

# POST-COVID-19 CONDITION IN SOLID ORGAN TRANSPLANT RECIPIENTS: A SINGLE-CENTER EXPERIENCE

ŽELJKA JUREKOVIĆ<sup>1</sup>, KSENIJA VUČUR ŠIMIĆ<sup>1</sup>, LADA ZIBAR<sup>1,2</sup>

<sup>1</sup>Department of Nephrology, Merkur University Hospital, Zagreb, Croatia; <sup>2</sup>Faculty of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia

Solid organ transplant (SOT) recipients who survived acute COVID-19 can develop post-COVID-19 condition. Post-COVID-19 condition can affect multiple organ systems, and its prevalence is up to 70% in general population. Data regarding post-COVID-19 condition in SOT recipients are scarce. The aim of our study was to investigate the prevalence and characteristics of post-COVID-19 condition in SOT recipients. The study included SOT recipients who had kidney transplantation in Merkur University Hospital between 2007 and 2020, and who survived COVID-19. Between July 2020 and June 2021, 78 transplanted patients (kidney only or combined with pancreas or liver) had acute COVID-19, of which 13 patients died. The study was conducted in the form of survey and included 60 patients who all gave informed consent for participation in the study. Post-COVID-19 condition experienced 40 (67%) patients, and most common symptoms were fatigue (43%) and shortness of breath (30%), followed by hair loss (27%), insomnia (22%), sweating (22%), and decline in the quality of life (20%). There was no difference between patients with post-COVID-19 condition and those without post-COVID-19 condition regarding gender, age, transplanted organ(s), time from transplantation to COVID-19, or need of hospitalization due to COVID-19. In conclusion, post-COVID-19 condition was frequent among SOT (kidney) patients, with fatigue and shortness of breath as the most common symptoms, as in general population. Thus, unfortunately, COVID-19 contributed to their comorbidity burden at longterm as well.

**Key words:** post-COVID-19, SARS-CoV-2, kidney transplantation

**Address for correspondence:** Željka Jureković, MD  
Department of Nephrology  
Merkur University Hospital  
Zajčeva 19  
10000 Zagreb, Croatia  
E-mail: zeljka.jurekovic@gmail.com

## INTRODUCTION

Solid organ transplant (SOT) recipients represent a frail population susceptible to various infective complications, including infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) responsible for coronavirus disease 2019 (COVID-19) (1). COVID-19 is a multi-organ disease with a broad spectrum of manifestations. Given the diversity of organ systems that can be affected by COVID-19, survivors might have persistent postinfection sequels, called post-COVID-19 condition (2). Post-COVID-19 is defined by Delphi consensus as a condition that occurs in patients with COVID-19 usually three months from the onset, with symptoms that last for at least two months, and cannot be explained by an alternative diagnosis (2). Given that post-COVID-19 is a relatively new condition, its exact prevalence in general population is unknown, but according to one study, up to 70% of patients experienced long-term consequences

of COVID-19 (3). It seems that the prevalence of post-COVID-19 condition does not depend of the severity of acute COVID-19, indicating that hospitalized patients and outpatients, including asymptomatic ones, are both at risk of experiencing long-term consequences of COVID-19 (4). Post-COVID-19 condition is often associated with multiple organ systems, although fatigue, shortness of breath, and cognitive impairment are reported as most common. Furthermore, negative impact on the quality of life and socioeconomic status is also relevant (3). It has been shown that kidney disease is associated with a higher risk of in-hospital mortality among COVID-19 patients (5). Kidney transplant recipients (KTR) have often allograft dysfunction and are more susceptible to acute kidney injury (6). Studies have reported higher mortality rate in KTR with COVID-19 compared to non-transplant patients (7-9). Immunocompromised patients, such as SOT recipients, are more susceptible to COVID-19, have a

greater risk of disease progression and prolonged recovery compared to non-transplant patients (10). It is expected that this population is at an increased risk of experiencing post-COVID symptoms. Nevertheless, data regarding post-COVID-19 condition in SOT recipients are scarce (3). The aim of our study was to investigate the prevalence and characteristics of post-COVID-19 condition in SOT recipients.

