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POST-COVID-19 COMPLICATIONS IN KIDNEY TRANSPLANT RECIPIENTS

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Abstract. *Background.* Although most people recover from acute COVID-19 within a few weeks, some have long-lasting clinical problems. The prevalence of these prolonged complications in kidney transplant (KT) recipients has not been determined. *Materials and methods.* Six months following of 148 patients with post-COVID-19 syndrome admitted to three centers in Iran (Tehran, Shiraz and Babol) that underwent KT were included in this study. Also, one-hundred COVID-19 patients without KT were included as the control group. The demographic data, medications, and disease course were recorded. The baseline and demographic characteristics were analyzed using the Chi-square test. Moreover, student's t-test were utilized to compare case and control groups. *Results.* The total number of patients was 248, of which 148 were in the case groups. Hospitalization associated with COVID-19 was for all patients; besides, there were 18 patients in control and 24 case groups admitted to an intensive care unit (ICU). The most commonly reported symptom was fever. Multivariate analysis identified the history of chronic kidney disease, hypertension, cerebral vascular accident, and diabetes mellites as predictors for developing post-COVID clinical complications. *Conclusion.* Evidence shows the high commonness of post-COVID-19 syndrome among kidney transplant patients after COVID-19, and the most common symptoms were fever, chills, and myalgia. So, all patients recovered from acute COVID-19 should undergo long-term monitoring to evaluate and treat possible complications.

Key words: *long-COVID-19, post-COVID-19, COVID-19, complications, kidney transplant, prolonged symptoms.*

ПОСТКОВИДНЫЕ ОСЛОЖНЕНИЯ У РЕЦИПИЕНТОВ ТРАНСПЛАНТИРОВАННОЙ ПОЧКИ

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Резюме. *Введение.* Хотя большинство людей выздоравливают от острой формы COVID-19 в течение нескольких недель, у некоторых заболевание приобретает затяжное течение с разного рода клиническими проявлениями. Распространенность таких вариантов COVID-19 у людей, перенесших трансплантацию почки (ТП), не установлена. *Материалы и методы.* В исследование было включено 148 пациентов с постковидным синдромом, госпитализированных в три центра в Иране (Тегеран, Шираз и Баболь). За шесть месяцев до

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этого им была проведена ТП. Контрольную группу составили 100 пациентов с COVID-19 без предшествующей ТП. Были проанализированы демографические данные, использованные лекарственные препараты и течение болезни. Исходные и демографические характеристики оценивались с использованием критерия хи-квадрат. Кроме того, для сравнения групп случаев и контрольных групп использовался t-критерий Стьюдента. *Результаты.* Все пациенты с COVID-19, включая перенесших ТП и лиц контрольной группы, были госпитализированны, причем лечение на отделении интенсивной терапии (ОИТ) потребовалось 24 больным с ТП в анамнезе и 18 пациентам контрольной группы. Наиболее частым симптомом была лихорадка. Многофакторный анализ обнаружил наличие в анамнезе хронических заболеваний почек, артериальной гипертензии, инсульта и сахарного диабета, которые являлись предикторами развития клинических осложнений после COVID-19. *Выводы.* Данные показывают высокую распространенность постковидного синдрома среди пациентов с трансплантацией почки после COVID-19. Наиболее распространенными симптомами были лихорадка, озноб и миалгия. Таким образом, все пациенты, выздоровевшие от острого COVID-19, должны проходить длительное наблюдение для оценки их состояния и терапии возможных осложнений.

Ключевые слова: *long-COVID-19, post-COVID-19, COVID-19, осложнения, трансплантация почки, пролонгированные симптомы.*

Introduction

On February 19, 2020, Iran reported its first COVID-19 mortality; by December 2022, more than 140,000 deaths were reported by SARS-CoV-2 infection [22]. In severe cases, multiple organ failure threatens patients with possible damage to vital organs such as the lungs, heart, liver, nervous system, and kidneys [18]. A condition known as "post-acute COVID-19 syndrome" or "long COVID-19," lasting for weeks or months, was observed in some recovered patients over time that was frequently manifested as persistent neurological, respiratory, or cardiovascular symptoms [17]. Persistent symptoms, such as fatigue, diffuse myalgia, and arthralgia, characterize Post-COVID-19 syndrome. These symptoms are linked mainly to mitochondrial dysfunction, oxidative stress, and low antioxidant levels [19]. Surprisingly, some patients with severe COVID-19 recover more quickly, whereas others with milder forms of the disease, or those who were asymptomatic, develop significant post-COVID-19 complications and require a long time to recover [24].

