KASTAMONU MEDICAL JOURNAL

Original Article

DOI: 10.51271/KMJ-0192

Kastamonu Med J. 2025;5(2):99-102

How did the COVID-19 pandemic period affect the patients on the cadaver waiting list? A single-center experience

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Cite this article as: Yönet F, Baloğlu İ, Pire B, et al. How did the COVID-19 pandemic period affect the patients on the cadaver waiting list? A single-center experience. *Kastamonu Med J.* 2025;5(2):99-102.

Received: 22.01.2025 ◆ **Accepted**: 20.02.2025 ◆ **Published**: 20.06.2025

ABSTRACT

Aims: During the COVID-19 pandemic, kidney transplantations have decreased worldwide and in Turkiye. This study aimed to explore the expected increase in the number of patients on the cadaver waiting list and the factors influencing this outcome.
Methods: We analyzed data from kidney transplant candidates during the pandemic period, focusing on mortality rates, causes of death, and patient behavior, such as attendance to routine transplant polyclinic visits.
Results: Although an increase in the number of patients on the cadaver waiting list was expected, a decrease was reported in some centers. Mortality rates were higher in kidney transplant candidates due to COVID-19, but the highest death rate was still attributed to cardiovascular diseases. Additionally, the number of patients attending routine transplant polyclinic visits decreased due to fear of infection.
Conclusion: The expected increase in patients on the cadaver waiting list was not observed, likely due to higher mortality rates and decreased clinic visits during the pandemic. The dilemma of transplantation and infection during the pandemic is a challenging issue, requiring careful follow-up in experienced centers.
Keywords: Chronic kidney disease, COVID-19, transplantation

INTRODUCTION

The COVID-19 pandemic has caused health policies to change all over the world. Transplant centers, especially dialysis centers, had to develop local strategies against the pandemic. Logistical constraints hampered hospitalization, hemodialysis access, and care from these centers. Since hemodialysis support is provided to COVID-19 infected patients in specific centers, the weekly hemodialysis time of uninfected patients has decreased.[1,2] Transplants have come to a standstill in many countries, including Turkiye, as the lack of COVID-19 testing, limited operating room conditions, and the lack of protective personnel equipment put the reliability of transplant operations at risk. Since the conditions for inclusion of hemodialysis patients who are under investigation for being placed on the waiting list have become more complex, the number of patients on the waiting list has gradually decreased in regions with a high COVID-19 burden.[3] In the United States, official records revealed a 41% drop in the waiting list during the first months of the pandemic. In addition, there has been an increase in the waiting period for transplantation due to the fact that the patients on the waiting list were infected or have had COVID-19, and hospital beds and operating rooms were insufficient during the pandemic.[4]

A kidney transplant is the most effective treatment for patients with chronic kidney disease (CKD). Renal replacement therapies (RRT), such as hemodialysis and peritoneal dialysis, are vital for patients when transplantation is delayed or not possible. Adverse effects of COVID-19 on the morbidity and mortality of patients undergoing RRT have been observed in our country and worldwide. Many patients died during this period while waiting for organ transplantation due to limited access to dialysis treatment, insufficient dialysis time, delay in being placed on the waiting list, not being included in the list, and prolonged waiting time.

In this study, we aimed to determine how patients waiting on the cadaver list for organ transplantation were affected by COVID-19.

METHODS

The study protocol was approved by the Necmettin Erbakan University Non-drug and Non-medical Device Researches Ethics Committee (Date: 21.07.2023, Decision No: 2023/4463). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

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This study included 398 patients registered in the organ transplant unit of Konya Necmettin Erbakan University Faculty of Medicine between March-2020 and June-2022. Information such as age, gender, duration of chronic kidney disease, waiting time on the list, blood group, comorbidities, cause of death, and date of death was accessed through the transplantation, dialysis, and monitoring systems (TDIS) system.

The clinical and laboratory evaluations of the patients on the waiting list during the pandemic period were retrospectively analyzed.

RESULTS

During the pandemic period, there were 398 patients (181 women, 217 men) registered in the organ transplant unit of our hospital. While the number of patients who were new applicants for transplantation was 37, it was found that only 28% of the patients who had previously registered on the waiting list came to their routine controls. In this period, it was observed that no kidney transplantation due to the decisions taken in our hospital and the fact that the hospital facilities were mostly used for patients with COVID-19.

When the patients on our waiting list were examined retrospectively, we found that 50 (12%) of our patients died during the pandemic. 19 (38%) of our deceased patients were female and 31 (62%) were male, and the mean age of the patients was 57.58 (±21.17). Among the deceased patients, A Rh(+) blood group was the most common with 58%, while the most common comorbidities were hypertension at 94% and diabetes mellitus at 44%.

