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Original article

Outcome of mild SARS-CoV-2-infected renal transplant recipients managed by supervised home-based self-monitoring

V. Vamsidhar , D. Bhadauria *, J. Meyyappan , M.R. Patel , M. Yaccha , A. Kaul , S. Shanmugam , N. Prasad

Department of Nephrology and Renal Transplantation, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India

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ABSTRACT

Objectives: We aimed to compare the outcomes of COVID-19 Renal Transplant Recipients (RTRs) managed on an ambulatory basis to that of inpatient management.
Design, setting, materials, and methods: We performed a retrospective study in Lucknow, India, comparing the ambulatory management with the historical cohort managed in the hospital.R RTRs with mild COVID-19 were managed by supervised home-based self-monitoring (HBSM), a strategy to manage this high-risk group on an outpatient basis during the second wave of the pandemic. The primary outcome was the clinical deterioration to a higher severity category among RTRs with mild COVID-19 managed by HBSM compared to hospitalized patients within two weeks of disease onset.
Results: Of the 149 RTRs with mild COVID-19, 94 (63%) and 55 (37%) were managed by HBSM and in the hospital, respectively. The proportion of RTRs who clinically deteriorated to a higher severity category (moderate or severe category) was similar among both groups (28.7% versus 27.2%, $P = 0.849$). Among RTRs with clinical deterioration, COVID-19-related death was reported in two patients of the HBSM group and in none of the patients of the hospitalized group. Graft dysfunction was higher in the hospitalized group (7.4% versus 27.2%, $P = 0.002$). Median time to complete clinical recovery (7 days in both groups), secondary bacterial infections (25% versus 33.3%, $P = 0.41$), and the mean decline in EQ-5D score from baseline at six weeks (−6.6 versus−4.3, $P = 0.105$) were found to be similar in both groups.

1. Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS CoV-2), has changed the way of living, health care systems, and the global economy. The burden was exceptionally high in India during the second wave, with officially more than 30 million confirmed infections and 400,000 deaths. In addition, India was responsible for more than half of the world's daily COVID-19 cases, setting a record-breaking pace of more than 400,000 new cases a day during the peak of the second wave in April-May 2021 [1].

Though the overall mortality rate of COVID-19 is 0.1–13%, it is relatively higher in high-risk populations such as immunosuppressed and solid organ recipients [2]. The mortality rate of COVID-19 in renal transplant recipients (RTR) is 13–30%, with the highest mortality of up to 38% seen in an hospitalized cohort [3]. This higher mortality in RTRs is attributed to the immunosuppressed state, the atypical presentation of disease, rapid worsening, and lack of expertise to manage this group of patients [3]. However, optimal admission and management strategies for RTRs with COVID-19 remain inconclusive. Many countries, including India, advise hospitalization of all RTRs with COVID-19 irrespective of disease severity [4]. However, the Centers for disease control and prevention (CDC) do not recommend universal admission. Instead, RTRs are considered at high risk of severe disease, and the CDC advise in-clinic evaluation in the presence of mild dyspnea [5].

However, home-based management of RTRs is complex due to multiple inherently associated issues such as titration of immunosuppression, maintenance of hydration during fever, drug interactions, steroid-induced worsening of glycemia, and blood pressure control apart from monitoring and managing the COVID-19 disease per se. Efficacy and safety data of the outpatient management of RTRs with COVID-19 are limited, with very few studies available that often displayed a limited sample size. In a study by Husain et al., 17 of 44 patients managed on an outpatient basis (32%) subsequently required hospitalization, although there was no mortality [6].

During the second wave of the COVID-19 pandemic in India, when the exponential increase in the case burden led to a scarcity

* Corresponding author at: Department of Nephrology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India.
E-mail address: drdharm1@rediffmail.com (D. Bhadauria).

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of hospital beds and other resources, transplant physicians were forced to provide home-based management to RTRs with mild diseases. This situation allowed us to study the outcomes of RTRs managed by supervised home-based self-monitoring (HBSM).

The current study aimed to compare the outcomes of RTRs with mild COVID-19 managed by supervised HBSM in the second pandemic wave in India with those hospitalized during the first wave.

2. Materials and methods

2.1. Study design and setting

This study was a single-center, observational study on RTRs who developed mild COVID-19 between March 2020 and June 2021 and either had home-based management or were admitted to a dedicated COVID-19 hospital. Though the study was designed retrospectively during the second wave, when many patients had to be managed on an ambulatory basis, all data were collected on a prospective basis.

2.2. Study population

2.2.1. Inclusion criteria

We included all confirmed COVID-19-positive RTRs with mild disease category and managed either at home or in the hospital.