Immunocompromised patients may present with unusual symptoms after SARS-CoV-2 infection. Therefore, the Centers for Disease Control and Prevention (CDC) identify immunocompromised patients, including those requiring immunosuppressive treatment after organ transplantation, as high-risk groups at risk of becoming severely ill with SARS-CoV-2 [13]. Kidney transplantation (KT) is the ultimate treatment for end-stage renal disease (ESRD) patients. KT recipients (KTRs) are at high risk due to chronic immunosuppression and comorbidities.

A significant temporal relationship has been observed between the increase in the severity of COVID-19 infection and the increase in the mortality in solid organ transplant patients. This decline has been seen most in KT, even in regions with few cases of COVID-19 [14]. The European Union database stated that about 21% of deaths from COVID-19 between February 1, 2020, and May 1, 2020, were in KTRs. Risk factors in KTRs with COVID-19 are older age, more significant weakness, obesity, and previous lung disease [15]. In KTRs with COVID-19, fever, cough, respiratory failure, fatigue, myalgia, and gastrointestinal symptoms have been reported as the most common manifestations [10, 15].

Several medical facilities stopped all immunosuppressive regimens for KTRs with COVID-19 and replaced them with methylprednisolone. Despite a reduction and change in baseline immunosuppression, no transplant rejection was reported in any patients [15]. A systematic review examining KTRs with COVID-19 from Asia, Europe, and America reported that compared to patients with mild or moderate disease, patients with severe disease had higher C-reactive protein (CRP), lactate dehydrogenase (LDH), ferritin, and D-dimer. Moreover, more prolonged time from transplantation to COVID-19 diagnosis, hypoxia, and elevated LDH were associated with higher mortality. Also, COVID-19 was associated with higher morbidity and mortality in KTRs. None of the specific COVID-19 treatments was associated with disease improvement in KTRs [11].

Little is known about the outcomes of COVID-19 infection and it`s residual complications in KTRs. Thus, this study aimed to describe complications following COVID-19 in KTRs from three referral centers in Iran.

Materials and methods

Study design and participants. By the end of August 2022, we identified 148 adult KTRs with COVID-19 at Shahid Beheshti hospital of Babol (C1) (35 patients), Shahid Namazi hospital of Shiraz (C2) (63 patients), and Shahid Labafinezhad hospital of Tehran, Iran (C3) (50 patients). Another 100 patients with COVID-19 who did not undergo a KT were included in the study as the control group. Patients with two negative reverse transcriptase-polymerase chain reaction (RT-PCR) tests for SARS-CoV-2 were eligible for further follow-up at our outpatient clinics. Then, all included patients were followed up for six months. Ethical approval for this study was obtained from the ethics committee of Babol University of Medical Sciences (Reference code: IR.MUBABOL.HRI.REC.1401.086).

Procedures and questionnaires. Patients were interviewed with a standardized survey by an infectious dis-

ease specialist to recount symptoms during the acute illness and whether they persisted or some new occurred to assess clinical complications, such as dry cough, headache, fever, chills, myalgia, sore throat, sputum discharge, dyspnea, hemoptysis, chest pain, rhinorrhea, nasal congestion, nausea, and vomiting. Individually, other diagnostic procedures were employed (laboratory and radiologic). Patient information includes demographic data, prescribed medications, disease course, paraclinical assays, computed tomography (CT) scan, time of KT, and immunosuppressive medications, including azathioprine, mycophenolic acid, cyclosporine, sirolimus, and tacrolimus, the need for dialysis during hospitalization, and their final outcome were recorded via a standardized questionnaire.

Statistical analysis. The primary outcomes included the presence of clinical complications or the occurrence of laboratory abnormalities. Multiple logistic regression statistical tests will be used to investigate the relationship between hematological and biochemical variables and the occurrence of death. The results will be calculated and reported as an odds ratio (OR) with 95% confidence intervals. The model's variables include all the variables affecting the occurrence of death, which have been proven in the literature review. A significance level of 0.05 was considered in all tests. IBM SPSS version 26.0 software was used for data analysis.

