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Evaluation of Kidney Transplant Patients Infected with COVID-19 in Turkey

Türkiye’de COVID-19 ile Enfekte Olan Böbrek Nakilli Hastaların Değerlendirilmesi

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Abstract

Objectives: Determining the clinical course of Coronavirus disease-2019 (COVID-19) infection in terms of mortality and morbidity in patients with kidney transplantation is of scientific importance in our country and in the world. Our aim in this study was to examine the epidemiological incidence and results of kidney transplant patients registered in the data system of the "Directorate of Tissue, Organ Transplantation and Dialysis Services" in Turkey after COVID-19 infection.

Methods: In this study, which was designed as a non-interventional, retrospective, and observational study; demographic information of patients, clinical and radiological parameters, life expectancy, hospital service and intensive care requirements and length of stay were analyzed in the information systems of the Ministry of Health. In the study, a total of 12,360 people with kidney transplants in Turkey were examined between March 2020 and March 2021 with suspected COVID-19.

Results: Between March 2020 and March 2021, 12,360 patients who received Kidney Transplants were examined in Turkey with COVID-19 symptoms. The rate of patients diagnosed with COVID-19 infection was 34.5% (4266) and their average age was 49.3 years. The number of patients who died from COVID-19 in patients with kidney transplantation was 288 (6.8%) and their average age was 60.7 years. In the intensive care unit, 446 patients (10.45%) were followed and 149 (3.5%) were intubated patients.

Conclusion: COVID-19 diagnosis, pneumonia cases and mortality rates were found to be higher in patients with kidney transplantation than in the general population. However, when many publications originating from abroad are examined, it is determined that we are well below the world average in the incidence of COVID-19 infection, hospitalization, intensive care hospitalization and mortality rates in those who have kidney transplants in our country.

Keywords: Kidney, transplantation, COVID-19, pneumonia, mortality

Öz

Amaç: Koronavirüs hastalığı-2019 (COVID-19) enfeksiyonun böbrek nakilli hastalarda mortalite ve morbidite açısından klinik gidişatını belirlenmesi bilimsel açıdan ülkemizde ve dünyada önem arz etmektedir. Ayrıca böbrek nakilli hastalardaki COVID-19 enfeksiyonunun dünya genelindeki popülasyondan, riskli hasta gruplarından farklı klinik seyre sahip olup olmaması koruyucu önlemler bakımından çok daha değerlidir. Bu çalışmada amacımız; Türkiye’de Doku, Organ Nakli ve Diyaliz Hizmetleri Başkanlığı veri sisteminde kayıtlı böbrek nakilli hastaların COVID-19 enfeksiyonu sonrası epidemiyolojik insidans ve sonuçlarının incelenmesidir.



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Öz

Yöntem: Girişimsel olmayan retrospektif gözlemsel dizayn edilen bu çalışmada; hastaların Sağlık Bakanlığı bilgi sistemlerine kaydedilmiş, demografik bilgileri, klinik ve radyolojik parametreleri, yaşam süresi, hastane servisi ve yoğun bakım gerekliliği ve kalış süreleri incelenmiştir. Çalışmada Mart 2020-Mart 2021 tarihleri arasında Türkiye'de COVID-19 şüphesiyle hastaneye başvuran toplam 12.360 böbrek nakilli kişi incelenmiştir. COVID-19 aşağıdaki durumlarda onaylanmıştır; Gerçek zamanlı revers-transkriptaz polimeraz zincir reaksiyonu tespiti pozitifliği veya Toraks bilgisayarlı tomografi (BT) COVID-19 pnömoni bulguları varlığı durumlarında COVID-19 olarak kabul edilmiştir. 2019-nCoV nükleik asit tespiti nazofarenks sürüntülerinde, balgamda ve gerekli durumlarda alt solunum yolu salgılarında tespit edilmiştir.

