

# Awareness and Concerns Among Adult Liver Transplant Recipients in the Current Pandemic Caused by Novel Coronavirus (COVID-19): Strategies to Safeguard a High-risk Population



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**Background:** The coronavirus disease 2019 (COVID-19) virus is spreading rapidly, and there are obvious concerns for the immunocompromised patient population including transplant recipients. Creating awareness and understanding patient concerns will play an important role in protecting this vulnerable group in developing timely and appropriate healthcare interventions. **Methods:** A cross-sectional online survey was conducted between 23rd March 2020 and 1st April 2020 among 154 liver transplant recipients, transplanted between October 2018 and February 2020. An 18-point questionnaire explored their knowledge of COVID-19, awareness of recipient's high-risk status, interventions to minimize cross-infections, and concerns of this patient group regarding the pandemic. **Results:** There were 112 (73%) respondents, with median age of 53 years (81% males). There was no difference in demographics between those who responded (n = 112) and those who did not respond to the survey (n = 42). Most of the recipients were aware of the main symptoms of COVID-19, such as fever (92%), breathlessness (86%), and dry cough (87%), but less than half were aware of diarrhea (39%) as a symptom. Awareness about spread from asymptomatic individuals was limited (26%). Majority (95%) understood their high-risk status, but worryingly, 23% of the respondents felt that there was no risk in visiting the hospital for routine clinic visit and blood tests. Concerns were raised by the recipients mostly regarding the uncertainties of COVID-19 infection and its treatment options, the quality of information on social messaging platforms, and lack of access to routine tests/immunosuppression levels because of lockdown/social distancing. **Conclusions:** Our liver transplant recipients have a reasonable awareness regarding COVID-19. Problems in accessing the healthcare system during prolonged periods of lockdown was a major concern. It is important for each transplant unit to educate, support, and remain accessible to this vulnerable patient cohort as the pandemic continues to progress worldwide. (J CLIN EXP HEPATOL 2020;10:540–547)

Coronavirus disease (COVID-19) caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has spread to 215 countries and affected over 4.5 million individuals, with 308,676 reported dead, as of May 16, 2020.<sup>1</sup> There is growing concern for the high-risk populations, especially the elderly and the immunocompromised.<sup>2</sup> The immune response of transplant recipients, particularly the T-cell immune response, is

significantly suppressed because of long-term use of immunosuppressive agents.<sup>3</sup> Clinical manifestations of COVID-19 in this cohort may hence be atypical and potentially more severe when compared with the nontransplant patients.<sup>4</sup>

Data on liver transplant recipients infected with SARS-CoV-2 are still limited to case reports and small series.<sup>4–8</sup> The first reported COVID-19 infection in a liver transplant patient was from Wuhan, in a 37-year old recipient, who developed severe COVID infection in the posttransplant period and was subsequently discharged after 2 months of hospitalization.<sup>6</sup> Lombardy, one of the most affected regions in Italy, reported 3 of their 111 long-term liver transplant patients died due to COVID-19, all of them transplanted more than 10 years ago, and they were more than 65 years old.<sup>9</sup> However, reports from the multiple centers from US have shown that the infection in transplant patients is much severe with higher mortality and affects much younger recipient population compared with non-transplant population.<sup>7,8</sup>

**Keywords:** COVID-19, coronavirus, transplant, liver transplant, immunosuppressed, recipient, survey

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**Abbreviations:** COVID-19: Coronavirus Disease 2019; DDLT: Deceased Donor Liver Transplantation; LDLT: Living Donor Liver Transplantation; MERS: Middle East Respiratory Syndrome; nCoV: Novel Coronavirus; SARS: Severe Acute Respiratory Syndrome

