COVID-19 Infection in Renal Transplant Recipients at Dubai Hospital: Incidence, Clinical Profile, and Outcome

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Abstract

Background: Renal transplant recipients are at risk to acquire COVID-19 infection quite frequently, owing to their immunocompromized state. Nevertheless, data on the effects of this infection on patients and graft function are sparse from the Arab world. Methods: This retrospective cohort study was conducted in Dubai Hospital from April 1, 2020, to August 1, 2021. We analyzed 42 COVID-19-positive renal transplant recipients’ data. Information concerning demographics, comorbidities, medications, clinical and laboratory data, and outcomes was collected from the electronic medical records. Univariate analyses were performed to determine the association of acute kidney injury (AKI) with in-hospital mortality. Results: Median age was 47.46 (17–66) years; about 59% of patients were male. Eleven (26.19%) patients developed AKI during hospitalization. On admission high ferritin, C-reactive protein, creatinine, and low absolute lymphocyte count are identified risk factors for in-hospital AKI. Seven (21.87%) patients had their calcineurin inhibitor levels touch a toxic peak possibly due to an interaction with antivirals. Mortality was 14.28%, and the same number of patients required mechanical ventilation during treatment. Conclusion: A significant number of renal transplant recipients suffered from AKI during COVID-19 infection, and the mortality rate in this study population was less than in studies from other countries in the region. More insights are required to manage this infection in renal transplant recipients.

Introduction

In December 2019, multiple cases of pneumonia with unknown etiology were reported in Wuhan city of China. Subsequently, these cases were attributed to severe acute respiratory syndrome secondary to coronavirus 2, which belongs to the Coronaviridae family [1–3]. Because of the rapid spread of COVID-19 across the globe, the World Health Organization declared it a pandemic on March 11, 2020. Patients with an impaired immune system, either from an underlying disease or due to treatment, are at risk of severe infection and superimposed infections (bacterial and fungal) with any viral respiratory tract infection.
as compared to immunocompetent counterparts [4, 5]. The Nephrology Department of Dubai Hospital has more than 300 renal transplant recipients in follow-up, and we received the first COVID-19-infected renal transplant recipient on April 13, 2020, who recovered after 37 days of hospital admission. So far, there are scanty published studies, especially from the Arab world. The object of our study is to report the incidence, clinical course, and outcome of renal transplant recipients who were admitted with COVID-19 infection in our hospital.

Material and Methods

We conducted an observational study to identify the incidence, risk factors, and prognosis of COVID-19 infection in renal transplant recipients, who were admitted to Dubai Hospital from April 1, 2020, to August 1, 2021. The requirement of informed consent was waived by the Ethical Committee since the nature of the study was observational. COVID-19 infection was diagnosed based on clinical presentation, radiographic abnormalities, and positive result of polymerase chain reaction on a nasopharyngeal swab. Patients less than 13 years old were excluded from this study. Two consecutive negative RT-PCR SARS-CoV-2 test results 24 h apart were used for the discontinuation of isolation.

Data Collection

Medical records of the study population were reviewed using electronic medical records (Epic Hyperspace, year 2019) to retrieve patients’ demographic characteristics, laboratory findings, and radiological features. Demographic characteristics include age, sex, and comorbidities. Laboratory data consists of full blood count, coagulation profile, liver function tests, renal functions, creatinine kinase, lactate dehydrogenase (LDH), and inflammatory markers including C-reactive protein (CRP), ferritin, and D-dimer. Pulmonary infiltration on chest X-ray was identified as an increased opacity or an infiltrate. The definition of acute kidney injury (AKI) is based on Kidney Disease Improving Global Outcomes [6]. AKI is defined as an absolute rise in creatinine by ≥0.3 mg/dL within 48 h or an increase in serum creatinine ≥1.5 times of the baseline value within 7 days. According to Kidney Disease Improving Global Outcomes, severity stages of AKI are an increase in serum creatinine of 1.5–1.9, 2–2.9, and >3 times the baseline defined as AKI stages 1, 2, and 3, respectively. Baseline serum creatinine was well known for most of our follow-up patients. For those without recent values, the measured serum creatinine on admission was considered as a baseline, and the highest value was used to categorize different stages of AKI. A decrease in serum creatinine below 1.2 mg/dL is defined as AKI recovery. Renal replacement therapy (RRT), mechanical ventilation, intensive care admission, duration of hospital stays, and inpatient mortality were the other studied outcomes.

