzuncu Yil University (Date: 01.03.2022/ Number 174273).

REFERENCES

Bowe B, Cai M, Xie Y, Gibson AK, Maddukuri G, et al. (2021). Acute kidney injury in a national cohort of hospitalized US veterans with COVID-19. *Clinical Journal of the American Society of Nephrology,* 16(1), 14.

Cappellini F, Brivio R, Casati M, Cavallero A, Contro E, et al. (2020). Low levels of total and ionized calcium in blood of COVID-19 patients. *Clinical Chemistry and Laboratory Medicine (CCLM)* 58(9), e171-173.

Chan JFW, Kok KH, Zhu Z, Chu H, To KKW, et al. (2020). Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerging Microbes &Infections* 9(1), 221-236.

Chan L, Chaudhary K, Saha A, Chauhan K, Vaid A, et al.(2021). AKI in hospitalized patients with COVID-19. *Journal of the American Society of Nephrology,* 32(1), 151.

Chen D, Li X, Song Q, Hu C, Su F, et al.(2020). Assessment of hypokalemia and clinical

characteristics in patients with coronavirus disease 2019 in Wenzhou, China. *JAMA Network Open* 3(6), e2011122.

Cheng Y, Luo R, Wang K, Zhang M, Wang Z, et al.(2020). Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney International* 97(5), 829-838.

De Baaij J. H, Hoenderop J. G. J, Bindels R. J. M, et al. (2015). Magnesium in man: implications for health and disease. Physiological Reviews, 95(1),1-46.

Fortenberry JD, Paden ML, Goldstein SL (2013). Acute kidney injury in children: an update on diagnosis and treatment. *Pediatric Clinics* 60(3), 669-688.

Ghosn M, Attallah N, Badr M, Abdallah K, Oliveira BD et al. (2021). Severe acute kidney injury in critically ill patients with COVID-19 admitted to ICU: incidence, risk factors, and outcomes. *Journal of Clinical Medicine,* 10(6), 1217.

Hong X, Chi Z, Liu G, Huang H, Guo S et al. (2020). Analysis of early renal injury in COVID-19 and diagnostic value of multi-index combined detection. *MedRxiv*: 2020.2003. 2007.20032599.

Hu W, Lv X, Li C, Xu Y, Qi Y, et al. (2021). Disorders of sodium balance and its clinical implications in COVID-19 patients: a multicenter retrospective study. *Internal and Emergency Medicine,* 16, 853-862.

Huang C, Wang Y, Li X, Ren L, Zhao J, et al. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* 395(10223), 497-506.

Karras A, Livrozet M, Lazareth H, Benichou N, Hulot JS, et al.(2021). Proteinuria and clinical outcomes in hospitalized COVID-19 patients: a retrospective single-center study. *Clinical Journal of the American Society of Nephrology,* 16(4), 514.

Kellum JA, Lameire N, Aspelin P, Barsoum R. S, Burdman EA, et al. (2012). Kidney disease: improving global outcomes (KDIGO) acute kidney injury work group. KDIGO clinical practice guideline for acute kidney injury. *Kidney International Supplements,* 2(1), 1-138.

Lai CC, Wang CY, Wang YH, Hsuen SC, Ko WC, et al.(2020). Global epidemiology of coronavirus disease 2019 (COVID-19): disease incidence, daily cumulative index, mortality, and their association with country healthcare resources and economic status. *International Journal of Antimicrobial Agents,* 55(4), 105946.

Larsenn CP, Bourne TD, Wilson JD, Saqqa O, Sharshir MA, (2020). Collapsing glomerulopathy in a patient with COVID-19. *Kidney International Reports,* 5(6), 935-939.

Martinez-Rojas MA, Vega-Vega O, Bobadilla N. A, (2020). Is the kidney a target of SARS-CoV-2? *American Journal of Physiology-Renal Physiology,* 318(6), 1454-1462.

Nakagawa, S. and T. Miyazawa, (2020). Genome evolution of SARS-CoV-2 and its virological characteristics. *Inflammation and Regeneration,* 40(1), 17.

Nieto-Torres JL, DeDiego ML, Verdia-Baguena C, Jimenez-Guardeno JM, Regla-Nava JA, et al. (2014). Severe acute respiratory syndrome coronavirus envelope protein ion channel activity promotes virus fitness and pathogenesis. *PLoS Pathogens* 10(5), e1004077.

Park SE (2020). Epidemiology, virology, and clinical features of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2; Coronavirus Disease-19). *Clinical and Experimental Pediatrics* 63(4), 119.

Rothan HA, Byrareddy SN, (2020). The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *Journal of Autoimmunity* 109, 102433.

Spasovski G, Vanholder R, Allolio B, Annane D, Ball S, et al. (2014). Clinical practice guideline on diagnosis and treatment of hyponatraemia. *Nephrology Dialysis Transplantation,* 29(suppl_2), 1-39.

Stasi A, Castellano G, Ranieri E, Infante B, Stallone G, et al. (2020). SARS-CoV-2 and viral sepsis: immune dysfunction and implications in kidney failure. *Journal of Clinical Medicine,* 9(12), 4057.

Su H, Yang M, Wan C, Yi L.-X, Tang F, et al. (2020). Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. *Kidney International,* 98(1), 219-227.

van Kempen TA, Deixler E (2021). SARS-CoV-2: influence of phosphate and magnesium, moderated by vitamin D, on energy (ATP) metabolism and on severity of

COVID-19. *American Journal of Physiology-Endocrinology and Metabolism,* 320(1), 2-6.

Yang X, Yu Y, Xu J, Shu H, Xia J, et al. (2020). Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. *The Lancet Respiratory Medicine,* 8(5), 475-481.

Yeşilbağ K, Aytoğu G (2020). Coronavirus host divergence and novel coronavirus (Sars-CoV-2) outbreak. *Clinical and Experimental Ocular Trauma and Infection,* 2(1), 6-14.