Results

Demographic features of the patients. Of 248 patients, 134 (54%) were men, with an age range of 11 to 96 and a median age of 51.04±15.67 years. The mean age of the participants in the control group was 53.68±17.31 years. The details of the mean age of each center are provided in Table 1. There was not a significant difference between the age of the case and the control groups.

Patients in C1, C2, and C3 have received a transplant since 7.15±4.09, 12.56±12.54, and 6.66±6.14 years ago, respectively. Hospitalization associated with COVID-19 was for all patients, besides that there were 18 patients in control, 6 patients in C1, 3 patients in C2, and 15 patients in C3 groups admitted to an intensive care unit (ICU) because they needed intense support for failing organ systems, treatment, constant monitoring, and frequent nursing care, with a mean hospital stay of 7.44±7.95, 7.50±6.41, and 8.00±10.25 days, respectively. Table 1 shows the detailed characteristics of the study population.

The major maintenance immunosuppressive agents currently used in various combination regimens for case groups were Prednisolone (120 patients, $p = 0.001$), Tacrolimus (58 patients, $p = 0.004$), Sirolimus (3 patients, $p = 0.453$), Cyclosporine (80 patients, $p = 0.321$), Cellcept (98 patients, $p < 0.0001$), and Azathioprine (3 patients, $p = 0.007$).

Radiographic findings. Bilateral interstitial pneumonia was seen in C1 (71.90%), C2 (41.30%), and C3 (44%) ($p = 0.013$). Unilateral involvement was seen in the control group sharply high (76 patients) but in other centers was not too high (27 patients, 18.8%), and Consolidation was not a lot between the centers (32 patients, 22.5%). In contrast, Ground-glass opacity (GGO) was an enormous amount between the centers (114 patients, 79.2%) and effective in centers ($p = 0.021$). Radiologic features of patients shown in Table 2.

Post-COVID-19 clinical complications and conditions. Fever, chills, and myalgia were the most common prolonged symptoms commonly reported in patients infected with COVID-19. Among these patients, fever (132 patients, 53.7%) was the most common symptom, and 65 patients were from the control group ($p = 0.003$).

Details of clinical complication was demonstrated in Table 2.

The average oxygen saturation (SpO_2) for C1 on admission was 91.20±6.17%, and in discharge was 96.68±1.66%, for C2 on admissions was 91.97±4.10&, and in discharge was 95.15±2.79%, for C3 on admissions was 91.96±7.11%, and in discharge was 88.26±19.15%, and for the control group on admissions was 95.40±4.48%, and in discharge was 88.26±19.15%, showing that SpO_2 was higher in the control group. Further data are summarized in Table 3.

Chronic kidney disease (CKD) before transplant also was massive among patients (54.9%, $p < 0.0001$). Following that, in C3, 54,2% did Hemodialysis and 10% did Continuous renal replacement therapy (CRRT), which shows that kidneys were failed to purifying the blood from waste products such as creatinine and urea and free water ($p = 0.017$ and $p = 0.006$, respectively). It was seen that minor individuals had Polycystic ovary syndrome (PCOS) before the transplant (4 patients, 2.7%), ($p = 0.036$). Our study diagnosed AHF in C2 (1 patient) and C3 (8 patients). Different types of issues are in Table 4.

Discussion

After the transplant, people in the hospital experienced persistent COVID-19-related symptoms. This study aims to check whether transplants can lead to prolongation of COVID-19 symptoms. Generally, it is difficult to estimate the prevalence, characteristics, and duration of this new condition called a post-COVID syndrome, primarily because there is currently no accepted case definition for post-COVID syndrome and consensus on diagnostic procedures [5]. Most of the early data on post-COVID syndrome emerged from the follow-up of hospitalized individuals with COVID-19 who had a more severe disease course and, consequently, reported a higher prevalence of persistent symptoms.