Statistical Analysis

Continuous variables are described as mean with standard deviation and median with interquartile range values for normally distributed and non-normally distributed data, respectively. Categorical variables were presented as frequency and percentage. The independent t-test and Mann-Whitney test were used for continuous variables (normally and non-normally distributed, respectively), and categorical data were compared with help of Pearson’s χ² test or Fisher’s exact test. A p value of <0.05 was considered statistically significant. Statistical Package for the Social Sciences version 20 (2011) was used for statistical analysis.

Results

A total of 307 renal transplant recipients are followed regularly in the transplant clinic in Dubai Hospital. Of these, 42 (13.68%) patients acquired COVID-19 infection in the study period; their baseline characteristics are depicted in Table 1. Twenty-six (61.9%) infected patients were male, with mean age of 47.46 (±11.03) years; also, 11 (26.19%) patients were UAE nationals. Diabetes and hypertension were common comorbidities, in 47.6% (n = 20) and 64.3% (n = 27) patients, respectively. Fever (47.6%), body aches (42.85%), shortness of breath (21.42%), cough (19.04%), and diarrhea (11.90%) were the main complaints. Regarding maintenance of immunosuppressive medications, 30 (71.42%) patients were using triple immunosuppression. Prednisolone, cyclosporine, tacrolimus, and mycophenolate were used by 78%, 31%, 71%, and 76% of patients, respectively. Favipiravir was the most common antiviral drug used to treat COVID-19 infection, and 20 (47.61%) patients were treated with it. Also, different forms of corticosteroids were used for treatment in 80.95% (n = 34) of patients, while tocilizumab was used in 12 (28.57%) patients. The median duration of hospital stay was 16.03 (1–90) days. Twenty-one (50%) patients maintained optimal oxygen saturation on room air, 14 patients required supplemental oxygen via high flow nasal cannula (5, 11.9%) or non-rebreather mask (9, 21.87%), and 16.66% (n = 7) required mechanical ventilation. The mortality rate among COVID-19-infected renal transplant recipients was 14.28% (n = 6). Acute Kidney Injury

Out of 42 renal transplant recipients, 11 (26.19%) patients suffered from AKI, 5 (44.4%) patients had AKI stage I and III each, and 1 patient had AKI stage II; characteristics of AKI and non-AKI patients are shown in Table 2. Their mean age was 44 (±8.47) years, and their median duration of hospital admission was 15.62 (7–24) days. Triple immunosuppression (prednisolone, tacrolimus, and mycophenolate mofetil) was used by 81.81% (n = 9) of patients; also 27.27% were on cyclosporine. Statistically significant predisposing factors causing AKI in COVID-19-infected renal transplant recipients were my-
Table 1. Patient’s baseline characteristics

