

Original Article

COVID-19 Impact on Lower Urinary Tract Symptoms of Kidney Transplantation Recipients

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HIGHLIGHTS

- Kidney transplantation recipients are one of the most vulnerable populations to COVID-19 infection.
- LUTS in kidney transplant recipients was significantly more intense in those affected by COVID-19 infection.
- The kidney transplant recipients with COVID-19 had a higher risk of moderate IPSS than those without COVID-19.

ARTICLE INFO

Receive Date: 30 April 2022

Accept Date: 13 June 2022

Available online: 21 June 2022

DOI: 10.22034/TRU.2022.345939.1113

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ABSTRACT

Introduction

Kidney transplantation recipients are one of the most vulnerable populations to COVID-19 infection and are more prone to develop complications. The lower urinary tract might be seriously affected by COVID-19 disease in this population. The present study aimed to assess the impact of COVID-19 disease on LUTS in kidney transplantation recipients.

Methods

All patients who underwent kidney transplantation at Sina Hospital (Tehran University of Medical Sciences, Iran) were included in this cross-sectional study. Covid-19 infection was confirmed by real-time polymerase chain reaction (PCR) of oropharyngeal swabs. All patients with urinary tract infections were excluded from the study. LUTS status was assessed by International Prostate Symptom Score (IPSS).

Results

The study involved 153 consecutive kidney transplant recipients; 67 (43.8%) and 86 (56.2%) patients were with and without Covid-19, respectively. The mean age of all patients was 49.7 ± 12.9 years, and 105 (68.6%) males were in the study. The mean IPSS in kidney transplant recipients with and without Covid-19 was 2.74 ± 3.0 and 1.96 ± 2.7 , respectively. A significant difference was observed in IPSS between patients with and without Covid-19 (P -value= 0.03). The kidney transplant recipients with COVID-19 had a higher risk of moderate IPSS (OR:1.5 CI 95%: 0.5-4.87) than those without COVID-19, but it is not significant (P -value=0.4).

Conclusions

We pioneering found that LUTS in kidney transplant recipients measured by the validated tool IPSS was significantly more intense in those affected by COVID-19 infection. Future studies are necessary to explore the long-term impact and potential sequels.

Keywords: Lower Urinary Tract Symptom; Covid-19; Kidney Transplantation; SARS-CoV-2

Introduction

The coronavirus disease 2019 (COVID-19) epidemic that results from infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an international

concern, showing a significant warning to public health (1). There is insufficient data about COVID-19 because it is a new disease, and all its symptoms are not entirely known (2).

The patients with COVID-19 present firstly with fever, cough, diarrhea, shortness of breath, and lack of taste. Although respiratory symptoms are the main sign of COVID-19, various organs are involved, including the central nervous system, gastrointestinal tract, cardiovascular system, bone marrow, liver, and kidney (3-5). In addition, the lower urinary tract is a possible SARS-CoV-2 target due to significant angiotensin-converting enzyme 2 (ACE2) expression in urothelial cells (6). Recently, Can et al. found that lower urinary tract symptoms (LUTS) might be one of the COVID-19 infection symptoms, and in elderly patients, the International Prostate Symptom Score (IPSS) significantly increased (7). The most common lower urinary tract involvement symptoms are urinary frequency, nocturia, and storage symptoms (8).

Kidney transplantation recipients are one of the high-risk groups for COVID-19 infection because of immunosuppression therapy (9). The number of kidney transplantation recipients with COVID-19 was 2–5 times greater than in the general population (10), and the mortality rate of COVID-19 in kidney transplantation recipients was approximately 20–28%, compared to 1–5% in the general population (11). Kidney transplantation recipients are one of the most vulnerable populations to COVID-19 infection and are more prone to develop COVID-19 complications, so that lower urinary tract would be seriously affected by COVID-19 disease in this population.

According to our knowledge, no studies assess the effect of COVID-19 on LUTS in kidney transplantation recipients. Therefore, the purpose of the current study was to evaluate the impact of COVID-19 disease on LUTS in kidney transplantation recipients using the IPSS, a validated tool.

Methods

This cross-sectional study included all consecutive patients who underwent kidney transplantation at Sina Hospital (Tehran University of Medical Sciences, Iran), and all donors were unrelated. This study was approved by the Tehran University of Medical Sciences ethics committee (IR.TUMS.MEDICINE.REC.1400.1488).

The Covid-19 infection was confirmed with oropharyngeal swabs' real-time polymerase chain reaction (PCR). All patients with urinary tract infections were excluded from the study. The treating medical staff obtained demographic and clinical data from patients' medical records and interviews. All participants filled out written informed consents. The study protocol was approved by the Tehran University of Medical Sciences Ethics Committee and carried out by the Declaration of Helsinki.