2.2.2. Exclusion criteria

We excluded patients with moderate and severe disease category and RTRs with failed graft.

Transplant recipients with confirmed COVID-19 were enquired regarding their symptoms, including duration of symptoms, fever, myalgias, sore throat, cough, breathlessness, anosmia, dysgeusia, vomiting, diarrhea, and oxygen saturation. Patients were then triaged into three categories (mild, moderate, and severe disease categories) as per the ICMR 2021 guidelines [7]. Admission to a dedicated COVID-19 hospital was advised to all patients. Patients under the mild category who could not get admitted due to a lack of beds in a dedicated COVID-19 care facility were assessed for supervised HBSM. If they were appropriate candidates for HBSM, both the patients and caregivers were given instructions regarding isolation, monitoring, and management techniques through smartphone messaging systems. Simultaneously, efforts for admission were also continued with an ongoing triage (Fig. 1).

2.2.3. Management of the supervised HBSM group

Patients and their caregivers were trained telephonically or directly regarding the isolation, monitoring of vital signs, including temperature, pulse rate, blood pressure, oxygen saturation (resting and 6-minute walk test), blood glucose, input-output monitoring, etc. The prescriptions, information charts regarding maintaining adequate hydration, fever control, and dietary precautions were sent over WhatsApp. Besides these, the self-administered questionnaires on vital signs and blood glucose level, as well as temperature monitoring charts routinely used in the inpatient care were also sent to improve the understandability and hence compliance apart from simulating the inpatient health care services. Patients/caregivers were advised to send back the charts every 12 hours through picture messages or scanned copies over WhatsApp, which were reviewed by the treating physicians. Further treatment suggestions/changes were sent back, and the same process was repeated until any signs/symptoms of warning were observed or two weeks after symptom onset, whichever was earlier. Patients were advised to look for various warning signs or symptoms as mentioned below under the management section. Text messages, voice messages, and video calling services were utilized as per the requirement to avoid any form of miscommunication. Various aspects of COVID-19 in transplant recipients were managed as follows.

2.2.4. Management of the disease per se

Home isolation, monitoring temperature, pulse rate, blood pressure, and oxygen saturation every 6–8 hours, monitoring for warning signs of worsening – drop in oxygen saturation to <94% or by >3% on a 6-minute walking test, persistent fever for >5 days, recurrent vomiting/diarrhea severe enough to require parenteral therapy.

2.2.5. Titration of immunosuppressive medications

Immunosuppression was modified and tailored as per immunological risk and symptom severity (Fig. 1). Calcineurin inhibitors (CNI) trough level was targeted at a lower range of 3–5 ng/ml for tacrolimus and 50–75 ng/ml for cyclosporine.

2.2.6. Other management

Caregivers were also trained to monitor blood glucose level and pressure, to maintain adequate hydration, and to monitor urine output. In addition, serum creatinine level and total leukocyte count were also monitored during the illness if the patient could get those investigations at the local laboratory.

2.2.7. Management of the hospitalized group

Patients with mild COVID-19 during the first wave and managed in-hospital constituted the historical control group (hospitalized group). Deterioration of oxygen saturation requiring supplementation of O_2 or new-onset breathlessness or clinical deterioration requiring intensive care unit (ICU) admission was considered worsening in this subgroup. Titration of the immunosuppression was done as per the same principles as for the HBSM group. Monitoring of vital signs, blood glucose level and intake-output, laboratory parameters, and the necessary treatment modifications were performed by physicians and nurses trained for managing COVID-19 patients under the supervision of a team of transplant physicians. The data of these patients were also collected prospectively during the first wave of COVID-19.

A clinical tool, the EQ-5D score, was used to measure long-term disability. Developed by the EuroQol group as a measure of health, it has five dimensions that describe the health-related quality of life (HRQoL)–Mobility, anxiety, self-care, pain/discomfort, and usual activities [8,9]. Each variable in the score was assigned a score between 0 and 100. The total average of all five variables was calculated for a maximum score of 100. The EQ-5D score has been well validated as a reliable measure of health status in renal transplant recipients [9]. The pre-COVID EQ-5D score was calculated at the patient's initial contact with the COVID-19 transplant team, and the post-COVID-19 score was calculated after 6 weeks from infection onset. Permission to use the EQ-5D score has been obtained from its developer, the EuroQol group. In addition, clearance from the institutional ethics board was applied with a request for a consent waiver. Finally, definitions of the confirmed COVID-19 and the various severity categories were described (section reports.)