| Characteristics                        | COVID-19-infected (n = 42) | Not infected (n = 265) |
|----------------------------------------|-----------------------------|------------------------|
| Age, years, mean (SD)                  | 47.46 (11.03)               | 51.78 (34.25)          |
| Gender, n (%)                          |                             |                        |
| Male                                   | 26 (61.90)                  | 161 (60.75)            |
| Nationality, n (%)                     |                             |                        |
| UAE                                    | 11 (26.19)                  | 181 (68.30)            |
| Philippine                             | 7 (16.66)                   | 8 (3.01)               |
| Pakistan                               | 6 (14.28)                   | 12 (4.52)              |
| Comor Island                           | 2 (4.76)                    | 6 (2.26)               |
| Egypt                                  | 3 (7.14)                    | 5 (1.88)               |
| India                                  | 3 (7.14)                    | 11 (4.15)              |
| Iran                                   | 3 (7.14)                    | 4 (1.50)               |
| Jordan                                 | 3 (7.14)                    | 3 (1.13)               |
| Syria                                  | 3 (7.14)                    | 3 (1.13)               |
| Afghanistan                            | 1 (2.38)                    | 1 (0.37)               |
| Others                                 | 0 (0)                       | 31 (11.69)             |
| Transplant duration, months, mean (SD)| 122.2 (96.6)                | 130.06 (127.08)        |
| Hospital stay, days, median (IQR)      | 16.03 (1–90)                | **                     |
| Comorbid, n (%)                        |                             |                        |
| Diabetes mellitus                      | 20 (47.61)                  | 164 (61.88)            |
| Hypertension                           | 27 (64.28)                  | 60 (22.64)             |
| Symptoms, n (%)                        |                             |                        |
| Fever                                  | 20 (47.61)                  | **                     |
| Vomiting                               | 4 (9.52)                    | **                     |
| Shortness of breath                    | 9 (21.42)                   | **                     |
| Cough                                  | 8 (19.04)                   | **                     |
| Diarrhea                               | 5 (11.90)                   | **                     |
| Body aches                             | 18 (42.85)                  | **                     |
| Immunosuppression, n (%)               |                             |                        |
| Triple                                 | 30 (71.87)                  | 198 (74.71)            |
| Dual                                   | 11 (26.19)                  | 24 (9.05)              |
| Prednisolone                           | 33 (78.57)                  | 189 (71.32)            |
| Cyclosporine                           | 13 (30.95)                  | 97 (36.60)             |
| Tacrolimus                             | 30 (71.42)                  | 190 (71.69)            |
| MMF                                    | 32 (76.19)                  | 188 (70.94)            |
| Antiviral and immunomodulator, n (%)   |                             |                        |
| Favipiravir                             | 20 (47.61)                  | **                     |
| Kaletra                                | 3 (7.14)                    | **                     |
| Remdesivir                             | 6 (14.28)                   | **                     |
| Corticosteroids                        | 34 (80.95)                  | **                     |
| Tocilizumab                            | 12 (28.57)                  | **                     |
| Plasma                                 | 2 (4.76)                    | **                     |
| Oxygen therapy, n (%)                  |                             |                        |
| Room air                                | 21 (50)                     | **                     |
| Nasal cannula                          | 5 (11.90)                   | **                     |
| Non-rebreather mask                    | 9 (21.42)                   | **                     |
| Mechanical ventilation                 | 7 (16.66)                   | **                     |
| Outcome, n (%)                         |                             |                        |
| Discharge to home                      | 32 (76.19)                  | **                     |
| Expired                                | 6 (14.28)                   | **                     |
| Transfer to another facility           | 4 (9.52)                    | **                     |
| CXR, n (%)                             |                             |                        |
| Bilateral infiltrates                  | 36 (86.67)                  | **                     |
| Unilateral infiltrates                 | 3 (7.14)                    | **                     |
| No pneumonia                           | 3 (7.14)                    | **                     |
cyclophosphamide immunosuppression (74 vs. 82%, \( p = 0.044 \)), need for mechanical ventilation (0 vs. 54%, \( p = 0.005 \)), lower median absolute lymphocyte count (0.52 vs. 7.77, \( p = 0.048 \)), high CRP (139.37 vs. 64.67, \( p = 0.02 \)), and high LDH (753.85 vs. 334.90, \( p = 0.05 \)). Favipiravir (4; 36.36%) and remdesivir (2; 22.2%) were the antiviral drugs used in the AKI group. Steroids and tocilizumab were used in 87.5 and 55.5% of AKI patients, respectively. AKI carries a high mortality rate (54.54%, \( n = 6 \)) among COVID-19-infected renal transplant recipients.

**Immunosuppressive Medications and Antiviral Drug Interaction**

Ten (21.87%) transplant recipients’ calcineurin inhibitor (CNI) levels rose to toxic levels during COVID-19 treatment. The interaction was noted with tacrolimus more than cyclosporine in 7 (70%) and 3 (30%) patients, respectively. Tacrolimus-favipiravir and tacrolimus-remdesivir interactions were noted in 3 patients each, while tacrolimus-lopinavir/ritonavir interaction was observed in 1 patient. On the other hand, cyclosporine-favipiravir and cyclosporine-remdesivir interactions were observed in 2 and 1 patients, respectively. CNI-antiviral interaction is associated with AKI in 4 (57.14%) and death in 3 (42.85%) patients.