Bulgular: Mart 2020-Mart 2021 tarihleri arasında Türkiye'de COVID-19 belirtileriyle hastanelere başvuran böbrek nakli olmuş 12.360 olgu incelenmiştir. COVID-19 enfeksiyonu tanısı konan hasta oranı %34,5 (4.266) olup ortalama yaşları 49,3 çıkmıştır. Böbrek nakilli 12.360 kişinin %11,7'si (1456) hastaneye yatırılmıştır. Hastaneye yatırılan kişilerin ortalama yaşı 51,5, toplam hastanede kalış süreleri ortalama 12,5 gün çıkmıştır. 12.360 COVID-19 şüpheli böbrek nakilli kişilerin toraks BT görüntülemeleri incelendiğinde 1.714 kişide (%13,8) BT uyumlu COVID-19 pnömonisi saptanmış olup hastaların yaş ortalaması 52,4 bulunmuştur. Böbrek nakilli hastalarda COVID-19'a bağlı ölen hasta sayısı 288 (%6,8) olup ortalama yaşları 60,7 çıkmıştır. Yoğun bakım ünitesinde 446 hasta (%10,45) takip edilmiş olup, 149'u (%3,5) entübe hastalardan oluşmaktadır. Yoğun bakım ünitesinde takip edilen hastaların yaş ortalaması 55,1 olup ortalama yatış süresi 11,45 gün çıkmıştır.

Sonuç: Böbrek nakilli olgularda COVID-19 tanısı, pnömoni olgularının mevcudiyeti ve ölüm oranları genel popülasyona göre daha yüksek saptanmıştır. Ancak yurtdışı kaynaklı birçok yayın incelendiğinde ülkemizde böbrek nakli olanlarda COVID-19 enfeksiyon varlığı, hastaneye yatış, yoğun bakım yatış ve ölüm oranlarında dünya ortalamasının oldukça altında olduğumuz tespit edilmiştir.

Anahtar Kelimeler: Böbrek, nakil, COVID-19, pnömoni, mortalite

Introduction

On December 31, 2019, a new coronavirus was detected in Wuhan, China, with unknown origin from the respiratory secretions of several patients presenting with a lower respiratory tract infection. The World Health Organization (WHO) identified this newly reported coronavirus as 2019-nCoV and later named it Severe acute respiratory syndrome-CoV-2. The resulting infection was declared a pandemic in the world on March 11, 2020 by the WHO after the rapid spread of the virus, which was called Coronavirus disease-2019 (COVID-19)⁽¹⁾.

When the 2020 data are examined, COVID-19-related mortality rates are thought to be between 1 and 5% in the normal population, while these rates are much higher in older adults, those with underlying chronic diseases and immunosuppressive patients. Kidney transplant recipients are on long-term immunosuppressive treatment and have a high risk of contracting serious respiratory infections after virus exposure and may receive clinically late diagnosis⁽²⁻⁷⁾.

More than 1.5 million people worldwide live with organ transplants, and kidney transplants account for almost 60% of these transplants. There is 5,759 people who received solid organ transplants in our country in 2019, of which 3.863 (67%) were people with kidney transplants. Of the 50,180 solid organ transplants performed in our country in the last decade, 34,936 (69%) consisted of kidney transplants⁽⁸⁾.

Kidney transplantation is the most effective treatment method for treating advanced chronic kidney disease and end-stage kidney diseases⁽⁹⁾. Determining the clinical progress of COVID-19 infection in terms of mortality and morbidity in patients with kidney transplantation is of scientific importance in our country and around the world. Additionally, whether COVID-19 infection in patients with kidney transplantation has different clinical courses from the population and risky patient groups is much more valuable in terms of preventive measures⁽¹⁰⁾.

Our aim in this study was to examine the epidemiological incidence and results of kidney transplant patients registered in the data system of the Directorate of Tissue, Organ Transplantation and Dialysis Services in Turkey after COVID-19 infection.

Materials and Methods

In this retrospective observational designed study, the demographic information, clinical and radiological parameters, life expectancy, hospital service and intensive care requirements and stay times of the patients with kidney transplants were examined in the information systems of the Ministry of Health following the ethical approval of the Ethics Committee of Ankara State Hospital (ethical approval number: E2-21-245) on March 30th, 2022.