When we examined the causes of death of our patients, the most common cause was cardiovascular disease (CVD) at 38%. While the second most common cause was pneumonia at 16%, we found that 6 (12%) patients died due to COVID-19. While the mean age of patients who deceased due to COVID-19 was 58.6, it was observed that the number of men and women was equal. The detailed demographic and clinical characteristics of the patients on the cadaver waiting list during the pandemic are presented in **Table**.

Table. Baseline characteristics of the study population

Category	Data
Total number of patients	398 (181 female, 217 male)
New applicants for transplant	37
Percentage attending routine controls	28%
Total deaths	50 (12%)
Gender distribution of deceased	19 female (38%), 31 male (62%)
Mean age of deceased patients	57.58 (±21.17)
Most common blood group	A Rh(+) 58%
Most common comorbidities	Hypertension 94%, diabetes mellitus 44%
Causes of death	1. Cardiovascular disease (38%)
	2. Pneumonia (16%)
	3. COVID-19 (12%)
Mean age of patients who died from COVID-19	58.6
Gender distribution of COVID-19 deceased	6 female, 6 male

DISCUSSION

This study had several significant findings. First, we saw that the rate of patients who were on the waiting list during the pandemic period came to their routine controls, and the number of new registrations was low. Second, the mortality rate in hemodialysis patients on the waiting list during the pandemic period was 12%, with a higher proportion of men. Third, cardiovascular diseases were the most common cause of death among the patients on our waiting list, while the number of patients who died due to COVID-19 infection was six. Finally, the most common comorbid diseases seen in deceased patients were found to be hypertension and diabetes mellitus.

Chronic kidney disease is a growing public health problem worldwide, causing end-stage renal disease and cardiovascular complications.[5] According to the CREDIT research conducted in Turkiye, CKD is a significant health problem in Turkiye and many countries. The relationships between CKD and various cardiovascular risk factors highlight that it is a significant public health problem and an essential determinant of overall morbidity and mortality.[5] Even though new developments in dialysis treatments, morbidity, and mortality are higher in CKD compared to the average population in all age groups.[6] Although diabetes mellitus and hypertension are the most common causes in the etiology of end-stage renal disease in hemodialysis patients, the increased cardiovascular risk is thought to be related to these underlying diseases. However, CKD alone has been proven to increase the risk of CVD independently.[7] More than half of the hemodialysis patients have CVD, and the risk of CVD-related death has increased 20 times compared to the average population.[8]

During the pandemic, mortality rates among patients on organ transplant waiting lists increased significantly due to COVID-19. Large-scale studies conducted in the United States reported that COVID-19-related mortality was 11% among kidney transplant waiting list patients and 16% among active transplant recipients. Moreover, kidney transplant candidates who contracted COVID-19 had a significantly higher rate of hospitalization and mortality compared to transplant recipients.[9]

Additionally, the COVID-19 pandemic has led to a substantial decline in organ transplantation rates worldwide. Studies from the United States have demonstrated a marked decrease in kidney transplant procedures, with waiting list patients experiencing increased mortality while the number of transplants performed significantly declined. This trend is consistent with our findings, which indicate a reduction in transplant activity and a concurrent rise in mortality among patients awaiting transplantation during the pandemic period.[10]

Despite concerns regarding immunosuppression in transplant recipients, studies have shown that kidney transplant recipients had better outcomes in terms of COVID-19-related morbidity and mortality compared to patients on the waiting list. This discrepancy is attributed to the fact that waiting list patients undergo frequent hemodialysis sessions, which increase their exposure to healthcare settings and subsequently elevate their risk of acquiring infections, including COVID-19. In contrast, transplant recipients have reduced healthcare interactions, which may contribute to their relatively better prognosis during the pandemic.[9]

The main reason for this decline is the multiple effects of the COVID-19 pandemic on the healthcare system. The disruptions in healthcare services due to the pandemic not only affected transplant rates but also contributed to an increased burden of cardiovascular disease in dialysis patients. Many factors have been held responsible for the pathogenesis of cardiovascular disease in dialysis patients. First of all, uremic toxins cause damage to myocardial and vascular functions by affecting the activities of leukocytes, endothelial cells, and platelets. Especially, uremic toxins such as p-cresol and indoxyl sulfate are responsible for chronic inflammation, hemostatic dysfunction, and vascular damage by reducing nitric oxide synthesis.[11] In addition, more reactive oxygen radicals are formed in these patients than in healthy controls through activating thrombocytes, complement, and leukocytes during hemodialysis.[12] Asymmetric dimethylarginine (ADMA) and symmetric dimethyl arginine (SDMA), which are among profibrotic cytokines IL-6 and methyl arginines, which are indicators of atherosclerosis and endothelial dysfunction, were found to be high in patients with CKD.[13,14] The best-defined CVD risk factor in CKD is vascular calcifications. It involves transdifferentiating vascular smooth muscle cells into cells resembling bone progenitor cells rather than a simple calcium phosphate crystal deposition.[15] Vascular calcifications cause left ventricular hypertrophy by causing aortic calcifications, increasing CVD mortality by 181% and all-cause mortality by 73%.[16] Apart from these risk factors, intradialytic weight changes cause left ventricular hypertrophy, and erythropoietin and lipoprotein carbamylation cause an increase in cardiovascular mortality in hemodialysis patients.[16,17]