**Mortality**

In our study population, six (14.28%) renal transplant recipients expired due to COVID-19-related complications during the study period (Table 3). 83.3% (\( n = 5 \)) were male with mean age of 48.8 (±5.76) years. All the patients were on triple immunosuppressive medications before acquiring COVID-19 infection (prednisolone = 6 [100%], MMF = 5 [83.3%], tacrolimus = 4 [66.67%], cyclosporine = 3 [50%]), also favipiravir and tocilizumab were used in 50% (\( n = 3 \)) and 66.67% (\( n = 4 \)), respectively. AKI (\( n = 6 \), \( p = 0.005 \), OR = 9.26) and need for mechanical ventilation (\( n = 6 \), \( p = 0.005 \), OR = 11.45) were statistically significant risk factors for mortality in our study population (Table 3), while association of other factors like comorbid conditions (diabetes and hypertension) and inflammatory (LDH, ferritin, D-dimer) and septic (C-reactive protein and procalcitonin) markers with mortality were not statistically significant.

**Discussion**

Hypothetically, there is a high risk of acquiring COVID-19 infection in the renal transplant recipients, and the reasons are multifactorial, including immunosuppressive medications, steroid therapy, comorbidities, frequent contact with the health care providers, and malnutrition. The incidence rate of COVID-19 infection in renal transplant recipients ranges from 9.5 to 17/1,000 transplants [7–10], whereas the incidence rate in our cohort is 13.68%. The number of renal transplant recipients infected with COVID-19 is higher (three times) than that of the general population [11]; a lower testing threshold may have contributed to better identification while many oligosymptomatic patients were not tested and do not appear in national statistics. The median age of our COVID-19-infected renal transplantation recipients was younger (47.46 vs. 60.9 years) than reported by other studies [7, 12]. Male predominance (59.25%) and distribution of comorbid (diabetes 47.6% and hypertension 64.3%) correlate with typical transplant patients’ characteristics. Among the latter, early publications proposed that hypertensive patients are highly susceptible to SARS-CoV-2 infection, with a drastic clinical course and increase in COVID-19-related deaths [13]. Regarding immunosuppressive medications in our cohort, our prac-
tice is to stop the antimetabolite and decrease the dose of CNI by 50%, if being treated with antiviral, with frequent monitoring of CNI levels in renal transplant recipients suffering from COVID-19 infection. Nevertheless, AKI was observed in 26% ($n = 11$) of our study population, and 66.67% of them recovered renal functions to base-

| Table 2. Comparison of patients’ characteristics: AKI versus non-AKI |
|---------------------------------------------------------------|
| Non-AKI ($n = 31, 73.80%$) | AKI ($n = 11, 26.19%$) | $p$ value |
| Age, years, mean (SD) | 47.95 (11.19) | 44 (8.47) | 0.353 |
| Gender, n (%) | | | | |
| Male | 17 (54.83) | 9 (81.81) | 0.113 |
| Transplant duration, months, mean (SD) | 111.63 (106.82) | 135 (104.78) | 0.511 |
| Hospital stay, days, median (IQR) | 16.18 (2–90) | 15.62 (7–24) | 0.743 |
| Comorbid, n (%) | | | | |
| Diabetes mellitus | 15 (48.38) | 5 (45.45) | 0.356 |
| Hypertension | 21 (67.74) | 6 (54.54) | 0.116 |
| Immunosuppression, n (%) | | | | |
| Triple | 21 (67.74) | 9 (81.81) | 0.075 |
|Dual | | | | |
|Prednisolone | 24 (77.41) | 9 (81.81) | 0.074 |
|Cyclosporine | 10 (32.25) | 3 (27.27) | 0.117 |
|Tacrolimus | 20 (64.51) | 10 (90.90) | 0.117 |
|MMF | 23 (74.19) | 9 (81.81) | 0.044 |
| Antiviral and immunomodulator, n (%) | | | | |
| Favipiravir | 16 (51.61) | 4 (36.36) | 0.470,101 |
| Kaletra | | 3 (27.27) | 0.001 |
|Remdesivir | 4 (12.90) | 2 (18.18) | 0.005 |
|Corticosteroids | 24 (77.41) | 8 (72.72) | 0.060 |
|Tocilizumab | 7 (22.58) | 5 (45.45) | 0.101 |
|Plasma | 0 | 2 (18.18) | 0.157 |
| Oxygen therapy, n (%) | | | | |
| Room air | 20 (64.51) | 2 (18.18) | 0.008 |
| Nasal cannula | 4 (12.90) | 1 (9.09) | 0.737 |
|Non-rebreather mask | 7 (22.58) | 2 (18.18) | 0.760 |
| Mechanical ventilation | 0 (0.00) | 6 (54.54) | 0.025 |
| Outcome, n (%) | | | | |
| Discharge to home | 29 (93.54) | 3 (27.27) | 0.001 |
| Transfer to another facility | 2 (6.45) | 2 (18.18) | 0.563 |
| Expired | 0 | 6 (54.54) | 0.025 |
| CXR, n (%) | | | | |
| Bilateral infiltrates | 27 (87.09) | 9 (81.81) | 0.667 |
| Unilateral infiltrates | 2 (6.45) | 1 (9.09) | 0.097 |
| No pneumonia | 2 (6.45) | 1 (9.09) | 0.097 |
| Lab investigations, median (IQR) | | | | |
| Absolute lymphocyte count | 0.77 (0.2–1.8) | 0.52 (0.2–0.9) | 0.048 |
| Procalcitonin, ng/mL | 0.38 (0.03–1.7) | 4.08 (0.2–28.2) | 0.327 |
| CRP, mg/L | 64.62 (3.5–159) | 139.37 (30–233) | 0.025 |
| Ferritin, ng/mL | 1,292 (58.3–6,809) | 3,586 (981–11,870) | 0.010 |
| D-dimer, μg/mL | 2.08 (0.2–20) | 2.50 (1.36–4.52) | 0.746 |
| LDH ($n = 28$), U/L | 334.90 (120–1,141) | 753.85 (463–1,606) | 0.055 |
| Interleukin-6 ($n = 15$), pg/mL | 387 (13.9–963) | 753.85 (463–1,606) | 0.055 |
| Creatinine at admission, mg/dL | 1.49 (0.6–4.5) | 2.83 (0.9–7.6) | 0.124 |
| Peak creatinine, mg/dL | 1.65 (0.7–5.2) | 4.07 (1.8–8.1) | 0.032 |
| Creatinine at discharge, mg/dL | 1.15 (0.6–3.6) | 2.11 (1.1–3.3) | 0.017 |

