Research Article / Araştırma Makalesi

Comparison of Acute Kidney Injury and Mortality in Variant B.1.1.7 Positive and Negative SARS-CoV-2 Infection

Varyant B.1.1.7 Pozitif ve Negatif SARS-CoV-2 Enfeksiyonunda Akut Böbrek Yetmezliği ve Mortalitenin Karşılaştırılması

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Abstract

Background: This study aimed to compare the acute kidney injury AKI) development and mortality rates in patients with variant B.1.1.7 positive and negative SARS-CoV-2 infection.
Materials and Methods: Variant B.1.1.7 negative (group I, n:92) and 57 variant B.1.1.7 positive (group II) SARS-CoV-2 patients were included in the study. Demographic data, comorbidities, the number of intensive care unit hospitalization days, the need for an invasive mechanical ventilator, number of mechanical ventilator days, whether acute renal failure developed, the day of acute renal failure development, and treatment outcome were recorded for each patient.
Results: Group I patients (31/92 -33.7%) developed acute kidney injury at a higher rate than group II patients (17/57 -29.8%) (p=0.04). 46/92 (50%) patients in group I and 38/57 (66.7%) patients in group II received invasive mechanical ventilation support (p <0.05). The mortality rate of patients without AKI development was higher in group II [22/40 (55%)] than group I [19/61 (31.2%)] (p<0.05).
Conclusions: C It was determined that the development of acute kidney injury in patients with critical illness and variant B.1.1.7 infection followed was less than in the other patients. This result suggested that the increase in mortality in variant B.1.1.7 infection occurred independently of the development of acute kidney injury.

Key Words: COVID-19, Variant B.1.1.7, Acute kidney injury, Mortality

ÖZ.

Amaç: Bu çalışmada varyant B.1.1.7 pozitif ve negatif SARS-CoV-2 enfeksiyonu olan hastalarda akut böbrek hasarı gelişimi ve mortalite oranlarının karşılaştırılması amaçlanmıştır.
Materyal ve Metod: Çalışmaya varyant B.1.1.7 negatif 92 (grup I) ve 57 varyant B.1.1.7 pozitif 57 (grup II) SARS-CoV-2 hastası dahil edildi. Her hastanın demografik verileri, komorbiditeleri, yoğun bakım yatış gün sayıları, invaziv mekanik ventilatör ihtiyacı, mekanik ventilatör gün sayısı, akut böbrek yetmezliği gelişip gelişmediği, gelişti ise kaçıncı günde akut böbrek yetmezliği geliştiği ve tedavinin sonlanım şekilleri kaydedildi.
Bulgular: Grup I hastalarda 31/92 (33.7%) Grup I hastalara 17/57 (29.8%) göre daha fazla oranda akut böbrek hasarı gelişti (p=0.04). Grup I'de 46/92 (50 %) grup II'de 38/57 (66.7%) hasta hasta invaziv mekanik ventilasyon desteğine alındı (p <0.05). Akut böbrek hasarı gelişmeyen hastaların mortalite oranı grup II'de 22/40 (55%) grup I'e 19/61 (31.2%) göre daha yüksekti (p<0.05).
Sonuç: aryant B.1.1.7 enfeksiyonu olan hastalarda akut böbrek hasarı gelişiminin diğer grup hastalara göre daha az olduğu saptanmıştır. Varyant B.1.1.7 enfeksiyonundaki mortalite artışının akut böbrek hasarı gelişiminden bağımsız olarak gerçekleştiğini düşündürmektedir.

Anahtar kelimeler: COVID-19, Varyant B.1.1.7, Akut böbrek hasarı, Mortalite

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Received / Geliş tarihi: 29.01.2022

Accepted / Kabul tarihi: 01.04.2022

DOI: 10.35440/hutfd.1064849

Introduction

COVID-19 disease remains a significant health problem. The clinical course of this disease may range in a broad spectrum from asymptomatic infection to multiple organ failure and death (1-3). Since there is a high rate of lung involvement in COVID-19 disease, patients developing acute hypoxic respiratory failure (AHRF) and acute respiratory distress syndrome (ARDS) have been the subject of most scientific studies (1,2,4). In Covid-19 disease, apart from the lungs kidney, heart, central nervous system and gastrointestinal system are also affected (1- 5).

The pathophysiology of acute kidney injury (AKI) due to COVID-19 disease has not been fully understood. Therewithal causes such as nephrotoxic drugs, renal hypoperfusion, viral cytopathic activity, cytokine storm, and microvascular thrombosis are emphasized (5).

AKI is considered the second most common cause of death in critically ill patients after ARDS (4,6). Although there are studies on the AKI development due to SARS-CoV-2, no study has been found in the literature on the AKI development in variant B.1.1.7 infection. This study aimed to compare the AKI development and mortality rates in patients with SARS-CoV-2 variant B.1.1.7 positive and negative.