2.3. Primary outcome

Clinical deterioration to a higher severity category among RTRs with mild COVID-19 managed by HBSM compared to hospitalized patients within two weeks of disease onset

2.4. Secondary outcomes

The secondary outcomes are:

- O Outcome among patients with clinical deterioration and who acquired a higher severity category;
- Time to clinical improvement;
- Secondary bacterial infections and need for antibiotic escalation;

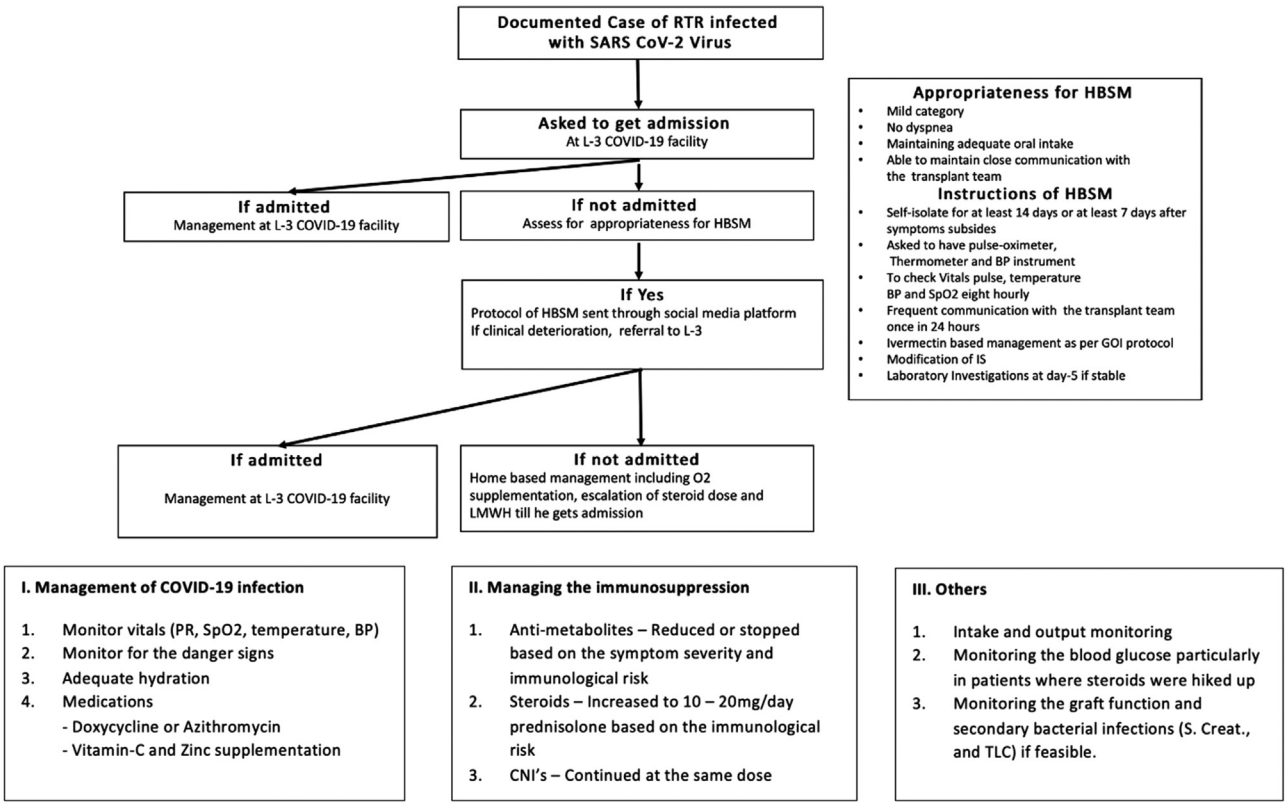

Fig. 1. Management protocol of mild category of SARS-CoV-2 RTRs managed by supervised HBSM. * RTR: renal transplant recipients; L-3 COVID-19 facility: tertiary care COVID-19 hospital; HBSM: home-based self-monitoring; LMWH: low molecular weight heparin; CNI: calcineurin inhibitors; GOI: Government of India; IS: immunosuppression; S. creat.: serum creatinine; TLC: total leukocyte count.

- Mean decline in the EQ-5D score at the end of 6 weeks from baseline;
- Acute graft dysfunction;
- Graft outcome 6 weeks post-COVID;
- Factors associated with clinical worsening among the HBSM group.