line; also, 33% of AKI patients had CNI toxicity. People with low absolute lymphocyte count, high CRP, and LDH and those who require mechanical ventilation were at high risk to develop AKI during their treatment. Cravedi et al. and Fava et al. [14, 15] reported a higher AKI incidence of 52 and 45.7%, respectively [3, 4], and
RRT was provided to 15 and 23% of AKI patients as mentioned by Aziz et al. and Marinaki et al. [16, 17], while in our cohort, only 1 patient required RRT. Urine studies in COVID-19-associated AKI usually indicate transient proteinuria and hematuria [18]. We also observed proteinuria and hematuria in 21% and 19% of COVID-19-infected renal transplant recipients who suffered from AKI, respectively. Acute tubular necrosis is the main histopathologic finding in AKI secondary to COVID-19 infection in the general population [19]. Additionally, glomerular lesions like minimal change disease, collapsing glomerulopathy [14, 15, 20–23], thrombotic microangiopathy, and pauci-immune crescentic glomerulonephritis are described in AKI associated with persistent proteinuria [14, 15, 21–25]. Information about histologic findings in AKI in transplant recipients is quite scarce. Case studies showed acute tubular necrosis, cortical necrosis [26], minimal change disease [27], and collapsing glomerulopathy [28]. Graft rejection is noted in very few cases, signifying a probable involvement of the COVID-19 virus in immune modulation [24, 26]. Graft biopsies were not performed in our cohort for logistic issues. Because of immunosuppression and comorbidities, there may be a higher risk of developing severe COVID-19 disease in renal transplant recipients; however, there are limited studies to compare acute respiratory distress syndrome (ARDS) in the general population and renal transplant recipients. In our cohort, 36 patients (86.67%) had radiological changes suggestive of pneumonia, 6 of 36 (16.66%) required mechanical ventilation.