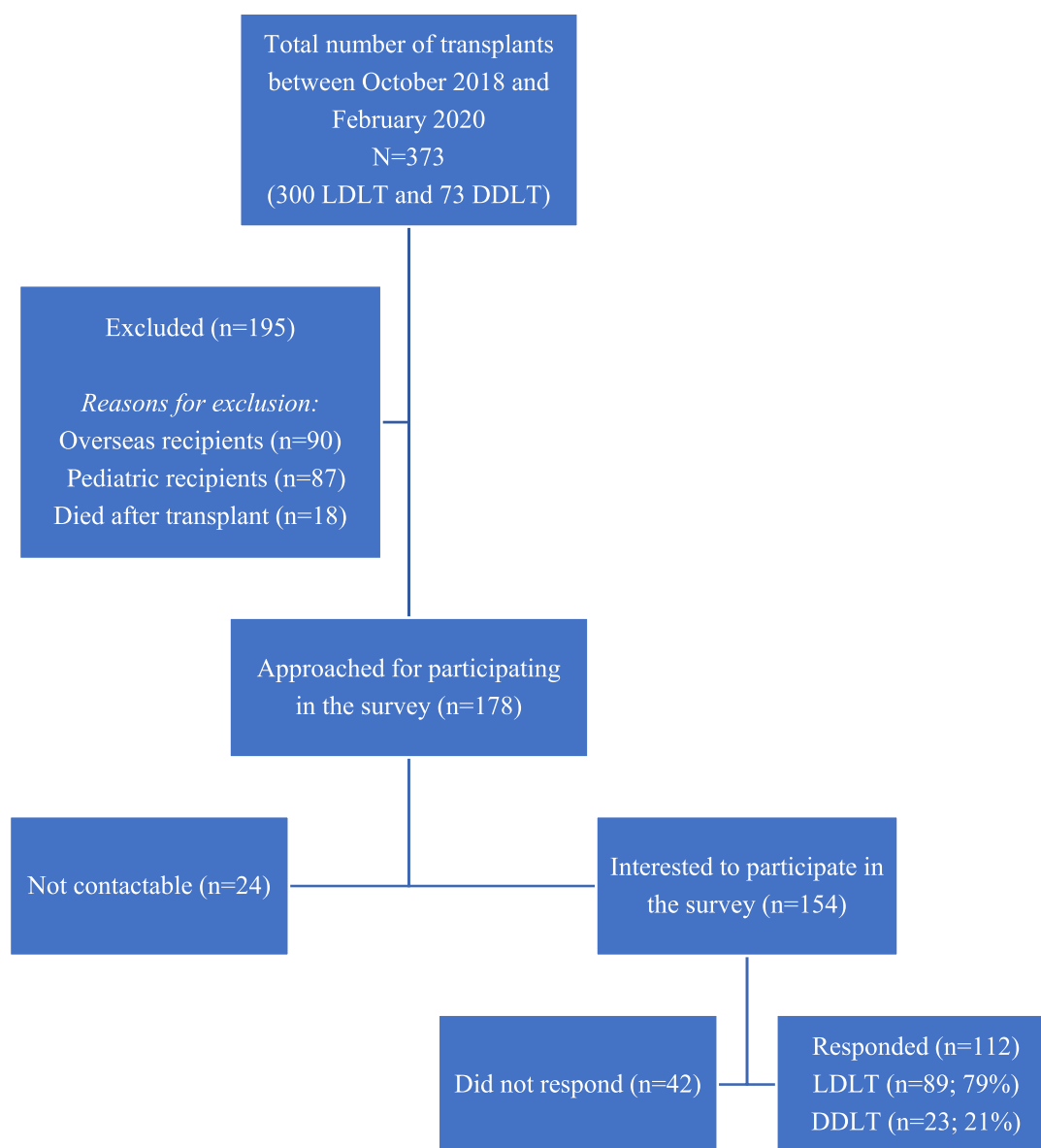
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Social distancing and personal hygiene seem to be the two main factors with the potential to prevent the spread of the virus.<sup>10</sup> Following a temporary lockdown period lasting 14 h on the 22nd of March 2020, the Indian Government extended the lockdown period to 21 days to prevent community spread of this highly infectious virus. For the transplant population on lifelong immunosuppression and accustomed to frequent clinic visits and routine blood tests, this is uncharted territory!

There is hence an urgent need for focused education of this patient cohort. We conducted an online survey to identify potential gaps in knowledge among the recipient population and their major concerns regarding the pandemic.

## MATERIALS AND METHODS

This study was conducted as a cross-sectional online survey using a commercially available online survey software ([www.surveymonkey.com](http://www.surveymonkey.com)). India's first case of COVID-19 was reported on 30th January. The largest COVID-19 national lockdown in the World started on 25th March for 21 days until 14th April, which was subsequently extended to 3rd May. The survey was initiated following the 14-hour curfew on the 23rd March and completed on the 1st of April. All recipients received an initial telephone call to explain the completely voluntary nature of the survey and asking them if they were interested to participate. The survey was then sent to them through



**Figure 1** Flowchart depicting the study inclusions and exclusions. DDLT, Deceased Donor Liver Transplantation; LDLT, Living Donor Liver Transplantation.