We found post-COVID syndrome in patients with a mild to moderate COVID-19 course. So far, only two studies have been published on the post-COVID long-term outcomes in KTR. In the prospective co-

Table 1. Characteristics of study participants

Characteristics	Center 1	Center 2	Center 3	Control group	P value
Age, years, mean±SD	47.37±12.26	49.35±13.90	50.44±16.00	53.68±17.31	0.029
Sex, n (%) Male	19 (54.3)	43 (68.3)	32 (64)	42 (44.2)	< 0.0001
Years since transplantation, years, mean±SD	7.15±4.09	12.56±12.54	6.66±6.14	0	0
Duration of hospitalization in ICU, days, mean±SD	7.50±6.41	0	8.00±10.25	6.33±4.73	0.955
Drug history					
Prednisolone, n (%)	30 (85.7)	58 (92.1)	32 (64)	0	0.001
Tacrolimus, n (%)	6 (17.6)	25 (39.7)	27 (54)	0	0.004
Sirolimus, n (%)	1 (2.9)	2 (3.2)	0 (0)	0	0.453
Cyclosporine, n (%)	13 (38.2)	34 (54)	23 (46)	0	0.321
Cellcept, n (%)s	29 (82.9%)	49 (77.8%)	20 (40%)	0	< 0.0001
Azathioprine, n (%)	3 (8.6)	0 (0)	0 (0)	0	0.007
Past medical history					
PCOS, n (%)	3 (8.8)	0	1 (2)	0	0.036
Chronic kidney infection, n (%)	7 (21.2)	6 (9.5)	2 (4.1)	0	0.042
ADPKD	0	1	0	0	0
Kidney cancer, n (%)	2 (6.1)	2 (3.2)	4 (8)	0	0.527
CKD, n (%)	8 (25.8)	28 (44.4)	43 (86)	0	< 0.0001
HTN, n (%)	16 (45.7)	43 (68.3)	35 (70)	19 (19)	< 0.0001
CVA, n (%)	2 (5.7)	1 (1.6)	0	21 (21)	< 0.0001
Cardiovascular surgery, n (%)	5 (14.3)	0	2 (4)	4 (4)	0.784
DM, n (%)	10 (30.3)	17 (27.0)	23 (46)	28 (28)	0.301
Malignancy, n (%)	0	0	1 (2)	3 (3)	0.154
Chronic liver disease, n (%)	0	0	3 (2)	1 (1)	0.529
Brain diseases, n (%)	1 (2.9)	1 (1.6)	5 (10)	1 (1)	0.103
Complications					
CKD, n (%)	1 (2.9)	1 (1.6)	1 (2)	0	0.152
AIDS, n (%)	0	0	0	0	0
COPD, n (%)	0	0	1 (2)	1 (1)	0.779
ARDS, n (%)	1 (2.9)	0	0	2 (2)	0.349
Pneumonia, n (%)	1 (2.9)	0	0	1 (1)	0.779

Abbreviations: ICU, Intensive care unit; PCOS, Polycystic ovary syndrome; ADPKD, Autosomal dominant polycystic kidney disease; CKD, Chronic kidney disease; HTN, Hypertension; CVA, Cerebrovascular accident; DM, Diabetes mellitus; AIDS, Acquired immunodeficiency syndrome; COPD, Chronic obstructive pulmonary disease; ARDS, Acute respiratory distress syndrome.

Table 2. Post-COVID-19 radiographic features of study participants

Types of problem	Center 1	Center 2	Center 3	Control group	P value
Bilateral lung involvement, n (%)	23 (71.9%)	26 (41.3%)	22 (44%)	0	0.013
Unilateral lung involvement, n (%)	8 (25.8%)	9 (14.3%)	10 (20%)	76 (83.5%)	0.389
Consolidation, n (%)	7 (23.3%)	9 (14.3%)	16 (32.7%)	0	0.069
GGO, n (%)	30 (96.8%)	48 (76.2%)	36 (72%)	0	0.021
Peripheral involvement, n (%)	15 (48.4%)	29 (46%)	20 (40%)	0	0.719
Peribronchovascular involvement, n (%)	6 (20%)	6 (9.5%)	8 (16%)	0	0.348
Involvement in lung base, n (%)	12 (40%)	3 (4.9%)	3 (6.1%)	0	< 0.0001
Cavitary lesions, n (%)	0	3 (4.9%)	0	0	0.134
Diffuse pulmonary nodules, n (%)	0	0	0	0	0
Tree-in-bud pattern, n (%)	0	0	13 (26%)	0	< 0.0001
Pleural effusion, n (%)	2 (6.7%)	10 (15.9%)	11 (22.4%)	0	0.181
Lymphadenopathy, n (%)	0	1 (1.6%)	8 (16%)	0	0.002
Linear opacities, n (%)	0	0	2 (4%)	0	0.152
Crazy paving, n (%)	12 (40%)	3 (4.8%)	22 (44%)	0	< 0.0001
Reversed halo sign, n (%)	0	2 (3.2%)	14 (28%)	0	< 0.0001

Abbreviations: GGO, Ground-glass opacity.