In the study, a total of 12,360 patients with kidney transplants were examined in Turkey between March 2020 and March 2021 with suspected COVID-19.

COVID-19 diagnosis is approved in the following cases: in cases with real-time RT-PCR detection positivity or the presence of COVID-19 pneumonia signs on the thorax computed tomography (CT). 2019-nCoV nucleic acid detection has been detected in nasopharynx swabs, phlegm and, where necessary, lower respiratory tract secretions. Patients' consent was waived due to the study.

Statistical Analysis

The data were recorded on the tabulation software and the frequency changes were calculated using the statistical formulas of the tabulation software.

Results

Between March 2020 and March 2021, 12,360 patients who received kidney transplants were examined in Turkey with COVID-19 symptoms. The number of patients diagnosed with COVID-19 infection was 4,266, and the percentage of patients with kidney transplantation admitted to the hospital was calculated as 34.5% (Table 1).

When the age analyses of patients with kidney transplantation were analyzed that the mean age of patients diagnosed with COVID-19 infection was 49.3, the average age of patients with COVID-19 pneumonia was 52.4, the average age of patients admitted to the hospitalized was 51.5 years, and the average age of those who died was 60.7 years (Table 2).

There were 1714 patients diagnosed with thorax CT-confirmed COVID-19 pneumonia. The pneumonia rate among all people with kidney transplantation (12,360) was 13.8% and the rate of patients with pneumonia was 40.17% among 4,266 people with COVID-19 infection (Table 3).

Table 1. Service hospitalization or ICU stay statistics in patients with kidney transplantation

Description	Numbers
Number of transplanted patients	12,360
COVID-19 infected transplants	4,266 (34.5%)
Number/rate of hospitalization in those diagnosed with COVID-19 infection	1,456 (34.1%)
Hospitalization rate among all patients admitted with suspected COVID-19	11.7%
Hospitalization time/average days	12.5
ICU hospitalization time/average days	11.45
Intubation time/average days	10.35
ICU: Intensive care unit, COVID-19: Coronavirus disease-2019	

1,456 patients with kidney transplantation had a hospitalized and the proportion of inpatients in all kidney transplants was found to be 11.7%. The rate of patients in 4,266 kidney transplant patients diagnosed with COVID-19 infection was 34.1%. COVID-19 pneumonia diagnoses (1,714) and hospitalized rates were 84.9%. Hospital stays were calculated as an average of 12.5 days (Table 1, Table 3).

The number, rate and length of hospitalization of 4,266 kidney transplant patients diagnosed with COVID-19 infection was examined. In patients with kidney transplantation length of stays intensive care unit (ICU) percentage was 10.45% (446) and the average length of stay in the ICU was 11.45 days. Intubated patient rate was also 3.5% (149). The average length of stay under intubation was 10.35 days.

The number rate of death in patients with kidney transplantation was examined. 284 (2.3%) people in all (12,360) cases with suspected COVID-19 with kidney transplantation died, and the mortality rate increased by 6.8% in patients with kidney transplantation (4,266) diagnosed with COVID-19 (Table 4).

Table 2. Age statistics of patients with kidney transplantation

Description	Numbers
Number of transplanted patients	12,360
Average age of COVID-19 infected patient	49.3
Average age of patients with COVID-19 pneumonia	52.4
Average age of hospitalized patients	51.5
Mean age of ICU stay	55.1
Average age of deceased patients	60.7
ICU: Intensive care unit, COVID-19: Coronavirus disease-2019	

Table 3. Pneumonia in patients with kidney transplantation

Description	Numbers
Number of total transplant patients	12,360
COVID-19 infected transplants	4,266
Number of patients diagnosed with COVID-19 pneumonia	1,714
Pneumonia diagnosis rate in COVID-19 infected transplant patients	40.17%
Pneumonia diagnosis rate among all transplants with suspected COVID-19	13.86%
Number (rate) of hospitalization of patients with pneumonia	1,456 (84.9%)
ICU: Intensive care unit, COVID-19: Coronavirus disease-2019	