Materials and Methods

This study was performed as a single-center, cross-sectional and retrospective study in the privatized intensive care unit of Samsun Training and Research Hospital for Covid-19 treatment between February 1, 2021, and March 31, 2021. The study was conducted following the approval of the Ministry of Health Scientific Committee (Local Ethics Committee dated 01.05.2021 and numbered Non-Interventional Clinical Research/2021/9/3).

Study population and procedure

Data were obtained from four separate privatized intensive care units for COVID-19 patient follow-up. Patients with chronic kidney failure, a history of renal transplantation, a creatinine value above 4 mg/dl at admission to the intensive care unit, less than 48 hours of hospitalization in the intensive care unit, patients who used radio contrast agent and patients younger than 18 years of age were excluded from the study.

Variant B.1.1.7 negative (group I, n: 92) and 57 variant B.1.1.7 positive (group II) SARS-CoV-2 patients with positive polymerase chain reaction test and hospitalized in intensive care unit were included in the study. In addition to the demographic data of each patient, comorbidities, the number of intensive care unit hospitalization days, the need for an invasive mechanical ventilator (IMV) support, number of days spent on a mechanical ventilator, daily creatinine values, and treatment outcome (exitus or transfer to service) were recorded.

Besides, whether AKI developed during the hospitalization, its level, and on which day it developed were recorded in the case of AKI development.

Diagnosis of coronavirus disease 2019

Bio-Speedy, SARS COV-2 Double Gene RT-qPCR kit was used to diagnose COVID-19. This kit was studied with the BioRad CFX96 RT-PCR device. "Bio-Speedy® SARS-CoV-2 + VOC202012/01 RT-qPCR/TURKEY" kit was used for COVID-19 variant detection.

Definitions

The AKI diagnosis was made by the Kidney Disease Improving Global Organization (KDIGO) criteria (7). According to these criteria; 1.5-1.9 times increase in serum creatinine level compared to basal value or 0.3 mg/dl increase in creatinine value was considered as stage 1, 2-2.9 times as stage 2, and at least 3-fold increase or serum creatinine level ≥ 4 mg/dl or the need for renal replacement therapy was considered as stage 3 (7).

Statistical analysis

The data collected in the study were analyzed using the statistical software package SPSS 24 (Statistical Package for the Social Sciences – IBM®). Descriptive statistics of independent variables depending on distribution were presented as numbers and percentages for categorical variables, mean, standard deviation, and median for numerical variables. The conformity to the normal distribution of continuous variables was evaluated with the Kolmogorov-Smirnow test and continuous variables with the Shapiro-Wilk test.

In comparing numerical variables between groups, the Mann-Whitney U test was used for two independent groups and the One Way Anova test or Kruskal- Wallis Method for more than two groups. While distribution correlation between categorical variables was examined by Chi-Square test, t-Test for Two Independent Group was used to compare the numerical data. Also, ROC Analysis was applied to determine the cut-off points for numerical variables. Results were evaluated by accepting the $p<0.05$ value as significant at a 95% confidence interval.

Results

Fifty of the ninety-two patients (50/92) (54.4%) in group I and 33/57 (57.9%) of the patients in group II were male, and there was no significant difference between the groups in terms of gender ($p >0.05$) (Table 1). Drug therapy and fluid replacement were similar for all patients. The mean age of the patients in both groups was similar (68.40 ± 14.37 years, 66.89 ± 13.60 years). The mean age of male patients (65.26 ± 14.15 years, 66.15 ± 13.48 years) and female patients (72.14 ± 13.88 years, 67.83 ± 14.18 years) in both groups were similar ($p >0.05$) (Table 1).

Table 1. Data on Gender and Age Averages of the Groups in the Study

		Group I (n:92)				Group II (n:57)				t-test	P value
		n	%	Mean±Std	Min-max	n	%	Mean±Std	Min-max		
Age (years)	Female	42	45.6	72.14±13.88	45-91	24	42.1	67.83±14.18	39-96	1,301	0,061
	Male	50	54.4	65.26±14.15	32-92	33	57.9	66.15±13.48	22-85		
	Total	92	100	68.40±14.37	32-92	57	100	66.89±13.6	22-96		

The comorbid disease was present in group I patients with 70/92 (76.1%) and 48/57 (84.2%) of group II patients. The most common comorbidities in group I patients was 34/92 (37%) hypertension and 24/92 (26.1%) diabetes mellitus, while 22/57 (38.6%) diabetes mellitus and 16/52 (28.1%) hypertension in group II patients. There was no statistically significant difference in the presence of comorbid disease in both groups (p>0.05) (Table 2).