WhatsApp messaging. Those who did not respond by 29th March were given a single reminder call. The recipients were asked to fill the questionnaire independent of any help from others. Survey by telephone was avoided because of the risk of adding unnecessary bias by the call from the transplant unit. By the time the lockdown started, the government was promoting information on the COVID-19, including importance of social distancing and hand hygiene practices and the daily update on positive cases within the country.

The questionnaire focused on the recipient's awareness of the COVID-19 symptoms, knowledge of the modes of transmission, and available means of prevention and treatment. In particular, we were keen to know their understanding of their high-risk status, hence questions were asked about their risk when compared with normal population and other nontransplant patients and what would they do if they or their family members have symptoms suggestive of COVID-19 infection. Given the current stress on social distancing, we wanted to know if they were aware of the risk of travelling to the hospital for consultations and blood tests and their readiness for video consultations. We used an 18-point questionnaire: demographics (3 questions), COVID-19 information (4 questions), high-risk status assessment (7 questions), and concerns (4 questions). Opportunity was also provided for conveying any additional concerns in a free-text format (survey questionnaire available as [Supplemental file](#)).

Descriptive methods of data presentation were used. Categorical variables are expressed as frequencies and proportions (%), and continuous variables are presented as median (range). Approval for this study was obtained from the institutional review board.

## RESULTS

The flowchart depicts the study inclusions and exclusions ([Figure 1](#)). Following exclusions, we were left with 154 (41.3%) adult liver transplant recipients (123 living donor liver transplantation [LDLT] and 31 deceased donor liver transplantation [DDLT]) of Indian origin, of which 112 (73%) responded to the survey. The median age of the respondents was 53 years (range 18–64 years), 81% were male, and majority were living donor recipients (79% LDLT versus 21% DDLT). Nine percent were transplanted in 2020, 63% in 2019, and 28% in 2018. Median time since transplant was 8.6 months. There was no difference in demographic characteristics with the cohort which did not respond to the survey (n = 42; 27%), which minimizes the risk of nonresponse bias ([Table 1](#)).

### Awareness of COVID-19 and Mode of Spread

The majority of the recipients were aware of the common symptoms of COVID-19, such as fever (92%), breathlessness (86%), and dry cough (87%), but less than half were

**Table 1 Demographic Characteristics of Those who Responded and Those who did not Respond to the Survey.**

|                                      | Responders<br>(n = 112) | Nonresponders<br>(n = 42) | P value |
|--------------------------------------|-------------------------|---------------------------|---------|
| Median age (years)                   | 53 (range 18–64 years)  | 51 (range 18–72 years)    | 0.068   |
| Gender (male)                        | 91 (81%)                | 30 (71%)                  | 0.193   |
| Education level                      |                         |                           |         |
| No education                         | 2 (2%)                  | 1 (2%)                    | 1.000   |
| School level education               | 27 (24%)                | 12 (29%)                  | 0.679   |
| Undergraduate                        | 54 (48%)                | 19 (45%)                  | 0.856   |
| Postgraduate                         | 29 (26%)                | 10 (24%)                  | 0.838   |
| State of India                       |                         |                           |         |
| Tamilnadu                            | 54 (48%)                | 21 (50%)                  | 0.858   |
| Andhra Pradesh                       | 11 (10%)                | 4 (10%)                   | 1.000   |
| Kerala                               | 6 (5%)                  | 3 (7%)                    | 0.705   |
| Karnataka                            | 10 (9%)                 | 4 (10%)                   | 1.000   |
| Maharashtra                          | 6 (5%)                  | 4 (10%)                   | 0.462   |
| West Bengal                          | 9 (8%)                  | 1 (2%)                    | 0.287   |
| Other states                         | 16 (15%)                | 5 (11%)                   | 0.797   |
| Type of transplant                   |                         |                           |         |
| LDLT                                 | 89 (79%)                | 34 (81%)                  |         |
| DDLT                                 | 23 (21%)                | 8 (19%)                   | 1.000   |
| Year of transplant                   |                         |                           |         |
| 2020                                 | 10 (9%)                 | 5 (12%)                   | 0.554   |
| 2019                                 | 71 (63%)                | 27 (64%)                  | 1.000   |
| 2018                                 | 31 (28%)                | 10 (24%)                  | 0.689   |
| Median time from transplant (months) | 8.6 (range 1–17 months) | 9.1 (range 1–18 months)   | 0.094   |