2.5. Definitions

- Confirmed COVID-19:
  - nasal/throat swab positive for SARS-CoV-2 by RT-PCR,
  - high-resolution computed tomography (HRCT) findings highly suggestive of COVID-19 (CO-RADS≥4);
- mild disease:
  - Fever≤5 days duration,
  - No history of breathlessness,
  - SpO2 >94% on room air (in patients with home-based SpO2 monitoring available),
  - Fall of SpO2 level by not more than 3% on 6-minute walk test, or its subjective equivalent in patients without home-based SpO2 monitoring (no exertional breathlessness/limitation in daily activities due to breathlessness);
- moderate disease:
  - persistent fever of >5 days duration,
  - breathlessness at rest,
  - SpO2 90-93% on room air,
  - respiratory rate ≥24/min,
  - fall of SpO2 level by more than 3% on 6-minute walk test, or its subjective equivalent (exertional breathlessness/limitation in daily activities due to breathlessness);
- severe disease:
  - SpO2 <90% on room air,
  - respiratory rate >30/minute;
- acute graft dysfunction is defined as an increase in serum creatinine of 15% from baseline [10].

2.6. Statistical analysis

All continuous data were expressed as means or medians depending on the normality of the data, assessed using the Kolmogorov-Smirnov test. Categorical data were expressed as proportions/ratios. Student's *t*-test was used to compare quantitative data if it was normally distributed. Else, Mann-Whitney's U-test was used. We used the Chi^2 test to analyze qualitative data. Factors associated with clinical deterioration were assessed by univariate and multivariate analyses using the Cox-proportional hazard model. Statistical analysis was done by SPSS software, version 25.

3. Results

A total of 262 RTRs were diagnosed and treated for COVID-19. Of these, 162 (61.8%) belonged to the mild disease category, and 100 (38.2%) to the moderate ($n=36$) and severe disease ($n=64$) categories. Of the 162 patients with mild COVID-19 assessed for HBSM appropriateness, 149 patients were found to be fit for HBSM. Of them, 55 (37%) and 94 (63%) were managed in the hospital (Hospitalized group) and on a supervised HBSM basis (HBSM group). While all 94 patients managed in the HBSM group were from the second wave (March 25, 2020 to January 31, 2021), the remaining 55 patients of the mild category managed in the hospital were from the first pandemic wave (March 1, 2021 to July 31, 2021). The study methodology and distribution of patients are shown in Fig. 2.

The mean age of the study population was 41.1 years, and 91.3% were males. The median duration since time of transplant was 60 months (IQR: 32–90 months) in the entire population. Both the