## PATIENTS AND METHODS

Kidney transplant recipients who had transplantation in Merkur University Hospital between 2007 and 2020 and who survived COVID-19 from July 2020 to June 2021 were asked to participate in the study. Data regarding COVID-19 were regularly documented in all KTRs who were followed-up at our outpatient clinic. The diagnosis of COVID-19 was confirmed by the reverse transcription polymerase chain reaction test from nasopharyngeal/oropharyngeal swab.

Between July 2020 and June 2021, 78 patients had acute COVID-19, of which 13 patients did not survive. All patients who survived acute COVID-19 were contacted to participate in the study, of which five refused it. So, 60 patients were included in the study. The study was conducted in the form of questionnaire on regular follow up, or in the form of telephone interview during the year 2021. All participants gave informed consent for participation in the study. The following post-COVID-19 symptoms were analyzed: fatigue, shortness of breath, cough, anosmia, arthralgia, myalgia, headache, dysgeusia, inappetence, hair loss, dizziness, insomnia, sweating, diarrhea, inability to concentrate, anxiety, depression, memory loss, and decline in the quality of life.

### Statistics

Continuous variables were expressed as median (interquartile range, IQR), and categorical variables as absolute number (percentage). Differences between the groups were analyzed with Mann-Whitney test for continuous variables, and using  $\chi^2$ -test or Fisher exact test when appropriate for categorical variables. Statistical analysis was performed using the STATISTICA (version 12.0 Stat Soft Inc, Tulsa, OK, USA) software.

## RESULTS

The study included 60 SOT recipients (65% of male), median age at transplantation 45 (IQR 37-55) years, who had COVID-19 during 2020 and 2021. There were 45 kidney only transplant recipients, 13 pancre-

as and kidney, and 2 liver and kidney transplant recipients. Median time from transplantation to acute COVID-19 was 5 (IQR 2-10) years. Twenty of them were hospitalized due to COVID-19. All participants survived COVID-19. Among the COVID-19 survivors, 40 (67%) had post-COVID-19 symptoms. The most common symptoms were fatigue (43%) and shortness of breath (30%), followed by hair loss (27%), insomnia (22%), sweating (22%), and decline in the quality of life (20%) (Figure 1). Regarding duration of post-COVID-19 symptoms, patients reported fatigue, hair loss, insomnia, and decline in the quality of life as most persistent (longer than three months), while none of the patients had anosmia, dysgeusia, or inappetence for more than three months. Among patients with post-COVID-19, hair loss was more common among females compared to males (70.6% vs. 17.4%;  $p=0.001$ ), whereas no gender difference was found in other post-COVID-19 symptoms. There was no difference between patients with post-COVID-19 condition and those without post-COVID-19 condition according to gender ( $p=0.15$ ), age ( $p=0.882$ ), transplanted organ(s) ( $p=0.562$ ), time from transplantation to COVID-19 ( $p=0.312$ ) or need of hospitalization due to COVID-19 ( $p=0.395$ ) (Table 1).

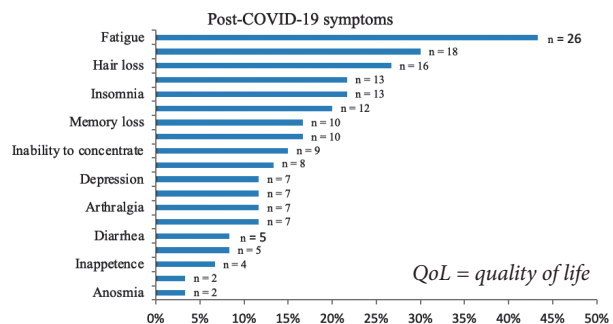


Figure 1. Prevalence of post-COVID-19 symptoms among solid organ transplant recipients (N=60).