Discussion

While the COVID-19 pandemic is still spreading around the world and continues to seriously affect societies, the high rates of morbidity and mortality are noticeable both in the normal population and in chronic immunosuppressive patients such as organ transplant recipients⁽²⁻⁷⁾. In our study, 12,360 cases of kidney transplantation presenting to health institutions with suspected COVID-19 in the year following the official declaration of the pandemic in Turkey, as well as the COVID-19 transmission, pneumonia presence, the hospitalization of patients with kidney transplantation internationally, hospitalizations, mechanical ventilation rates, mortality rates were examined.

In a study reported by Akalin et al.⁽¹¹⁾ from the United States (USA) at a Medical Center in New York, 36 kidney transplant patients were followed, 78% of these patients were hospitalized, 96% of the admitted patients were found to have symptoms consistent with viral pneumonia in their lung imaging, 39% were intubated and 28% mortality was determined.

Most of the studies in Europe were from Italy, Spain and France, which are the epicenters of the pandemic. In the Brescia-based studies of Alberici et al.⁽¹²⁾ 19% mortality was reported in patients with kidney transplantation diagnosed with COVID-19 infection. In the studies of Benotmane et al.⁽¹³⁾ 83.7% hospitalization, 34.2% condensation and 22% mortality data were reported in patients with kidney transplantation. Although many studies consist of single-centered studies, studies with national and international clinical results have also been reported. The TANGO international consortium reported the results of 144 kidney transplant recipients in 12 centers in the USA, Italy and Spain, and the mean age of the patients followed was 57, pneumonia was seen in 86% of cases diagnosed with COVID-19, acute renal failure in 52%, respiratory failure requiring intubation in 29% and mortality in 32%⁽¹⁰⁾.

In a study examining French COVID Registry including 279 patients with kidney transplantations, it was observed that 87% of the cases were hospitalized, 36% of the inpatients were admitted to ICU and the 30-day mortality rate was 23%⁽¹⁴⁾.

When the University of Washington records were examined, 66% (318) cases with kidney and kidney-pancreatic transplantation, 15.1% (73) liver transplants, 11.8% (57) hearts and 6.2% (30) lung transplants were examined. A total of 478 patients were evaluated, 78% of the cases were hospitalized, 31% were intubated and 20.5% mortality was reported⁽¹⁷⁾. In five additional studies from USA centers, mostly involving kidney transplant recipients, hospitalization rates were reported between 67 and 87%, mechanical ventilation needs were reported between 30 and 35%, and mortality rates were 7-24%^(15,16).

A total of 4.578 people with solid organ transplants were examined in a Swedish study and only 53 people were diagnosed with COVID-19 infection in total. The distribution of the cases by organ transplant types was as follows: 31 of the patients had kidney transplantation, 8 patients had liver, 5 patients had lungs, 5 patients had heart, 3 patients had kidney and livers together, and 1 patient had heart and kidney transplants. The mean age was 56, 56% were male, 22% of the patients were intubated during the follow-up and the mortality rate was 10%⁽¹⁷⁾.

Another study by Columbia University examined 90 patients with solid organ transplantation, with 57% of the patients reported as male. Forty-six (52%) of the patients with kidney transplantation, 17 (19%) lung transplant patients, 13 (14%) liver transplant patients, 9 (10%) heart transplant patients, 3 (3%) heart-kidney transplant patients, 1 (1%) liver-kidney transplant patient and 1 (1%) kidney-pancreatic transplant patients. 76% of the patients were hospitalized, 35% were intubated. During the same period, the mortality rate in the general population increased by 18%, and 24% of patients who got a kidney transplant and were admitted to the ICU died during the 3-week study period⁽¹⁸⁾. Bossini et al.⁽¹⁹⁾ Examined the clinical course of 7 infected kidney transplant patients and found that 57% of patients needed an ICU due to COVID-19 pneumonia and had a mortality rate of 14%.