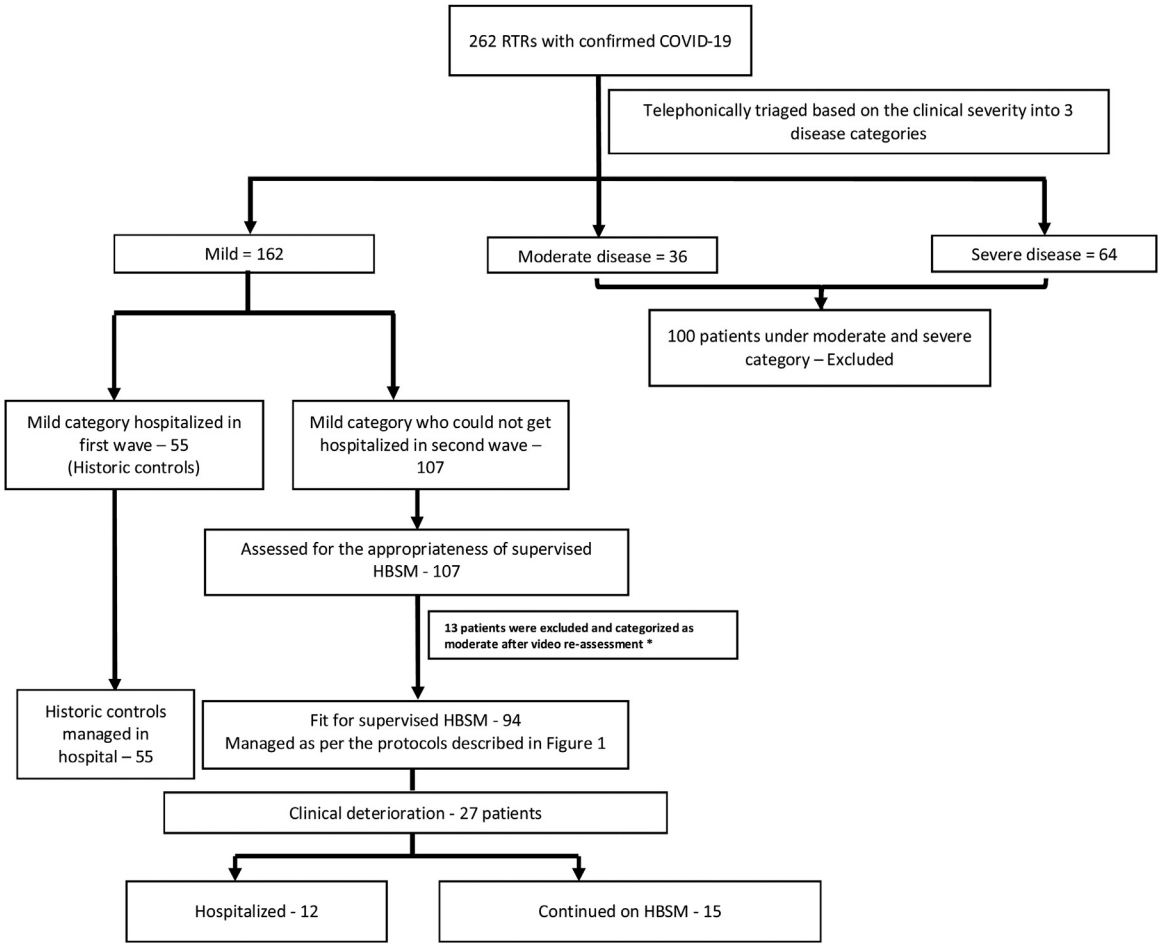

Fig. 2. Methodology. RTR: renal transplant recipients; HBSM: home-based self-monitoring.

groups matched in most of the baseline characteristics such as age, gender distribution, and comorbidities

(Table 1). The median duration since transplant and type of transplant, maintenance immunosuppression regimen used, and baseline creatinine level was also similar in both groups. However, the induction regimen used was significantly different among the two groups ($P = 0.02$) as a significantly higher number of patients had received antithymocyte globulin (ATG) in the hospitalized group. The mean EQ-5D score in the hospitalized group was significantly higher than in the HBSM group (95.9 versus 94.4, $P < 0.001$).

The most common symptom was fever (87.2%), followed by cough (44.9%) and myalgia/arthralgia (33.5%), and it was found to be similar in both groups. The mean time from symptom onset to contact with the transplant team or health care worker was 3.2 days (±2.1) and was similar in both groups.

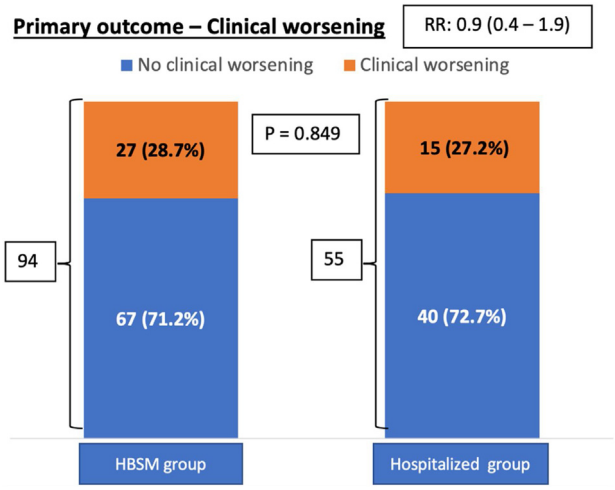

Fig. 3. Comparison of the primary outcome between the HBSM and hospitalized groups. *HBSM: home-based self-monitoring.

4. Outcome analysis

4.1. Primary outcome

Twenty-seven of 94 patients (28.7%) of the HBSM group and 15 of 55 (27.2%) patients of the hospitalized group experienced clinical worsening from a baseline mild COVID-19 ($P = 0.849$). The relative risk of clinical worsening to a higher severity category was 0.9 (CI: 0.4–1.9) (Fig. 3).

4.2. Secondary outcomes and analysis

4.2.1. Six-week outcome, clinical improvement, and secondary bacterial infections

Of the 27 patients in the HBSM group who experienced clinical worsening, all had worsened from mild category to moderate category of disease severity. However, only 12 were admitted to a

Table 1
Baseline characteristics of RTRs with mild COVID-19.