DDLT, deceased donor liver transplantation, LDLT, living donor liver transplantation.

aware of diarrhea (39%) as one of the main symptoms. It is worrying that only 26% of the recipients felt that the COVID-19 infection can be spread by asymptomatic patients similar to those with symptoms, whereas 16% felt that asymptomatic individuals were no risk to the community. The majority of the recipients were aware of the droplet spread by coughing/sneezing (89%), spread through surfaces (77%), and spread through touching infected person/secretions (78%). But only 18% were aware of the oral/feco-oral route as one of the modes of transmission. Ninety-four percent of the recipients understood the importance of social distancing and felt this as the best means of preventing COVID-19 infection ([Table 2](#)).

### Understanding Their High-risk Status

Majority of the recipients felt that coronavirus infection can affect transplant patients more than the normal

**Table 2 Survey Questionnaire With Liver Transplant Recipient Responses.**

|  | No. of Responses<br>(n = 112) | %  |
|--|-------------------------------|----|
| <b>What are the main symptoms of Coronavirus infection (COVID-19)?<sup>a</sup></b>   |                               |    |
| Fever  | 103                           | 92 |
| Breathlessness   | 96                            | 86 |
| Dry cough  | 97                            | 87 |
| Wheezing   | 42                            | 38 |
| Running nose   | 55                            | 49 |
| Diarrhea   | 44                            | 39 |
| <b>Can an adult or child without any symptoms of the infection transmit the virus?</b>   |                               |    |
| Never  | 18                            | 16 |
| Possible   | 51                            | 46 |
| Very less when compared with those with symptoms   | 14                            | 13 |
| Can spread the infection similar to those with symptoms  | 29                            | 26 |
| <b>What are the modes of transmission of infection in COVID-19?<sup>a</sup></b>  |                               |    |
| Direct (Droplet) infection by coughing/sneezing  | 100                           | 89 |
| Touching surfaces contaminated with respiratory secretions   | 86                            | 77 |
| Touching someone infected with the virus   | 87                            | 78 |
| Through the food you eat   | 20                            | 18 |
| <b>Which is the best means available at present to prevent COVID-19 infection?</b>   |                               |    |
| Vaccination  | 2                             | 2  |
| Antibiotic prophylaxis   | 0                             | 0  |
| Wearing face masks   | 5                             | 4  |
| Avoid contact with other people and gatherings (social distancing)   | 105                           | 94 |
| <b>In terms of severity, do you think that coronavirus infection affects transplant patients more than normal population?</b>          |                               |    |
| Strongly agree   | 83                            | 74 |
| Agree  | 23                            | 21 |
| Neutral  | 6                             | 5  |
| Disagree   | 0                             | 0  |
| Strongly disagree  | 0                             | 0  |
| <b>In terms of severity, do you think that coronavirus infection affects transplant patients more than the nontransplant patients?</b> |                               |    |
| Strongly agree   | 73                            | 65 |
| Agree  | 34                            | 30 |
| Neutral  | 4                             | 4  |
| Disagree   | 1                             | 1  |
| Strongly disagree  | 0                             | 0  |
| <b>What are the precautions you are currently taking in view of the COVID-19 situation?</b>  |                               |    |
| Staying isolated at home   | 80                            | 71 |
| Minimising contact with visitors and family members  | 22                            | 20 |
| Going out of home, but with a mask   | 7                             | 6  |
| Not following any additional restrictions  | 3                             | 3  |
| <b>What will you do if you or one of your family members develop symptoms of flu such as fever, cough or running nose?</b>             |                               |    |
| Treat with home remedies which have been effective before  | 1                             | 1  |
| Will contact my doctor or the transplant unit for advice   | 92                            | 82 |

(Continued on next page)