Studies in many countries were examined, and our study was seen as the most exhaustive study in terms of the number of cases compared with other studies in patients with kidney transplantation.

Table 4. Cooperation of intubation/death from patients with kidney transplant COVID-19 in ICU

Description	Numbers
COVID-19 infected transplant patients	4.266
Number (rate) of patients admitted to ICU	446 (10.45%)
Number (rate) of intubated patients	149 (3.5%)
Number (rate) of death	290 (6.8%)
ICU: Intensive care unit, COVID-19: Coronavirus disease-2019	

Although we look at the incidence of COVID-19 infection in patients with kidney transplantation, international studies show notifications between the ages of 48–62^(9,19,20). In our study, the average age of patients with kidney transplantation infected with COVID-19 was 49.3 years.

While we looked at the transplants performed in the last decade, it was seen that kidney transplantation was the most transplanted organ (69%). International studies have shown that these rates are between 52% and 74%^(20,21).

When we screened kidney transplant cases with COVID-19 infection in terms of pneumonia, this rate increased to 40.17% in our study. In similar studies, we found that rates ranged from 76% to 96%⁽⁹⁻¹¹⁾. These values show us that COVID-19 may rapidly progress to pneumonia in kidney transplant cases.

As we examined hospitalizations, the hospitalization rate increased by 34.1% in kidney transplant cases with COVID-19 infection in our country. The rate ranges from 22% to 76% internationally. While the hospitalization rate in our country was 83.6% in cases with pneumonia, internationally this rate varies between 32 and 100%^(9,12,16). We observed that the rate of hospitalization to the ICU was 10.45% in our country and the rate of patients followed up with intubation was 3.5%. In international studies, it was observed that the follow-up rate in the ICU ranged from 26% to 39%, and the cases followed by intubation were between 22% and 39%. According to international studies, it has been observed that the rates of patients who are both inpatient and intubated in the ICU are low. According to our examined mortality rates, 284 deaths have been reported in our country. In kidney transplants infected with COVID-19, this rate was 6.8%, and many international studies showed that mortality rates ranged from 10% to 32%. Although mortality rates in our country are low compared with internationally reported mortality rates, all national and international studies show us the high mortality rates, pneumonia rates, service and intensive care hospitalization and mortality rates in patients with kidney transplant infected with COVID-19 according to the general population^(9,22).

Restrictions or accessibility issues of PCR tests in some countries may lead to falsely lower infection rates. The criteria for hospitalization, admission to the ICU and discharge probably differ between countries.

Study Limitations

The limitation of the study is the lack of additional data such as administered drug treatments or doses during the study group's hospitalization in inpatient clinics and ICUs.

Conclusion

COVID-19 diagnosis, pneumonia cases and mortality rates were found to be higher in patients with kidney transplantation than in the general population. However, when many publications originating from abroad were examined, it was determined that those who have kidney transplants in Turkey had better outcomes than the world average in terms of the presence of COVID-19 infection, hospitalization, intensive care hospitalization and mortality rates. Immuno-suppressed patients often show signs of atypical or opportunistic infections, which often lead to late admissions or missed diagnoses and potentially worse outcomes overall. Literature shows that higher mortality rates, advanced age, presence of comorbidities are related to immunosuppression in patients with kidney transplantation. In conclusion, this study reflects the adverse effects of immunosuppression in patients infected with COVID-19 and shows that good management of immunosuppression in transplant recipients can be one of the most effective steps for better outcomes.

Ethics

Ethics Committee Approval: The study were approved by the Ankara State Hospital of Ethics Committee (ethical approval number: E2-21-245) on March 30th, 2022.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: H.D., Design: H.D., Y.Y., Data Collection or Processing: H.D., Analysis or Interpretation: H.D., Literature Search: Y.Y., Writing: H.D., Y.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

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