Baseline characteristics	Total (n = 149)	HBSM group (n = 94, 63%)	Hospitalized group (n = 55, 37%)	P value
Age	41.1 (±11.6)	40.2 (±11.09)	42 (±12.5)	0.23
Gender				0.9
Male	136 (91.3%)	86 (91.4%)	50 (90.9%)	
Female	13 (8.7%)	8 (8.5%)	5 (10%)	
Median duration since transplant, Months (IQR)	60 (32-90)	59 (28.2–88.5)	68 (40–96)	0.96
Comorbidities	112 (75.2%)	72 (76.6%)	40 (72.7%)	0.59
Hypertension	94 (63.1%)	58 (61.7%)	36 (65.5%)	0.64
Diabetes mellitus	40 (26.8%)	27 (28.7%)	13 (23.6%)	0.49
Induction agent				0.02
basiliximab	92 (61.7%)	68 (72.3%)	24 (43.6%)	
ATG	34 (22.8%)	17 (18%)	17 (30.9%)	
No induction agent	23 (15.4%)	9 (9.5%)	14 (25.4%)	
Type of transplant				
Live	147 (98.6%)	92 (97.8%)	55 (100%)	0.27
Cadaveric	2 (1.4%)	2 (2.2%)	0	0.3
ABO compatible	136 (91.2%)	82 (87.2%)	50 (90.9%)	
ABO incompatible	13 (8.7%)	12 (12.7%)	5 (10%)	
Baseline serum creatinine level	1.31 (±0.49)	1.24 (±0.44)	1.44 (±0.55)	0.159
Maintenance immunosuppression				
Dual	3 (2%)	1 (1.1%)	2 (3.6%)	
Triple	146 (98%)	93 (98.9%)	53 (96.3%)	
prednisolone	149	94	55	
CNI	149	94	55	
MMF	141	91 (96.8%%)	50 (90.9%)	
azathioprine	5	1 (1.1%)	4 (7.2%)	
Symptoms				
Fever	130 (87.2%)	83 (88.2%)	47 (85.4%)	0.6
Cough	67 (44.9%)	39 (41.4%)	28 (50.9%)	0.26
Myalgia/arthralgia	50 (33.5%)	35 (37.2%)	15 (27.2%)	0.21
Dyspnea at rest	27 (18.1%)	18 (19.1%)	17 (30.9%)	0.1
Gastrointestinal symptoms	26 (17.4%)	17 (18%)	9 (16.3%)	0.3
Mean time from symptom onset to HCW contact, Days (SD)	3.2 (±2.1)	3.1 (±1.9)	3.4 (±2.1)	0.93
Mean EQ-5D score at baseline (SD)	95.9 (±5.4)	94.4 (±5.79)	98.5 (±3.3)	< 0.001

RTR: renal transplant recipients; HBSM: home-based self-monitoring; ATG: antithymocyte globulin; CNI: calcineurin inhibitors; MMF: mycophenolate mofetil; HCW: health care worker.

Table 2
Comparison of primary and secondary outcomes between HBSM and hospitalized groups.

Variable	HBSM group	Hospitalized group	p value
Primary outcome–Clinical worsening until two weeks after symptom onset			
Percentage of clinical worsening	27 (28.7%)	15 (27.2%)	0.849
Secondary outcomes			
1. Median time to clinical recovery, Days (IQR)	7 days (5–14)	7 days (5–16)	–
2. Acute graft dysfunction, n (%)	7 (7.9%)	15 (27.2%)	0.002
3. Persistent graft dysfunction at 6 weeks post-COVID-19, n (%)	4 (4.4%)	7 (13.2%)	0.058
4. Mean EQ-5D score at 6 weeks post- COVID-19 (SD)	87.8 (±10.5)	94.0 (±11.6)	0.001
5. Mean decline in the EQ-5D score at 6 weeks post- COVID-19 compared to baseline (SD)	−6.6 (±7.3)	−4.3 (±9.8)	0.105
6. Secondary bacterial infections requiring higher doses of antibiotics after admission, n (%)	3 of 12 (25%)	6 of 15 (33.3%)	0.41

HBSM: Home-based self-monitoring.

dedicated COVID-19 hospital, and the remaining 15 patients had to continue on HBSM treatment due to the non-availability of beds (Fig. 2). There were two and no deaths among RTRs who deteriorated to higher COVID-19 severity in the HBSM and hospitalized groups, respectively (2.1% versus 0, P = 0.27). All deaths occurred in the HBSM group after hospitalization. The median time to clinical improvement, secondary bacterial infections requiring antibiotic escalation, and the mean decline of EQ-5D at 6 weeks from baseline were similar among the two groups (Table 2).

4.2.2. Graft dysfunction and graft outcomes

The rate of graft dysfunction during COVID-19 illness in the hospitalized group was significantly higher than in the HBSM group (7.9% vs 27.2%, P = 0.002). Persistent graft dysfunction was observed in four patients of the HBSM group and in seven patients of the hospitalized group (4.3% versus 12.7%, P = 0.059). Secondary outcomes are shown in Table 2.