Table 1. Solid organ transplant recipients with post-COVID-19 and without post-COVID-19 (N=60)

Variable	Post-COVID-19 Yes (n=40)	Post-COVID-19 No (n=20)	p
Gender (male), n(%)	23 (57.5)	16 (80)	0.15 <sup>†</sup>
Age <sup>#</sup> (years)	48 (36.0-53.5)	41 (36.5-56.5)	0.882 <sup>†</sup>
Type of transplantation, n (%)			
Kidney	30 (75)	15 (75)	0.562 <sup>‡</sup>
SPKT	8 (20)	5 (25)	
SLKT	2 (5)	0	
Time from transplantation to COVID-19 (years) <sup>#</sup>	6.3 (2.6-19.5)	3.9 (1.9-9.3)	0.312 <sup>†</sup>
Need of hospitalization, n (%)	15 (37.5)	5 (25)	0.395 <sup>†</sup>

\* $\chi^2$ -test or Fisher exact test; #median (interquartile range, IQR); †Mann-Whitney test; SPKT = simultaneous kidney-pancreas transplantation; SLKT = simultaneous liver-kidney transplantation

## DISCUSSION

A meta-analysis which included 47 950 patients showed a prevalence of 80% of post-COVID-19 in general population (3). We analyzed post-COVID-19 symptoms in SOT recipients, of which three-quarters were only kidney recipients, while the rest had combined SOT. Our research showed a high prevalence of post-COVID-19 among SOT recipients (67%), without taking into account the severity of acute COVID-19. To date, small observational studies on post-COVID-19 condition in SOT recipients have been published (11,12). According to the Polish study which included 67 KTRs, the prevalence of post-COVID-19 syndrome was 70%, similar as in our research (12). Another study reports clinical complications in 45% of KTR following acute COVID-19, whereas laboratory abnormalities were found in 71% of patients (11). In our study, self-reported fatigue and shortness of breath were most common, followed by hair loss, insomnia, sweating, and reduced quality of life. On the other hand, anosmia and dysgeusia were uncommon. In line with our results, Malinowska *et al.* report that fatigue (43%), dyspnea (34%) and hair loss (31%) were the most common symptoms, whereas smell disorder was the least common one (3%) (12). In addition, Basic Jukic *et al.* also report shortness of breath and tiredness as the most common clinical complications among KTRs (11). In a meta-analysis which included 15 studies with 47 910 patients, almost 60% of patients had fatigue, followed by headache (44%), attention disorder (27%), hair loss (25%), and dyspnea (24%) (3). According to published studies, it seems that post-COVID-19 symptoms including fatigue and dyspnea are frequent in general population and in SOT recipients. One-quarter to almost one-third of patients will experience hair loss after acute COVID-19 (3,12). We found a significantly higher prevalence of hair loss among female patients. Several studies also report a higher prevalence of hair loss after acute COVID-19 among female patients from general population (13-15). Hyperinflammatory response, called cytokine storm occurring during acute COVID-19, may initiate hair loss, together with other factors such as depression and anxiety, which can occur afterwards (18). Numerous clinical complications in KTRs, such as worsening of hypertension, *de novo* diabetes mellitus, skin changes, etc., can occur following acute COVID-19, but they seem to be infrequent (11). Not all sequels of post-COVID-19 last equally. In a study conducted among KTRs in India, fatigue was the most common symptom but its prevalence decreased significantly with time (17). Also, improvement in the quality of life was observed in the majority of patients as follow up time was prolonged (17). On the other hand, in our research, fatigue, hair loss, insomnia, and decline in the quality of life were the most persistent symptoms (lasting beyond three

months). In both studies, duration of anosmia was short. This difference in the duration of symptom persistence could be because of the characteristic of the study population, younger patients in India compared to our population, and severity of acute COVID-19 (17). All patients in India required hospitalization *versus* 37.5% of our patients who had post-COVID-19 symptoms (17). We did not find any difference according to gender, age, type of transplanted organ(s), time from transplantation to COVID-19, or need of hospitalization due to acute COVID-19 between patients who developed post-COVID-19 condition and those who did not experience any of post-COVID-19 symptoms. Our results on the prevalence of post-COVID-19 in SOT recipients, with fatigue and shortness of breath being most common, are comparable to the previously published results in general population, as well as in KTRs (3,12).