The IPSS, a previously validated assessment (11), assessed LUTS symptoms. Participants were asked to

score their condition regarding the COVID-19 duration. The IPSS scores of all patients were recorded. IPSS was categorized into mild (0–7), moderate (8–19), and severe symptoms (20–35) (12).

Statistical analysis

Continuous and categorical variables were described as mean \pm SD and frequency (%). The chi-square and Fisher's exact were applied to find the association between demographic and clinical characteristics of kidney transplant recipients with and without Covid-19. Also, the Mann–Whitney U was used to compare the continuous variables between these two groups. Finally, LUTS were categorized into two groups, and OR (95%CI) was calculated based on univariate logistic regression analysis.

Results

The demographic and clinical information are described in Table 1. Totally 153 patients participated in the study; 67 (43.8%) and 86 (56.2%) patients were kidney transplant recipients with and without Covid-19. Of all patients, the mean age was 49.7 ± 12.9 years, the mean body mass index (BMI) was 26.8 ± 4.7 kg/m², 105 (68.6%) males, and the mean graft duration was 9.7 ± 6.6 years. As displayed in Table 1, there were no significant differences in sex, age, BMI, graft duration, the type of graft donor, transplantation frequency, comorbidities distribution, and drug treatments between kidney transplant recipients with and without Covid-19 (P-value > 0.05).

The mean IPSS in kidney transplant recipients with and without Covid-19 was 2.74 ± 3.0 and 1.96 ± 2.7 , respectively. There were significantly higher IPSS scores in patients with Covid-19 (P-value=0.03) (Table 2). The odd ratios for IPSS in kidney transplant recipients with COVID-19 are shown in Table 3. The kidney transplant recipients with COVID-19 had a higher risk of moderate IPSS (OR:1.5 CI 95%: 0.5-4.9) than those without COVID-19, but it is not significant (P-value=0.4).

Discussion

According to our knowledge, no studies assess the effect of COVID-19 on LUTS in kidney transplantation recipients. Therefore, the present study evaluated the impact of COVID-19 disease on LUTS in kidney transplantation recipients and found significantly higher LUTS in COVID-19 kidney transplantation recipients.

Kidney transplant recipients are more vulnerable to several infections because of immunosuppression therapy to avoid allograft rejection (13). Therefore, immunosuppression drugs increase the risk and severity of infections in kidney transplant recipients, leading to reasonable worry about the impacts of COVID-19 disease on this population. On the other hand, cell-surface protein ACE2, the essential receptor for SARS-CoV-2, is highly expressed in the urothelial cells, which might be a

Table 1. Demographic and Clinical Characteristics between kidney transplant recipients with and without COVID-19

	Total n=153	Covid patients n= 67(43.8%)	Non-Covid patients n= 86(56.2%)	P-value
Baseline characteristics				
Mean Age, years	49.7 ± 12.9	48.5 ± 12.4	50.6 ± 13.3	0.3
Sex, n (%)				
Male	105 (68.6)	41 (62.7)	63 (73.3)	0.1
Female	48 (31.4)	25 (37.3)	23 (26.7)	
Mean BMI, Kg/m²	26.8 ± 4.7	26.9 ± 4.6	26.7 ± 4.7	0.8
Graft duration, years	9.7 ± 6.6	9.5 ± 6.6	9.9 ± 6.6	0.7
Type of graft donor, n (%)				
Alive donor	72 (47.1)	40 (46.5)	32 (47.8)	0.8
Brain death	81 (52.9)	35 (52.2)	46 (53.5)	
Transplantation frequency, n (%)				
Once	137 (89.5)	57 (85.1)	80 (93.0)	0.1
Twice	16 (10.5)	10 (14.9)	6 (7.0)	
Transplantation rejection, n (%)	53 (34.6)	26 (38.8)	27 (31.4)	0.3
Comorbidities, n (%)				
Hypertension	81 (52.9)	32 (47.8)	49 (57.0)	0.2
Cardiovascular disease	15 (9.8)	3 (4.5)	12 (14.0)	0.051
Diabetes	39 (25.5)	17 (25.4)	22 (25.6)	0.9
Stroke	5 (3.3)	2 (3.0)	3 (3.5)	0.9
Kidney problem	80 (52.3)	40 (59.7)	40 (46.5)	0.1
CMV infection	16 (10.5)	8 (11.9)	8(9.3)	0.5
Drug treatment, n (%)				
Cell cept	98 (64.1)	43 (64.2)	55 (64.0)	0.9
Tacrolimus	61 (39.9)	27 (40.3)	34 (39.5)	0.9
Azuthripsin	21 (13.7)	9 (13.4)	12 (14.0)	0.9
Rapamicin	14 (9.2)	7 (10.4)	7 (8.1)	0.6
Prednisolone	147 (96.1)	62 (92.5)	85 (98.8)	0.08
Cyclosporin	84 (54.9)	37 (55.2)	47 (54.7)	0.9

P-values were calculated based on Mann–Whitney U, Chi-Square tests, or Fisher's Exact Test

possible link with LUTS (6). Therefore, we hypothesized that the COVID-19 disease would seriously affect the lower urinary tract in kidney transplant recipients.