**Table 2** (Continued)

|  | No. of Responses<br>(n = 112) | %  |
|--|-------------------------------|----|
| Will start a course of antibiotics which was previously given for a similar infection  | 2                             | 2  |
| All of the above   | 17                            | 15 |
| <b>What will you do with the immunosuppressant medications if you have flu like symptoms?</b>  |                               |    |
| Will stop the medications upfront as there is infection  | 0                             | 0  |
| Will halve the dose as there is infection  | 4                             | 3  |
| Will skip a few doses and restart when the I am fine   | 1                             | 1  |
| Will consult transplant centre for advice  | 107                           | 96 |
| <b>Do you think routine blood tests (liver function test, immunosuppression levels) need to be deferred as there is a risk of contact with someone infected with COVID-19?</b>   |                               |    |
| No, I don't feel there is a risk and routine tests can be done   | 26                            | 23 |
| There is a definite risk and I want to defer the labs  | 8                             | 7  |
| There is a risk, so will contact the transplant centre for advice  | 78                            | 70 |
| <b>In view of the current restriction in travel, I will be happy to do video consultation with my transplant team</b>  |                               |    |
| Strongly agree   | 72                            | 64 |
| Agree  | 36                            | 32 |
| Neutral  | 2                             | 2  |
| Disagree   | 0                             | 0  |
| Strongly disagree  | 2                             | 2  |
| <b>Have you had any respiratory illness in the last 4 weeks which worried you because of the current COVID-19 problem?</b>   |                               |    |
| Yes  | 3                             | 3  |
| No   | 109                           | 97 |
| <b>In India, access to testing for COVID-19 is very limited. Do you believe that all transplant patients should be considered as high-risk and offered testing for symptoms?</b> |                               |    |
| Strongly agree   | 41                            | 37 |
| Agree  | 42                            | 38 |
| Neutral  | 18                            | 16 |
| Disagree   | 10                            | 9  |
| Strongly disagree  | 1                             | 1  |
| <b>Which medium do you commonly depend on for getting information regarding COVID-19 problem?<sup>a</sup></b>  |                               |    |
| Television   | 91                            | 81 |
| WhatsApp   | 44                            | 39 |
| Facebook   | 19                            | 17 |
| Newspaper  | 42                            | 38 |
| Books  | 3                             | 3  |
| Direct discussion with a doctor  | 32                            | 29 |
| Others (if any)  | 13                            | 12 |
| <b>Please list up to five questions regarding the current COVID-19 scenario which you believe are important<sup>b</sup></b>  | See Table 3                   | –  |

<sup>a</sup>These questions have multiple responses.

<sup>b</sup>Selective responses from this have been tabulated into Table 3.

population (Strongly agree 74% and Agree 21%) and the nontransplant patients (Strongly agree 65% and agree 30%). In compliance with current social distancing guidelines and the Government of India lockdown restrictions, 71% of the recipients stayed at home, and a fifth (20%) minimized contact with other family members and visitors. Only a small percentage ventured out of the home with mask (6%), and a minority (3%) did not follow any additional restrictions. Eighty-two percent of the respondents were clear that they would contact their doctor or the transplant unit for advice, if they or their family members develop symptoms of flu such as fever, cough, or running nose. It is reassuring that 96% will not stop or modify immunosuppression and would rather consult their transplant unit for advice, for any flu-like illness (Table 2).

### Understanding the Risk of Routine Hospital Visits

The majority of the recipients (70%) understood the risk of acquiring the infection during travel to the hospital for routine appointments and blood tests and would rather contact the transplant unit by telephone for advice. It is worrying that 23% of the respondents felt that there is no risk, and they would be happy to visit hospital for routine tests. Ninety-six percent of the respondents liked the idea of video consultation during this period of social distancing and lockdown (Table 2).