Our study had several limitations. First was a small study sample. Second, we did not have data on treatment during acute COVID-19. Third, timing of follow up after recovery from acute COVID-19 at our outpatient clinic was not equal in all patients. Fourth, we did not use a widely and validated questionnaire regarding post-COVID-19 symptoms. Fifth, the nature of telephone interview could influence data quality compared to data obtained by face to face interview. However, the main strength of the study are particular epidemiological data on Croatian SOT patients in COVID-19 pandemic during the first pandemic years, inadequately present in the literature so far. Additional strength is that we analyzed miscellaneous post-COVID-19 symptoms (a total of 19 symptoms). Further studies should focus on investigating this relatively new syndrome, risk factors and its consequences in immunocompromised patients such as SOT recipients.

In conclusion, kidney transplanted patients frequently experienced post-COVID-19, irrespective of their gender, age, kidney only or combined SOT or time from transplantation, or even hospitalization, with fatigue and shortness of breath as the most common symptoms, as in general population. Unfortunately, COVID-19 also contributed to their comorbidity burden at longterm.

## R E F E R E N C E S

1. Bruchfeld A. The COVID-19 pandemic: consequences for nephrology. *Nat Rev Nephrol.* 2021;17(2):81-2.
2. Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV; WHO Clinical Case Definition Working Group on Post-COVID-19 Condition. A clinical case definition of post-

COVID-19 condition by a Delphi consensus. *Lancet Infect Dis* 2022;22(4):e102-e107.

3. Lopez-Leon S, Wegman-Ostrosky T, Perelman C, Sepulveda R, Rebolledo PA, Cuapio *Aetal*. More than 50 long-term effects of COVID-19: a systematic review and meta-analysis. *Sci Rep* 2021;11(1):16144.

4. Townsend L, Dowds J, O'Brien K, Sheill G, Dyer AH, O'Kelly B *et al*. Persistent poor health post-COVID-19 is not associated with respiratory complications or initial disease severity. *Ann Am Thorac Soc* 2021;18:1431-2.

5. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L *et al*. Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int* 2020;97(5):829-38.

6. Goldberg RJ, Weng FL, Kandula P. Acute and chronic allograft dysfunction in kidney transplant recipients. *Med Clin North Am* 2016;100(3):487-503.

7. Akalin E, Azzi Y, Bartash R, Seethamraju H, Parides M, Hemmige V *et al*. COVID-19 and kidney transplantation. *N Engl J Med* 2020;382(25):2475-7.

8. Pereira MR, Mohan S, Cohen DJ, Husain SA, Dube GK, Ratner LE *et al*. COVID-19 in solid transplant organ recipients: initial report of the US epicenter. *Am J Transplant* 2020;20(7):1800-8.

9. Alberici F, Delbarba E, Manenti C, Econimo L, Valerio F, Pola A *et al*. A single center observational study of the clinical characteristics and short-term outcome of 20 kidney transplant patients admitted for SARS-CoV2 pneumonia. *Kidney Int* 2020;97(6):1083-8.

10. Caillard S, Chavarot N, Francois H, Matignon M, Greze C, Kamar N *et al*. Is COVID-19 infection more severe in kidney transplant recipients? *Am J Transplant* 2021;21(3):1295-303.

11. Basic-Jukic N, Juric I, Furic-Cunko V, Katalinic L, Radic J, Bosnjak Z *et al*. Follow-up of renal transplant recipients after acute COVID-19 – a prospective cohort single-center study. *Immun Inflamm Dis* 2021;9(4):1563-72.

12. Malinowska A, Muchlado M, Ślizień Z, Biedunkiewicz B, Heleniak Z, Dębska-Ślizień A *et al*. Post-COVID-19 syndrome and decrease in health-related quality of life in kidney transplant recipients after SARS-COV-2 infection – a cohort longitudinal study from the north of Poland. *J Clin Med* 2021;10(21):5205.