The present study indicated that the mean IPSS of kidney transplantation recipients with COVID-19 was significantly greater than without COVID-19. Also, in our research, the kidney transplant recipients with COVID-19 had a 1.5 times higher risk of moderate IPSS than those without COVID-19, but this correlation was not significant because of the small sample size.

Previous studies assessed the impact of COVID-19 infection on LUTS in different populations, which presented the COVID-19 most likely effect on the lower urinary tract (7, 14, 15). Nabeeh et al. evaluated

the impact of COVID-19 on LUTS in patients with benign prostatic hyperplasia (BPH) and presented that COVID-19 infection significantly affected LUTS in BPH patients. They showed that after COVID-19 infection, there were significant increases in IPSS, post voiding residual urine (PVR), and quality of life (Qol) compared to before infection. Also, the maximum flow rate (Qmax) significantly decreased after the COVID-19 infection (14, 16).

Can et al's., study in elderly patients found that LUTS was significantly higher after COVID-19 infection, and they suggested that older adults with increased LUTS had better be assessed for COVID-19 (7). On the other hand, LUTS has also been recommended to predict the severity

Table 2. IPSS between kidney transplant recipients with and without Covid-19

Outcomes	Covid patients n=67(43.8%)	Non-Covid patients n=86(56.2%)	P-value
IPSS (mean ± SD)	2.74 ± 3.0	1.96 ± 2.7	0.03

Table 3. Odds ratios (CI 95%) for IPSS in COVID-19 patients

Outcomes	Non-Covid patients (Reference)	Covid patients	OR	P-value
IPSS (Moderate)	6 (7%)	7 (10%)	1.5 (0.5-4.87)	0.44

of COVID-19 in patients with BPH (17).

Recent documents have described that SARS-CoV-2 is found in animal and human urine (18, 19), and frequent urination was indicated as a common sign of COVID-19 (20). Additionally, Kaya et al. showed that LUTS might be one of the early signs of COVID-19 disease (21). However, in the Marand et al. study, COVID-19 patients did not report having any LUTS, even those with a positive SARS-CoV-2 in the urine (22), suggesting that not all patients did have might develop COVID-19-related LUTS.

Last but not least, although the LUTS evaluation is limited to the IPSS, it is the most used tool in the clinical practice, in addition to measuring the quality-of-life impact in a scenario where no ideal tool exists (20), and invasive methods should be avoided due to transplant-related immunosuppression.

The strength of the present study is that it is the first study to show the impact of COVID-19 on LUTS in kidney transplant recipients. There were some limitations to the current research:

1. The relatively small sample size of the study.
2. Urine analyses were not performed to assess the presence of the SARS-CoV-2 in the urine to indicate bladder COVID-19 invasion.
3. While COVID-19 kidney transplanted patients showed significantly higher LUTS measured by the validated tool IPSS, the current cross-sectional study design lacks the power to define cause and effect.

Therefore, while we hypothesized that SARS-CoV-2 might affect the lower urinary tract function in kidney transplanted patients, those with more LUTS might be more susceptible to COVID-19.

Future studies with greater sample size and SARS-CoV-2 urine analysis are necessary to evaluate the effect of COVID-19 on the lower urinary tract in kidney transplant recipients and further explore the long-term impact and potential sequels.

Conclusions

We pioneering found that LUTS in kidney transplant

recipients measured by the validated tool IPSS was significantly more intense in those affected by COVID-19 infection. Future studies are necessary to explore the long-term impact and potential sequels.

Authors' contributions

RR designed the study, AM wrote the manuscript; EM performed the analysis; PZ and VS collected the data; LOR reviewed and edited the manuscript.

Acknowledgments

Special thanks to Urology Research Center at Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Conflict of interest

All authors declare that there is no potential competing or conflict of interest.

Funding

There was no funding.

Ethics statement

This study was approved by the ethics committee at Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1400.1488).

Data availability

Data will be provided on request.

Abbreviations

BPH	Benign prostatic hyperplasia
IPSS	International Prostate Symptom Score
LUTS	Lower Urinary Tract Symptoms
PCR	Polymerase chain reaction
PVR	Post voiding residual urine
Qol	Quality of life

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How to cite this article

Oliveira Reis L, Mohammadi A, Zahmatkesh P, Kazemi R. COVID-19 Impact on Lower Urinary Tract Symptoms of Kidney Transplantation Recipients. *Translational Research in Urology*. 2022 June;4(2):77-82.

DOI:10.22034/TRU.2022.345939.1113

URL: https://www.transresurology.com/article_151435.html