Table 2. Data on Comorbid Diseases of the Groups in the Study

		Group I (n:92)		Group II (n:57)		t-test	P value
		n	%	n	%		
Comorbid disease	Present	70	76.1	48	84.2	1,701	0.095
	Absent	22	23.9	9	15.8		
DM*	Present	24	26.1	22	38.6	1,104	0.834
	Absent	68	73.9	35	61.4		
Hypertension	Present	34	37.0	16	28.1	-0,745	0.460
	Absent	58	63.0	41	71.9		
COPD*	Present	7	7.6	7	12.3	1,170	0.866
	Absent	86	92.4	50	87.7		
CAD*	Present	21	22.8	7	12.3	0,565	0.574
	Absent	71	77.2	50	87.7		
Liver Cirrhosis	Present	2	2.2	1	1.8	0,270	0.788
	Absent	90	97.8	56	98.2		
CANCER	Present	5	5.4	5	8.8	0,634	0.529
	Absent	87	94.6	52	91.2		
Ischemic CVD*	Present	6	6.5	4	7.0	0,481	0.632
	Absent	86	93.5	53	93		
Alzheimer's	Present	7	7.6	9	15.8	0,846	0.401
	Absent	85	92.4	48	84.2		

**CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CVD, Cerebrovascular disease; DM, diabetes mellitus*

When the groups included in the study were compared in the development of AKI and duration of AKI development, it was found that 31/92 (33.7%) of group I patients and 17/57 (29.8%) of group II patients developed AKI (p=0.04). While there was no significant difference in AKI levels for stage 1 [13/92 (14.1%) and 9/57 (12%) (p>0.05)], a significant difference was determined for stage 2 [11/92 (12%), 6/57 (respectively) 10.5%) (p=0.03)] and stage 3 [7/92 (7.6%), 2/57 (3.5%) (p=0.01)) (Table 3). Durations of AKI development were similar in both groups [4.61± 2.59 days, 4.41 ± 2.58 days, respectively, (p>0.05)]. Hemodialysis need of patients in both groups was similar 7,6% (7/92) and 3,5% (2/57) (p>0,05).

While invasive mechanical ventilation (IMV) support was 46/92 (50%) in group I patients during intensive care unit hospitalization, it was 38/57 (66.7%) (p<0.05) in group II patients. In addition, the duration of IMV was 11.39± 11.35 (1-56) days in group I, while 9.44 ± 6.15 (1-29) days in group II (p>0.05). Furthermore, the number of hospitalization days in the intensive care unit was similar in both groups [13.80 ± 11.0 (4-57) days, 12.93 ± 7.70 (4-32) days, respectively (p>0.05)].

When considering all patients included in the study, the mortality rates were 48.9% (45/92) in Group I and 63.2% (36/51) in Group II (p=0.348) (Table 3). In patients developing AKI, the mortality rate was similar in both groups [83.9% (26/31), 82.4% (14/17) (p>0.05), respectively]), but the mortality rate in patients not developing AKI was 31.2% (19/61) in group I while 55% (22/40) in group II (p<0.05).

Table 3. Mortality and Acute Kidney Injury Development Status of the Groups in the Study

		Group I (n:92)		Group II (n:57)		P value
		n	%	n	%	
Mortality	Present	45	48.9	36	63.2	0.348
	Absent	47	51.1	21	36.8	
AKI	Present	31	33.7	17	29.8	**0.043***
	Absent	61	66.3	40	70.2	
S1	Present	13	14.1	9	15.8	0.418
	Absent	79	85.9	48	84.2	
S2	Present	11	12	6	10.5	**0.031***
	Absent	81	88	51	89.5	
S3	Present	7	7.6	2	3.5	**0.014***
	Absent	85	92.4	55	96.5	

AKI: Acute Kidney Injury, S1: stage 1, S2: stage 2, S3: stage 3

Discussion

This study determined that AKI development in critically ill patients with variant B.1.1.7 infection followed in the intensive care unit was less than in other patients. In addition, it was determined that the need for IMV in variant B.1.1.7 patients and the mortality rates in variant B.1.1.7 patients not developing AKI were both higher. This suggested that the increase in mortality due to the longer duration of variant B.1.1.7 infection in the respiratory tract occurred independently of the AKI development.

In December 2019, a viral origin diffuse respiratory disease outbreak occurred in Wuhan, China (8). After the causative agent of this disease was identified as SARS-CoV-2, the World Health Organization (WHO) named this disease as 'Coronavirus Disease 2019 (COVID-19) (2,9). While the whole world is struggling with this disease, it has also had to struggle with newly emerged mutant infections. Variant B.1.1.7 infection of SARS-CoV-2 was first identified in England in December 2020 and spread worldwide (10).