### Concerns Raised by the Recipients

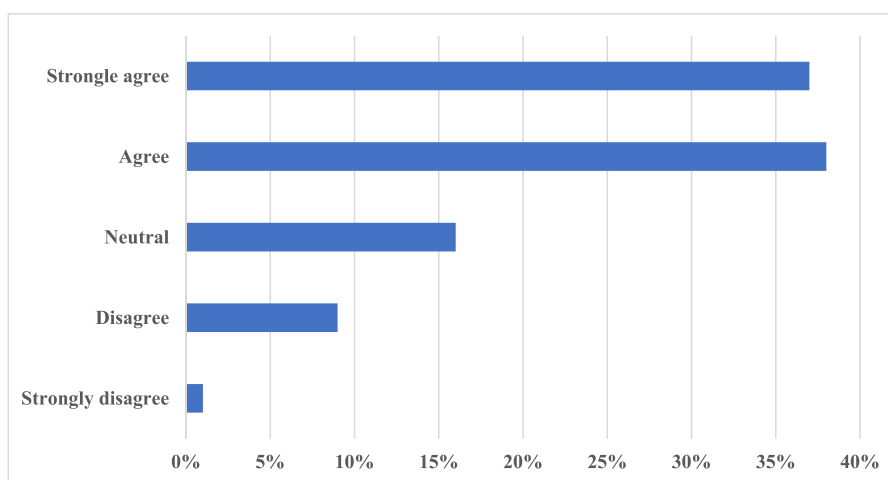
Three percent of respondents have had self-limiting respiratory illness in the last 4 weeks, which had caused them some concern to them in the background of the coronavirus outbreak. Seventy-five percent of the respondents felt that the Indian Government should offer testing to trans-

plant patients for any flu-like symptoms in view of their high-risk status even in the absence of other high-risk criteria such as international travel (Figure 2). The majority of them obtained their COVID-19 news from television (81%), WhatsApp (39%), and newspaper (38%) though a third (29%) had already contacted their doctor for information on COVID-19. Patients reported wrong information received on social media platforms, difficult access to healthcare, and disruption of their supply of immunosuppressive medications because of the prolonged lockdown as major concerns (see Table 3).

### DISCUSSION

Severe infections in transplant recipients has been previously reported with severe acute respiratory syndrome and Middle East Respiratory Syndrome viruses.<sup>11,12</sup> Respiratory virus infection in transplant recipients can cause more than just a cold, with reports of prolonged illness, extended viral shedding, progression to severe disease with resultant higher morbidity and mortality.<sup>13</sup> Because of their immunosuppressed state, these patients may also present with atypical symptoms.<sup>14</sup>

Our survey has demonstrated that liver transplant recipients have reasonable knowledge about the COVID-19 pandemic, and most are aware of their high-risk status. However, they are concerned about the current situation and to an extent confused by the information available on various social platforms. Their concern with the current situation was apparent with 285 questions being asked by 85 recipients, an average of 3.4 questions per person. It is heartening that most recipients reported their intention to contact the transplant unit for any advice when faced with doubts regarding their graft. Data from this survey have informed us during the preparation of a detailed



**Figure 2** In India, access to testing for COVID-19 is very limited. Do you believe that all transplant patients should be considered as high-risk and offered testing for symptoms?

**Table 3 An Illustrative Selection of Questions Put Forward by the Recipients Regarding the COVID-19 Pandemic.**

|   |
|---|
| <b>Concerns regarding COVID-19:</b>   |
| “Is COVID-19 airborne?”   |
| “How dangerous is this virus?”  |
| “How long it will stay in our body?”  |
| “Newspaper touching should be avoided?”   |
| “If COVID-19 affect any transplant patients will any treatment be effective to cure it?”                                      |
| “If a transplant recipient gets infected by COVID-19, what is the prognosis?”   |
| “When the vaccine will be available for covid-19?”  |
| “How far can COVID-19 transmit in the mode of air how much distance should we maintain.                                       |
| Is staying at home for the next 15 days sufficient? Or is it necessary to isolate oneself at home from other family members?” |
| <b>Misinformation on COVID-19:</b>  |
| “Can I use air conditioner in night, some of the information I came to know is to avoid cold things and AC is that true?”     |
| “Can I have egg and chicken as there is news about bird flu?”   |
| “Why so much fear created by Government?”   |
| “Sunlight will destroy the virus?”  |
| “What is special diet chart to prevent Corona for us?”  |
| <b>Concerns regarding prevention and cure:</b>  |
| “Any major precautions I have to take?”   |
| “Can I take Tablet. Plaquenil and Tablet. Hydroxychloroquine”   |
| “I need to go to shop for business but I am using sanitizer and wearing mask (N95), is that fine?”                            |
| “What should I do with the immunosuppressant medications if I have flu like symptoms?”  |
| “Should we wear masks even when we are at home?”  |
| <b>Concerns due to lack of access and lockdown:</b>   |
| “How to procure immunosuppressive and other medicines in case of the courier services being stopped?”                         |
| “My check-up is due now. How long should I wait for next check-up?”   |
| “How can take liver function tests and tacrolimus level tests?”   |
| “Where to get blood tests as no transport available?”   |
| “Can centre help to get important medicine for transplant patients if they are facing shortage of meds?”                      |
| “For how many days tentatively we should stock up the medicines for?”   |
| “In a lockdown situation with limited food resources what should my diet be?”   |
| <b>Other general concerns:</b>  |
| “Should I inform my situation with the local health authorities?”   |
| “Does the donor has to follow the same instructions given for recipient?”   |
| “Can I use alcohol based sanitizer?”  |
| “What should I do if there is an emergency?”  |