4.2.3. Factors associated with clinical worsening in the HBSM group

Within the HBSM group, the characteristics of patients who had worsened were compared with those who had not declined to a higher category (Table 3). Among various baseline characteristics analyzed, a significantly higher number of patients with clinical deterioration were found to be hypertensive (81.5% vs 53.7%, P = 0.01). In addition, a significantly higher number of patients with clinical deterioration were found to have myalgia as one of the symptoms at presentation (81.5% vs 19.4%, P < 0.001). The mean decline in the baseline EQ-5D score was also higher in patients without clinical deterioration (6.1% vs 4.23%, P = 0.002).

5. Discussion

This is the largest single-center observational study assessing the outpatient management by supervised HBSM of RTRs with mild COVID-19. Studies conducted so far on the ambulatory treatment

Table 3
Factors associated with clinical worsening in the HBSM group ($N = 94$).

Baseline characteristics	Clinical deterioration ($n = 27$, 28.7%)	No Clinical deterioration ($n = 67$, 71.3%)	p–value
Age	40.3 (±9.15)	40.1 (±11.8)	0.23
Gender			0.5
Male	24 (88.9%)	62 (92.5%)	
Female	3 (11.1%)	5 (7.5%)	
Median duration since transplant, Months (IQR)	56 (21–101)	60 (29–88)	0.29
Comorbidities	22 (81.5%)	50 (74.6%)	0.47
Hypertension	22 (81.5%)	36 (53.7%)	0.01
Diabetes mellitus	5 (18.5%)	22 (32.8%)	0.16
Induction agent			0.44
basiliximab	22(81.5%)	46 (68.7%)	
ATG	3 (11.1%)	14 (20.9%)	
No induction agent	2 (7.4%)	7 (10.4%)	
Type of transplant			
Live	27 (100%)	65 (97%)	0.36
Cadaveric	0	2 (3%)	
ABO Compatible	24 (88.9%)	58 (86.6%)	
ABO incompatible	3 (11.1%)	9 (13.5%)	
Baseline serum creatinine level	1.26 (±0.32)	1.23 (±0.48)	0.52
Maintenance immunosuppression			0.64
Dual	0	1 (1.5%)	
Triple	27 (100%)	66 (98.5%)	0.36
prednisolone	27 (100%)	94 (100%)	0.66
CNI	27	67	
tacrolimus	27 (100%)	65 (97%)	
cyclosporine	0	2 (3%)	
Anti-metabolite			
MMF	27 (100%)	65 (97%)	
azathioprine	0	1 (1.5%)	
None		1 (1.5%)	
Symptoms			
Fever	26 (96.3%)	57 (85.1%)	0.55
Cough	13 (48.1%)	26 (38.8%)	0.4
Myalgia	22 (81.5%)	13 (19.4%)	<0.001
Mean time from symptom onset to HCW contact, Days (SD)	3.14 (±1.76)	3.13 (±2.05)	0.62
Mean EQ-5D score at baseline (SD)	92.2 (±4.23)	95.3 (±6.1)	0.002

RTR: renal transplant recipients; HBSM: home-based Self-monitoring; ATG: Antithymocyte globulin; CNI: calcineurin inhibitors; MMF: mycophenolate mofetil; HCW: health care worker.

Table 4
Predictors of clinical worsening among transplant patients with mild COVID-19 managed at home.

Variable	Odds Ratio (95% CI)	p-value
Cox Univariate analysis		
Hypertension	3.7 (1.2–8.2)	0.01
Rejection within the past year	1.8 (1.1–3.5)	0.03
Severe myalgia at presentation	2.8 (1.2–4.2)	0.03
Graft dysfunction at presentation	3.3 (1.4–7.2)	0.01
Baseline Eq5D score <92 (vs >92)	2.8(1.5–4.9)	0.02
Cox multivariate regression analysis		
Hypertension	2.7 (1.5–6.6)	0.03
Graft dysfunction at presentation	1.6 (1.1–2.5)	0.03

95% CI: 95% confidence interval. Factors with significant association in univariate analysis were taken for multivariate regression analysis.

of COVID-19 in the general population using telemedicine and various apps reported similar rates of clinical deterioration in patients managed on an ambulatory basis [11–13]. Our study is probably the first to assess the outcomes of ambulatory treatment compared to hospitalized treatment of solid organ transplantation patients with mild COVID-19 (Table 4).

We found that the rates of clinical deterioration within the first two weeks of illness and the 6-week outcomes in patients managed by HBSM (second wave) were similar to those managed in the hospital (historical controls in the first wave). Comparing the two groups managed in two different periods is acceptable because both groups had similar baseline characteristics and were treated by the same transplant team using identical management strategies. Moreover, data were collected prospectively for the historical control group. However, the comparability of the two groups might be limited by the potential differences in the viral strains seen across the two pandemic waves [14,15], although data on viral strains were unavailable in our study. As the study was conducted before the implementation of a full-fledged vaccination programme in India [16], none of the patients was vaccinated. This thereby might not have led to any COVID-19 specific differences in the immune status of patients across the two groups.