| Table 3. Comparison of patient’s characteristics (survived and deceased): univariate logistic regression-mortality prediction |
|---------------------------------------------------------------|
| Deceased (n = 6, 14.28%) | Survived (n = 36, 85.71%) | p value | Odds ratio | 95% CI of odds ratio |
|-----------------------------|-----------------------------|---------|------------|---------------------|
| **Age, years, mean (SD)**   | 48.8 (5.76)                | 46.14 (11.8) | 0.455 | 0.311, 0.601 | 2.096, 8.81 |
| **Gender, n (%)**           | 5 (83.34)                  | 21 (58.33)    | 0.243 | 0.067, 0.75 | 0.001, 7.33 |
| **Transplant duration, months, mean (SD)** | 175.1 (122.55) | 104.8 (89.68) | 0.038 | 7.9, 1.115 | 56.289 |
| **Hospital stay, days, median (IQR)** | 16.6 (7–23) | 15.14 (1–90)    | 0.766 | 1.192, 0.323 | 4.39 |
| **Immunosuppression, n (%)** | 6 (100)                  | 24 (66.66)    | 0.007 | 0.069, 0.005 | 9.382 |
| **Antiviral and immunomodulator, n (%)** | 3 (50)                | 17 (47.22)      | 0.854 | 0.994, 0.945 | 1.046 |
| **Oxygen therapy, n (%)**   | 0 (40)                     | 0              | 0.171 | 0.25, 0.23  | 4.423 |
| **Lab investigations, median (IQR)** | 0.58 (0.2–0.9) | 0.7 (0.2–1.8) | 0.399 | 0.083, 0.001 | 12.606 |
| **Procalcitonin, ng/mL**    | 6.36 (0.27–28.7)           | 0.36 (0.037–1.7) | 0.344 | 0.986, 0.884 | 1.1 |
| **CRP, mg/L**               | 149.2 (62–233)             | 73.18 (3.6–189) | 0.087 | 0.328, 0.103 | 1.051 |
| **Ferritin, ng/mL**         | 4,228 (1,257–2,819)        | 1,455 (58–6,809) | 0.226 | 0.493, 0.192 | 1.264 |
| **D-dimer, pg/mL**          | 3.15 (1.8–4.5)             | 1.96 (0.2–20)   | 0.198 | 0.171, 0.31  | 4.423 |
| **LDH, U/L**                | 969.5 (463–1,606)          | 344.9 (120–1,141) | 0.075 | 0.56, 0.104  | 1.064 |
| **Interleukin-6 (n = 15), pg/mL** | 907 (60–3,124)         | 260.37 (16–963) | 0.438 | 0.763, 0.128 | 2.254 |
| **Creatinine at admission, mg/dL** | 3.3 (0.9–7.6)           | 1.54 (0.6–4.5)   | 0.001 | 9.263, 1.658 | 52.083 |
| **Peak creatinine, mg/dL**  | 5.4 (3.1–8.1)              | 1.68 (0.7–5.2)   | 0.001 | 0.55, 0.169  | 2.089 |
| **Creatinine at discharge, mg/dL** | 2.6 (1.4–3.3)            | 1.16 (0.6–3.6)   | 0.001 | 0.963, 0.259 | 3.221 |
but nevertheless, the same patients expired. Incidence of ARDS in renal transplant recipients up to 68% was reported by Elias et al. [29]. Spanish multicenter study and Bossini et al. [30] found higher odds of developing ARDS in renal transplant recipients with obesity (OR 2.63) and tacrolimus (OR 2.77), respectively [10, 30], whereas patients with >10-year-old renal grafts and GI symptoms at the onset of COVID-19 disease have a lesser risk of developing ARDS (OR: 0.37 and 0.21) [30]. Despite the high incidence of ARDS in renal transplant recipients, more studies are needed to prove that transplant recipients on chronic immunosuppression are more prone to have ARDS than the general population.

During the first wave of the pandemic, agents with presumed antiviral activity, i.e., hydroxychloroquine, antibiotics, and protease inhibitors, did not exhibit a beneficial response in prevention or treatment in either the general population [2, 31–33] or in renal transplant recipients [1–4, 24, 25] and rather interacted with immunosuppressive and other medications [34]. Twenty (47.61%) patients were treated with favipiravir, and five of them had toxic CNI levels. Remdesivir may succeed to reduce in-hospital stay of COVID-19 patients but had no effect on mortality reduction; however, initially, its use was considered unsafe in patients with a glomerular filtration rate less than 30 mL/min/1.73 m² [35], but later, its safety was confirmed by small-scale studies in the transplant population [36, 37]. In our cohort, 6 (15.62%) patients were treated with remdesivir, 2 of them suffered AKI, and also 4 patients had drug interaction with immunosuppressive medications, leading to increase in CNI levels (tacrolimus-remdesivir: n = 3, cyclosporine-remdesivir; n = 1). Large-scale randomized trials are needed to prove its efficacy in the transplant population. Regarding COVID-19 infection progression, it is observed that the two most important factors are viral eluding of immune response and cytokine storm, so attempts are made to modulate immune response with the use of immunomodulators. Large studies are available to advocate the potential role, safety, and efficacy of immunomodulators in the management of severe COVID-19 disease [38]. In our population, corticosteroids and tocilizumab were the two immunomodulators used in 34 and 12 (81 and 28%) transplant recipients with moderate to severe pneumonia, respectively; the mortality rate was 17.6% (6 out of 34) and 33.33% (4 out of 12) in patients on corticosteroid and tocilizumab treatment, respectively.