Table 3. Self-reported symptoms by study participants.

Symptoms	Center 1	Center 2	Center 3	Control group	P-value
Fever, n (%)	2 (5.7%)	44 (69.8%)	21 (42%)	65 (65%)	0.003
Chills, n (%)	1 (3.1%)	45 (71.4%)	16 (32%)	64 (64%)	0.001
Myalgia, n (%)	2 (6.1%)	21 (33.3%)	18 (36%)	44 (44%)	0.01
Headache, n (%)	1 (3%)	10 (15.9%)	4 (8%)	6 (6%)	0.239
Dry cough, n (%)	3 (9.1%)	40 (63.5%)	24 (48%)	34 (34.3%)	0.072
Sore throat, n (%)	1 (2.9%)	9 (14.3%)	2 (4%)	0	0.003
Sputum discharge, n (%)	2 (5.7%)	1 (1.6%)	4 (8%)	6 (6%)	0.337
Dyspnea, n (%)	1 (3%)	40 (63.5%)	33 (66%)	47 (47%)	0.570
Hemoptysis, n (%)	0	1 (1.6%)	0	1 (1%)	0.787
Chest pain, n (%)	0	2 (3.2%)	1 (2%)	6 (6%)	0.105
Rhinorrhea, n (%)	1 (2.9%)	1 (1.6%)	2 (4%)	0	0.149
Nasal congestion, n (%)	0	2 (3.2%)	1 (2%)	0	0.002
Nausea Vomiting, n (%)	2 (6.1%)	24 (38.1%)	14 (28%)	11 (11%)	0.002
Diarrhea, n (%)	0	17 (27%)	7 (14%)	8 (8%)	0.053
Constipation, n (%)	6 (18.2%)	1 (1.6%)	2 (4%)	0	0.011
Loss of appetite, n (%)	1 (3%)	8 (12.7%)	3 (6%)	7 (7%)	0.725
Arthralgia, n (%)	0	8 (12.7%)	0	0	0.017
Stomachache, n (%)	0	1 (1.6%)	3 (6%)	5 (5%)	0.354
Vertigo, n (%)	0	11 (17.5%)	2 (4%)	0	0.002
Attention disorder, n (%)	0	3 (4.8%)	0	1 (1%)	0.521
Memory disorder, n (%)	0	3 (4.8%)	0	0	0.133
Depression, n (%)	2 (6.1%)	4 (6.3%)	0	0	0.196
Anosmia, n (%)	0	5 (7.9%)	0	0	0.033
Ageusia, n (%)	0	1 (1.6%)	0	0	0.515
Dermatologic manifestations, n (%)	0	2 (3.2%)	0	0	0.263
Hair loss, n (%)	2 (6.1%)	13 (20.6%)	0	0	0.001
Sleep disturbances, n (%)	1 (3%)	2 (3.2%)	0	0	0.450
Weight loss, n (%)	6 (18.2%)	9 (14.3%)	0	0	0.011
Weight gain, n (%)	1 (3%)	2 (3.2%)	0	0	0.450
Cardiac manifestations, n (%)	1 (3%)	1 (1.6%)	10 (20%)	0	0.001
Decreased sense of touch, n (%)	1 (3%)	1 (1.6%)	0	0	0.499
CNS manifestations, n (%)	1 (3%)	0	11 (22%)	0	< 0.0001
Cyanosis in lips and face, n (%)	1 (3%)	0	0	0	0.178

Table 4. Post-COVID-19 conditions

Conditions, mean±SD	Center 1	Center 2	Center 3	Control group	P value
SpO_2 on admission, mean±SD	91.20±6.17	91.97±4.10	91.96±7.11	95.40±4.48	< 0.0001
SpO_2 on discharge, mean±SD	96.68±1.66	95.15±2.79	88.26±19.15	0	0.005
BUN on admission, mean±SD	34.09±24.03	76.24±48.47	44.58±30.93	20.56±12.46	< 0.0001
BUN on discharge, mean±SD	29.33±20.76	110.36±218.38	43.38±26.29	0	< 0.0001
Creatinine on admission, mean±SD	1.59±1.27	4.31±17.68	3.25±2.28	1.48±3.60	< 0.0001
Creatinine on discharge, mean±SD	1.23±0.69	1.97±1.46	2.26±1.18	0	< 0.0001
LDH on admission, mean±SD	720.30±253.00	459.02±183.70	707.17±439.63	442.39±168.24	0.003
AKF, n (%)	0	0	14 (28%)	0	0.002
Hemodialysis, n (%)	1 (2.9%)	10 (15.9%)	13 (26%)	0	0.017
CRRT, n (%)	0	0	5 (10%)	0	0.006