The two groups only differed in the first-line treatment used and in baseline EQ-5D scores. While more patients in the HBSM group received basiliximab, a significantly higher number of patients in the hospitalized group received depleting antibodies (ATG). As the median duration of COVID-19 since transplantation was 60 months, the induction agent would not have affected the disease severity or the study outcome. Even though the hospitalized group had a significantly better EQ-5D score than the HBSM group, outcomes of the HBSM group were similar to those of the hospitalized group. It could be because the lower EQ-5D score in the HBSM group is only relative, as the absolute score is 94.4, which suggests a good baseline functional status. In addition, clinical worsening rates in the HBSM group (28.7%) in our study are comparable to that of the study by Husain et al. (32%) though with a bigger sample size [6]. Finally, the short mean time interval between symptom onset and contact with health care workers (3.2 days ± 2.1) could have resulted in the successful outcome for the HBSM group.

Time to clinical recovery, mortality at 6 weeks, secondary bacterial infections requiring higher doses of antibiotics, and the mean decline in EQ-5D score was found to be similar among the two groups. The EQ-5D score at 6 weeks of follow-up was significantly lower in the HBSM group compared to the hospitalized group. However, this could be due to the lower baseline EQ-5D score in the

former, as the mean decline in EQ-5D score from baseline was similar among the two groups.

The rate of acute graft dysfunction in the inpatient group was higher than the HBSM group despite a similar baseline creatinine level. This could be due to the difference in the primary physicians treating the two groups of patients. While the HBSM group was directly under the care of the transplant physician team, the hospitalized group was under the care of other multidisciplinary teams, although under the direct supervision of the transplant team. However, the graft dysfunction was transient as the 6-week graft dysfunction rate was not significantly different between the two groups. Still, to avoid graft complications, RTRs with COVID-19 are best managed under the close supervision of a transplant physician. Furthermore, hypertension at presentation and a lower baseline EQ-5D score were associated with deterioration in the HBSM group.

6. Strengths and limitations

This study was a large, single-center study with a good sample size of 149 RTRs with mild COVID-19. In addition, this study is the first to compare the outcomes of ambulatory and hospitalized RTRs with COVID-19. Though the study was designed retrospectively, data collection was performed prospectively.

One limitation of the study could be that the patients or caregivers provided data in the HBSM group while it was taken directly by the transplant team in the inpatient group. However, most data were objective and collected using the monitoring charts sent through smartphone messaging systems. Also, the patient's clinical status was assessed by video calls whenever possible to prevent observational bias. Comparing one wave with another in an ongoing pandemic may have limitations due to changes in virulence patterns, vaccination, past-immunity patterns and slightly different management protocols in the two pandemic waves. Nevertheless, the baseline characteristics, including age, gender, and various symptoms, were similar between the two groups. Furthermore, the similar clinical deterioration rate in the two groups despite possible different virulent strains might suggest that this difference might not influence the disease nature in transplant patients with mild COVID-19. The study is not powered to comment on the non-inferiority of the HBSM strategy compared to the inpatient management. Most patients of the study population were males (91.3%), reflecting the gender disparity in renal transplantation in India [17,18]. As such, result applicability to the female gender may be limited.

To conclude, the supervised home-based self-monitoring strategy resulted in similar outcomes as the inpatient management of RTRs with mild COVID-19. However, as the study is not powered to analyze non-inferiority, additional substantial evidence in the form of randomized controlled trials or prospective studies is required to re-affirm the findings. Nonetheless, the outpatient management of RTRs with mild COVID-19 with a supervised HBSM strategy might be a good alternative, especially in limited inpatient services.

Human and animal rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well as in accordance with the EU Directive 2010/63/EU for animal experiments.

Informed consent and patient details

The authors declare that the work described does not involve patients or volunteers.

Disclosure of interest

The authors declare that they have no competing interest.

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Authorship contribution statement

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Dharmendra Bhadauria, Narayan Prasad, and Anupma Kaul participated in the research design.

Vamsidhar Veeranki, Dharmendra Bhadauria, and Jey Kumar participated in the writing of the paper.

Manas Ranjan Patel, Monika Yaccha, Anupma Kaul, and Sabarinath Shanmugham participated in the performance of the research.

Narayan Prasad, Sabarinath Shanmugham participated in data analysis.

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