information leaflet regarding COVID-19 for our recipients. We have also started video consultations to minimize the need for hospital visits and increased home visits by phlebotomists for collecting blood samples. Reliable access to immunosuppressive medications during the period of lockdown was also identified as a major concern, and we are undertaking measures to ensure home delivery of medications for these recipients.

For those who are not infected with COVID-19 or are asymptomatic, we did not advise any change in immunosuppression, and the immunosuppressant dosage levels were titrated as per the trough levels. We also did not alter the frequency of our follow-up from our routine posttransplant protocol, but ensured patients were reviewed in the virtual clinics. For those patients who do need a face to face clinic review, for example to check their wounds or to get an ultrasound scan, we ensured their visit was planned in advance, and their stay in hospital is short, adhering to all social distancing measures. Based on the guidance available, we do not advise COVID-19 testing for asymptomatic recipients.<sup>15</sup>

Transplantation involves a lifelong contract between the patient and the transplant team. Confidence in the healthcare system is essential so that in extreme situations such as this, the patient knows that the most reliable advice is easily available from the transplant team. We believe that questionnaires such as these not only help us in understanding the immediate and urgent concerns of our patients but only periodically remind patients about our commitment to their well-being. Most of the interventions which we have undertaken have also been suggested in the recently published American Association for the Study of Liver Diseases (AASLD) guidelines.<sup>13</sup> A survey done on 640 liver transplant recipients in Milan, Italy, showed that 81% of them adhered to at least two COVID-19 preventive measures (frequent handwashing, sanitization, avoiding crowded places, and wearing masks), with only 8 recipients (1.25%) diagnosed with novel coronavirus infection. This survey elucidated the importance of preventive measures in this high-risk population, which eventually led this group to move to telemedicine to deliver care to liver transplant recipients.<sup>16</sup>

The major strength of this survey is its generalizability to all transplant patients. Given the rapid pace at which the COVID-19 pandemic is progressing and the uncertainty regarding its future course, it is vitally important that the transplant community is prepared to prevent dangerous consequences in a vulnerable patient group. Although there might be minor variations based on local practice across centers Worldwide, our study has underscored the need to interact with recipients and respond to their needs. Measures to minimize nonessential hospital visits for the recipient maintain open channels of communication with the treating team and ensuring an

uninterrupted supply of immunosuppressive medications during periods of lockdowns are key issues to address during these uncertain times.

## AUTHORS' CONTRIBUTION

A.R.H., J.M., N.S., and M.S.R. planned and designed the study. H.P., S.K., and S.M. disseminated the survey and collected the responses for the study. A.R.H. performed the statistical analysis and wrote the manuscript. J.M., N.S., D.J., and M.S.R. reviewed and revised the study design and the manuscript, which was finalized by M.R.

## CONFLICTS OF INTEREST

The authors have none to declare.

## CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

**Abdul R. Hakeem:** Conceptualization, Methodology, Data curation. **Hrishikesh Padmanaban:** Investigation. **Srinath Karthikeyan:** Investigation. **Sivakumar Murugesan:** Investigation. **Jagadeesh Menon:** Conceptualization, Methodology. **Naresh Shanmugam:** Conceptualization, Methodology, Project administration. **Dinesh Jothimani:** Conceptualization, Methodology, Project administration. **Mettu S. Reddy:** Conceptualization, Methodology, Project administration, Visualization. **Mohamed Rela:** Supervision.

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## SUPPLEMENTARY DATA

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jceh.2020.06.001>.