Abbreviations: SpO_2, Oxygen saturation; BUN, Blood urea nitrogen; LDH, Lactate dehydrogenase; AKF, Acute kidney disease; CRRT, Continuous renal replacement therapy.

hort study by Basic-Jukic et al., only 11.53% of 104 KTR who survived acute mild to moderate COVID-19 had no clinical symptoms or were free from any laboratory abnormality during the median follow-up of 64 days (range: 50–76 days) after recovery [6].

In our study, prolonged symptom duration and clinical complications were present in 0 to 10% of patients in C1, but in C2 and C3 range in too varied but in control group in average was higher than centers like fever (65%). In contrast, a small number of individuals had one or more laboratory abnormalities, and the most significant abnormalities were HTN which in C3 was 70%. Many patients require ICU admission for severe complications. In a study, Chauhan et al. reported their investigation regarding the long-term consequences of COVID-19 in KTR from India. Even in individuals with a mild course of COVID-19, persistent symptoms and deterioration in the quality of life were observed up to 6 months after follow-up. Fatigue, alopecia, sleep disturbances, and loss of appetite were the most frequently reported symptoms, and anxiety/depression was the worst affected component of quality of life [8].

Previous studies used various diagnostic methods (questionnaires, laboratory or imaging tests) and focused on different groups of patients. As a result, data on the majority of the post-COVID syndrome in the total population vary greatly, ranging from 75–93% in hospitalized patients [7, 12, 21], to 10–20% in patients with a mild course of the disease [2, 20]. On the contrary, at least one persistent symptom at six months post-disease was observed in only 8% of KTR in the recent study from India. Notably, the studied cohort was significantly younger than our patients, and the most remarkable thing is the age that is so widely varied from 22 to 96.

Moreover, the percentage of patients with a severe course of COVID-19 was not significant and amounted only to 12% [8]. Most of the conditions that happened to patients were fatigue and weakness. also we found that fatigue was the most common persistent symptom in KTR, consistent with data from the long-term follow-up study of Huang et al. in the general population and KTR from India [8, 12].

However, the course of COVID-19 in our research was mainly moderate, without significant respiratory involvement. As in other studies, hair loss, sleep difficulties, myalgia, and memory disturbances were some of the most frequently reported persistent symptoms [1, 8]. Hair loss was the other most frequently reported complaint, which in transplant may result from the cumulative effects of COVID-19, and the side effects of immunosuppressants, particularly tacrolimus or other drugs [23, 25].

Basic-Jukic et al.'s study demonstrated that complications were more frequent in KTR with diminished glomerular filtration and those with diabetes mellitus [6]. Older age, gender, and initial dyspnea were found to be significantly associated with an increased risk of the post-COVID syndrome in the general population [3, 9, 16]. In a controlled cohort investigation, including 47.780 citizens of England, Ayoubkhani et al. displayed that people released from hospital after COVID-19 had increased rates of multiorgan dysfunction (particularly respiratory and cardiometabolic) compared with a matched control group from the general population without COVID-19 in history [4].

Conclusion

In conclusion, recovery from acute COVID-19 is associated with different clinical and laboratory complications in the renal transplant population, regardless of the age or severity of initial symptoms. The constant symptoms, weakness, hair loss, dyspnea, mental disorders, myalgia, and headaches were more frequent in older patients and those with more significant comorbidity. Finally, we can say transplants can reduce immunity in patients with COVID-19. Our results highlight the need for a long-term follow-up of convalescences in this population for diagnostic and rehabilitation programs. All patients who recovered from COVID-19 should undergo long-term monitoring to evaluate and treat complications. Further studies with long-term follow-up are needed.

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Availability of data and materials

All relevant data are within the paper however, any question or other file data is required you can contact us using the email address, upon reasonable request.

Declarations

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