13. Xiong Q, Xu M, Li J, Liu Y, Zhang J, Xu Y *et al*. Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. *Clin Microbiol Infect* 2021;27(1):89-95.

14. Monari P, Gualdi G, Bettoni G, Costa R, Ragni G, Zani F *et al*. Post-SARS-CoV-2 acute telogen effluvium: an expected complication. *J Clin Med* 2022;24;11(5):1234.

15. Abdulwahab RA, Aldajani BM, Natto NK, Janabi AM, Alhijaili OI, Faqih NT *et al*. Prevalence of hair loss after COVID-19 infection in Makkah Region, Saudi Arabia. *Cureus* 2022;14(9):e29285.

16. Sharquie KE, Jabbar RI. COVID-19 infection is a major cause of acute telogen effluvium. *Ir J Med Sci* 2022;191(4):1677-81.

17. Chauhan S, Meshram HS, Kute V, Patel H, Desai S, Dave R. Long-term follow-up of SARS-CoV-2 recovered renal transplant recipients: a single-center experience from India. *Transpl Infect Dis* 2021;23(6):e13735.

## SAŽETAK

### STANJE POST-COVID-19 U PRIMATELJA BUBREŽNOG PRESATKA: ISKUSTVO JEDNOG CENTRA

Ž. JUREKOVIĆ<sup>1</sup>, K. VUČUR ŠIMIĆ<sup>1</sup>, L. ZIBAR<sup>1,2</sup>

<sup>1</sup>Zavod za nefrologiju, Klinička bolnica Merkur, Zagreb, Hrvatska; <sup>2</sup>Medicinski fakultet, Sveučilište Josipa Jurja Strossmayera, Osijek, Hrvatska

Bolesnici s presađenim organom koji su preboljeli COVID-19 mogu razviti sindrom post-COVID-19. Sindrom post-COVID-19 obilježen je mogućnošću zahvaćanja više organskih sustava, a javlja se u do 70 % bolesnika u općoj populaciji. Podatci o sindromu post-COVID-19 među bolesnicima s presađenim organom su oskudni te je stoga cilj ovoga istraživanja bio utvrditi učestalost i obilježja sindroma post-COVID-19 u navedenoj populaciji. Istraživanje je uključilo bolesnike koji su imali presadbu bubrega u Kliničkoj bolnici Merkur u razdoblju od 2007. do 2020. godine i koji su preživjeli COVID-19. U razdoblju od srpnja 2020. do lipnja 2021. godine 78 bolesnika (s presađenim samo bubregom ili bubregom i gušteračom ili bubregom i jetrom) preboljelo je COVID-19, od kojih je 13 umrlo. Istraživanje je provedeno u obliku ankete, a uključilo je 60 bolesnika koji su dali dobrovoljni pristanak za sudjelovanje. Sindrom post-COVID-19 razvilo je 40 (67 %) ispitanika, a najčešći simptomi bili su umor (43 %), kratkoća daha (30 %), gubitak kose (27 %), nesanica (22 %), znojenje (22 %) i smanjenje životne kakvoće (20 %). Nije nađeno razlike između bolesnika sa sindromom post-COVID-19 i onih koji nisu razvili sindrom post-COVID-19 s obzirom na spol, dob, vrstu presađenog organa, vrijeme od presadbe organa do COVID-19 ili potrebe za hospitalizacijom zbog COVID-19. Zaključno, prema rezultatima našeg istraživanja možemo reći da je sindrom post-COVID-19 čest među bolesnicima s presađenim solidnim organom (bubregom) te da su umor i kratkoća daha najčešći simptomi, kao i u općoj populaciji. COVID-19 je tako, nažalost, i dugoročno doprinio njihovom ukupnom pobolu.

**Ključne riječi:** post-COVID-19, SARS-CoV-2, transplantacija bubrega