Although attempts are made to reduce these cardiovascular risk factors with hemodialysis treatment, there is no complete recovery. Mortality due to CVD is very high in hemodialysis patients, even compared to healthy controls. Conversely, transplantation leads to the regression of uremic cardiomyopathy and reduces cardiovascular deaths. For this reason, it has been reported that the long-term mortality rate of transplant recipients is much lower compared to dialysis patients on the waiting list.[18] Despite the increased mortality risk associated with COVID-19, cardiovascular diseases remained the leading cause of death among patients on the transplant waiting list and dialysis patients. Recent evidence suggests that while COVID-19 posed a significant short-term mortality risk, cardiovascular complications continue to be the predominant long-term cause of mortality in this patient group.[10] Long-term survival is higher in transplant patients because it reduces mortality and morbidity in the long term. Dialysis patients who are placed on the waiting list are selected quite well, and they are selected from patients who are younger, healthier, have a higher socioeconomic status, and have lower comorbid conditions than those not included in the list. Therefore, the survival rates of patients on the waiting list are better than all dialysis patients but lower than transplant recipients.[19] In their study, Robert et al.[20] found the long-term mortality rate per 100 patient-years to be 3.8 in transplant patients, 6.3 in waiting list patients, and 16.1 among all dialysis patients. In addition, Schnuelle et al.[21] determined the annual incidences of death in the 3rd, 5th, and eighth years on the waiting list as 0.37-0.43-0.52, respectively, and showed that the death rates in the waiting list increased as the time lengthened.

In the registry data published by the Turkish Society of Nephrology in 2020, it was reported that the number of patients who lost their lives after undergoing hemodialysis was 994. 42.55% of these patients died of cardiovascular causes. The number of transplant patients who had COVID-19 and died for this reason is 50.[21] In addition, according to the registry data published by the Turkish Society of Nephrology in 2022, 2492 patients who received hemodialysis treatment died in 2021, while 649 of them died due to COVID-19 (26.04%) and 842 (33.79%) due to cardiovascular causes. The number of transplant patients who died due to COVID-19 infection in 2021 was 141.[22]

According to the registry data published by the Turkish Society of Nephrology in 2021, 2499 kidney transplantations were performed in 2020. It is seen that the total number of transplants has decreased significantly compared to the number of 3858 transplants performed in the previous year. In addition, the rate of transplantation from a cadaver donor was reported to be 10% in this period. With the decrease of the effect of the pandemic in 2021, the number of transplants increased to 3375, but still could not reach the pre-pandemic numbers. In 2021, the transplant rate from a cadaver donor was 8.8%. The declining cadaveric transplantation rate, up to 10% last year, has further decreased.[22] This rate indicated a serious decrease in cadaver transplant activity, which is already low and generally remains at the level of 18-25%.

The main reason for this decline is the multiple effects of the COVID-19 pandemic on the healthcare system. The pandemic has severely affected our patients waiting for cadavers registered in our center. Nevertheless, we found that the most common cause of death was cardiovascular causes, with 38%. The COVID-19-caused mortality rate of kidney recipient candidates who died during the pandemic was nearly two times higher than the healthy population.

Limitations

This study was conducted on 398 patients registered in the organ transplant unit of Konya Necmettin Erbakan University Faculty of Medicine. Therefore, the results are limited to patients from this center, which makes it difficult to generalize the findings to the broader population of Turkiye or the world. Additionally, as the data from the pandemic period were collected retrospectively, there is a possibility of missing or inaccurate information. The data used in the study were obtained from the TDIS database, but potential data entry errors within the system may affect the results. Clinical evaluations were based solely on routine follow-ups, and sudden changes in patients' conditions and how these changes were managed were not considered.

CONCLUSION

As a result, we found that the number of transplants decreased during the pandemic period and the patients on the waiting list for transplants did not come to their regular check-ups. Consistent with the literature, we observed that although mortality rates due to COVID-19 were high in this population, the highest mortality rate was still due to cardiac pathologies. For this reason, we think that suitable patients on the waiting list for cadaver transplantation should not be kept waiting for transplantation, and cardiac controls of patients who did not receive transplantation should be followed more closely during pandemic periods.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Necmettin Erbakan University Non-drug and Non-medical Device Researches Ethics Committee (Date: 21.07.2023, Decision No: 2023/4463).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Acknowledgments

We would like to acknowledge the contributions of the staff at Konya Necmettin Erbakan University Faculty of Medicine for their support during this study.

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