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Taking care of kidney transplant recipients during the COVID-19 pandemic: experience from a medicalized hotel

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/CTR.14132 This article is protected by copyright. All rights reserved Running head: Alternative management for COVID19 transplant recipients

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MAIN BODY

To the editor:

The global overload that health systems are undergoing since the start of the COVID-19 pandemic has forced hospitals to explore sustainable alternatives to treat vulnerable patients that require closer monitoring and higher use of resources, such as Kidney Transplant Recipients (KTRs)^{1,2}. The use of telemedicine and hospital-like infrastructures represent a valid option for most patients with mild-moderate COVID-19, as well as for patients in the recovery phase who cannot be discharged from hospital^{3,4}. Herein we present our experience with KTRs infected by SARS-CoV-2 in the *Hotel Salut* (Health Hotel, HH), which was set-up within 2.5 km from the Hospital on March 25th 2020, coinciding with the main COVID-19 outbreak in Spain. At full capacity, the HH could accommodate up to 300 patients across 6 floors of 50 single-rooms each floor. The HH was equipped with both human and material resources from the Hospital Clínic of Barcelona, including 24-hour medical and nurse attention, availability of high-flux oxygen, a pharmacy and the same IT equipment.

By the end of May, 45 KTRs who were followed-up at our center developed COVID-19, of which 28 were hospitalized at the Hospital Clínic. Twelve patients were transferred to the HH according to the following criteria: i) >6 days from symptoms onset, ii) temperature below 37.3°C, iii) Respiratory rate <22 per minute and FiO2 < 0.35, iv) C-Reactive Protein< 5mg/dl or descending, LDH <240UI/L or descending, lymphocytes >1000/mm3 or increasing and v)without radiological progression. Baseline characteristics and treatment are highlighted in Table 1 and are described as median [interquartil range], frequencies and percentages. Differences were explored the with Mann-Whitney test or Fisher's exact test with SPSS 25.0 (SPSS inc, Chicago, US). The study has been approved by the local Ethical Committee (code HCB/2020/0641). The treatment protocol used in the HH was the same as the one carried out in the Hospital, and already described by our group⁵. Mycophenolate and/or mTOR inhibitors were discontinued in all patients. Calcineurin inhibitors were also suspended in case lopinavir/ritonavir was prescribed. KTRs were transferred to HH after 8.0[4.25-13.50] days of hospitalization; at that stage none of them had fever and 20% were still needing oxygen. Hospital stay was significantly shorter for patients treated at HH than for those discharged directly from the hospital (12.50[8.25-19.50] days, P=0.001). Median stay at the HH was 9.50[6.50-12.50] days, and only one patient was readmitted to the Hospital for respiratory deterioration 3 days after HH admission, being discharged from the hospital 9 days afterwards. Evolution of clinical parameters reflected progressive recovery after infection (Figure 1). It should be noted that stay at HH also allowed the gradual reintroduction of immunosuppression despite the challenging interactions between calcineurin inhibitors (CNIs) and the antiviral agents^{6,7}. Therefore, tacrolimus was restarted 9[8-11] days after withdrawal, with trough levels of 4.85[3.92-5.55]ng/ml at the time of HH discharge. The rest of immunosuppressant drugs were introduced gradually afterwards, tapering the steroids simultaneously.

In conclusion, although our study was conducted among a small proportion of all the COVID-19 infected KTRs, treating them at a medicalized hotel facility allowed us to monitor their progress closely, thus obtaining positive clinical outcomes as well as the ability to safely reintroduce immunosuppression.

Disclosure: The authors of this manuscript have no conflicts of interest to disclose as described by Clinical Transplantation.

Data availability statement: The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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REFERENCES

- Cravedi P, Suraj SM, Azzi Y, et al. COVID-19 and Kidney Transplantation: Results from the TANGO International Transplant Consortium [published online ahead of print, 2020 Jul 10]. *Am J Transplant*. 2020
- Guillen E, Pineiro GJ, Revuelta I, et al. Case report of COVID-19 in a kidney transplant recipient: Does immunosuppression alter the clinical presentation?. *Am J Transplant*. 2020;20(7):1875-1878
- Hollander JE, Carr BG. Virtually Perfect? Telemedicine for Covid-19. N Engl J Med. 2020;382(18):1679–81.
- Abuzeineh M, Muzaale AD, Crews DC, et al. Telemedicine in the Care of Kidney Transplant Recipients With Coronavirus Disease 2019: Case Reports [published online ahead of print, 2020 Jul 16]. *Transplant Proc.* 2020;S0041-1345(20)32629-4.
- Montagud-Marrahi E, Cofan F, Torregrosa JV et al. Preliminary data on outcomes of SARS-CoV-2 infection in a Spanish single center cohort of kidney recipients [published online ahead of print, 2020 May 5]. Am J Transplant. 2020;10.1111/ajt.15970. doi:10.1111/ajt.15970