Fernandez-Ruiz et al. and Pérez-Sáez et al. [39, 40] observed in their nonrandomized trial that tocilizumab offers some benefit in critically ill patients in the general population and renal transplant recipients, respectively, whereas prospective randomized trials in COVID-19 pneumonia patients showed that tocilizumab may reduce chances of progression to mechanical ventilation without improving survival [41, 42]. Recovery trial depicts that dexamethasone decreases 28-day mortality in mechanically ventilated patients and on oxygen alone but not in those who do not require oxygen support [43]; therefore, future research must focus not only on effective immunomodulatory strategy but also on the timing of intervention to achieve maximum results. Carbajo-Lozoya et al. [44] observed the in vitro inhibitory effect of cyclosporine A and FK 506 on replication of SARS-CoV-1 and other human coronaviruses. Nonetheless, clinical evidence of the protective effect to decrease COVID-19 severity or to treat cytokine storm is lacking. This approach seems safe since the incidence of acute rejection is quite low with a change in immunosuppression. In our transplant population infected with COVID-19, 6 (14.28%) patients required mechanical ventilation, and none of them survived. A recent systematic review of 20 studies from different countries revealed that mortality in renal transplant recipients ranges from 18 to 43% and suffered higher mortality than the general population [45]. Old age [24, 34], plasma viral load [46], and high plasma biomarkers such as CRP, interleukin-6, LDH, and D-dimer [2, 4, 41] are associated with high mortality. In our cohort population, the requirement for mechanical ventilation was also an indicator of poor prognosis. Early intervention in the form of reducing immunosuppression may help in reducing mortality and improving prognosis in the transplant recipients and require further studies to prove. The epidemiological situation regarding COVID-19 is changing across the globe; it is recommended to carry out renal transplant recipient evaluation case by case while treating COVID-19 infection according to available resources.

We understand that our study has limitations as treatment protocol changes with the emergence of new insights in COVID-19 guidelines. Also there is possible underreporting of COVID-19 cases in renal transplant recipients as mild cases were being treated at home with teleconsultation. Our findings are derived from hospitalized cases, so the conclusion may not be applied to all as patients were diagnosed and treated in outpatient facilities. In summary, Dubai Hospital data provide applicable input in the management and outcome of COVID-19 infection in renal transplant recipients and may help to improve outcomes in the region and globally.
Conclusion

A significant number of renal transplant recipients suffered from AKI during COVID-19 infection, and the mortality rate in our study population was less than in other countries in the region (possibly due to early intervention and better health facilities). More insights are required to handle this infection in renal transplant recipients.

Statement of Ethics

This research complies with the guidelines for human studies and is conducted ethically in accordance with the Declaration of Helsinki. The study was approved by Dubai Scientific Research Ethics Committee, Decision DSREC-05-2,021_03, Date May 20, 2021. Patients who visited Dubai Hospital in Dubai Health Authority signed a general informed consent submitted in the EMR (SALAMA) to use their de-identified data for Research and Education purposes.

Conflicts of Interest Statement

The authors have no conflict of interest to declare.

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Author Contributions

Kashif Gulzar: conceived the idea of research, proposal writing, data collection, data analysis, and manuscript writing. Fakhrinya Alalawi: conceived the idea of research, proposal writing, and data collection. Dileep Nanik Ram Kumar: conceived the idea of research and data collection. Hebah Rami Al Jaghoub: data collection. Amna Alhadari: conceived the idea of research, supervision of the study, and creative input.

Data Availability Statement

The data that support the findings of this study are not publicly available due to privacy and security reasons. However, they are available from the corresponding author upon reasonable request.
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