It has been determined that the first step in SARS-CoV-2 infection is the entry of the virus into the cell by binding the host cell receptor. At the same time, it has also been determined that this virus has a spike protein binding to the angiotensin-converting enzyme 2 (ACE2) receptor located on the cell membrane. In publications, it has been indicated that lung type II alveolar epithelial cells, renal tubular epithelial cells, intestinal epithelial cells, and myocardial cells rich in ACE2 receptors are target cells of the virus (11-13).

The pathophysiology of AKI formation in SARS-CoV-2 infection has not been clarified (5). The viral cytopathic effect, cytokine storm, some nephrotoxic drugs, renal micro-thrombosis, hypoperfusion due to ischemia, and some comorbidities (diabetes mellitus, hypertension) are assumed in the etiology (3,5,14). Although it has been reported that COVID-19 infection did not result in AKI in the first published studies in the literature (2,15,16), varying ratios of AKI development have been reported in subsequent studies. In a meta-analysis, it has been reported that the AKI incidence was approximately 15% in COVID-19 patients during their hospital stay and 50% in critically ill patients (3). In a study by Gabarre et al., it has been reported that AKI developed in 42 (42.9%) of 99 critically ill patients (5).In our study, similar to the studies in the literature, the AKI development ratios in SARS-CoV-2 infection with and without variant B.1.1.7 were found to be 33.7% and 29.8%, respectively.

There are a limited number of studies in the literature on the development time of AKI. Li et al. (6) reported the development time of AKI as seven days after admission to the hospital and in another study 9 days after the onset of the disease (17). In our study, the development times of AKI were 4.61±2.59 and 4.41±2.58 days, respectively. Since our study population consisted of intensive care patients, some part from emergency service applications, and some part from patients developing the need for intensive care during their follow-up, the development time of AKI may be expected to be short compared to other studies.

Although the AKI development (5,18), an indicator of poor prognosis and a reason for increased mortality in COVID-19 patients, was significantly higher in patients without variant B.1.1.7 in our study, the mortality rates did not significantly differ between the two groups. Many studies have investigated the AKI development in intensive care patients with COVID-19 infection, but as far as we know, no study is investigating the AKI development and its affecting factors in SARS-CoV-2 patients with and without B.1.1.7 variant infection. We think that this study will contribute to a better understanding of SARS-CoV-2 infection.

In our study, the AKI development (especially stage 2 and 3) was lower in variant B.1.1.7 infection than SARS-CoV-2 infection. This may be due to a longer stay of variant B.1.1.7 infection in the respiratory tract.

A meta-analysis reported that the mortality risk in mutant infections was significantly higher than in regular SARS-CoV-2 infections (19). Studies have reported that the reason for this increase in mortality in mutant infections is the high viral load and longer stay in the respiratory tract

(20-21). Another study conducted in London reported that more severe hypoxia was observed in patients with B.1.1.7 variant, and this status has increased mortality together with increased virulence (22). In our study, the higher need for IMV in patients with variant B.1.1.7 supports the fact that this variant stays in the respiratory tract longer. In addition, in our study, the duration of IMV was similar in both groups, and there was no difference between the two groups in terms of mortality rate. This situation may be due to extensive organ involvement of SARS-CoV-2 infection such as kidneys, heart, central nervous system, and gastrointestinal system other than lungs, causing multiorgan failure.

Limitations

There are some limitations to our study. First, our study was conducted in a limited time and with a limited number of patients. The reason for this was that while the B.1.1.7 mutation, which started to be seen in our country at the beginning of February, was routinely studied in suspected PCR samples, it was not routinely studied after March. The second limitation is that the data used in our study were obtained from four different intensive care units. Therefore, a complete homogeneity may not have been achieved in the patients' treatment, fluid support management, and ventilator strategies.

Conclusion

For the first time in the literature, our study showed that AKI development in patients with B.1.1.7 mutation was less than in patients without it. The higher mortality and need for IMV in variant B.1.1.7 infection suggests that this variant increases mortality due to respiratory causes rather than AKI development. We think that close follow-up of renal functions and successful treatment of respiratory complications that may develop in SARS-CoV-2 infection may reduce mortality. In addition, we believe that further studies with a large number of cases on this subject in the broader period will be needed.

Ethical Approval: The study was approved by Samsun Training and Research Hospital Ethics Committee dated 01.05.2021 and numbered Non-Interventional Clinical Research/2021/9/3

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Concept: Ç.E.Ö
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Data acquisition: Ç.E.Ö.
Analysis and interpretation: D.Y, Ç.E.Ö
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Conflict of Interest: *The authors have no conflicts of interest to declare.*

Financial Disclosure: *Authors declared no financial support.*

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