Total population	Transferred	Discharged from	P-value
(n=28)	to HH	the Hospital	

- Bartiromo M, Borchi B, Botta A, et al. Threatening drug-drug interaction in a kidney transplant patient with coronavirus disease 2019 (COVID-19). *Transpl Infect Dis.* 2020;22(4):e13286
- López V, Vázquez T, Alonso-Titos J, et al. Recommendations on management of the SARS-CoV-2 coronavirus pandemic (Covid-19) in kidney transplant patients. *Nefrologia*. 2020;40(3):265-27

FIGURE LEGENDS

Table 1 - Baseline characteristics and treatment of KTRs total population. Comparison between

 KTRs who were transferred to the *Hotel Salut* (Health Hotel, HH) and those who were

 discharged directly from the Hospital.

Figure 1 – Evolution of COVID-19-related laboratory parameters before and after HH admission.

		(n=12)	(n=16)	
Age	52.50 [46.25-68]	48.50 [43.75-57.25]	58 [47.25-72.75]	0.110
Sex (% males)	18/28 (64.3%)	7/12 (58.3%)	11/16 (68.8%)	0.698
Time from transplant	56.46 [22.01-125-45]	42.56 [12.21-74.75]	65.15 [26.11-134.92]	0.423
Baseline immunosuppr	ession			
- TAC + MPA	14/28 (50.0%)	5/12 (41.7%)	9/16 (56.3%)	0.240
- TAC + mTORi	9/28 (32.1%)	6/12 (50.0%)	3/16 (18.8%)	
- Other	5/28 (17.9%)	1/12 (8.3%)	4/16 (25.0%)	
Creatinine at baseline	1.55 [1.15-2.18]	1.93 [1.44-2.54]	1.29 [1.13-2.10]	0.093
(mg/dl)				
Positive PCR swab	23/28 (82.1%)	9/12 (75.0%)	14/16 (87.5%)	0.624
(%yes)				
Symptoms (%yes)				
- Fever	26/28 (92.9%)	10/12 (83.3%)	16/16 (100.0%)	0.175
- Cough	18/28 (64.3%)	9/12 (75.0%)	9/16 (56.3%)	0.434
- Dyspnea	9/28 (32.1%)	2/12 (16.7%)	7/16(43.8%)	0.223
- Gastrointestinal	7/28 (25.0%)	2/12 (16.7%)	5/16 (31.3%)	0.662
- Dysgeusia	3/28 (10.7%)	1/12 (8.3%)	2/16 (12.5%)	1
Pneumonia	25/28(95.3%)	9/12 (75.0%)	16/16 (100.0%)	0.067
AKI	19/28 (67.9%)	9/12 (75.0%)	10/16 (62.5%)	0.687
Need of dialysis	3/28 (10.7%)	0/12 (0.0%)	3/16 (18.8%)	0.238
Treatment				
- Lopinavir/Ritonavir	24/28 (85.7%)	9/12 (75.0%)	15/16 (93.8%)	0.285
- Hydroxicloroquine	27/28 (96.4%)	12/12 (100.0%)	15/16 (93.8%)	1
- Azithromycin	27/28 (96.4%)	11/12 (91.7%)	16/16 (100.0%)	0.429
- Tocilizumab	18/28 (64.3%)	6/12 (50.0%)	12/16 (75.0%)	0.243
- Steroids (bolus)	8/28 (28.6%)	3/12 (25.0%)	5/16 (31.3%)	1
ICU Admission	8/28 (28.6%)	3/12 (25.0%)	5/16 (31.3%)	1
Death	5/28 (17.9%)	0/12 (0.0%)	5/16 (31.3%)	0.053
Length of stay				
- At the Hospital	12.50 [8.25-19.50]	8 [4.25-13.50]	15.50 [12-25.50]	0.001
- At the Hotel	/	9.50 [6.50-12.50]	/	
- Total	18 [13-24]	19.00 [16.25-24]	15.50 [12-25.50]	0.631



-15

g)

800

Ferritin [ng/mL]

-15

-10

-5

Days

Ó

-10

Hospital

-5

Days

Ó











10

10

5

Hotel

5