

# SARS-Cov-2 Seroprevalence in a French Kidney Transplant Center Located Within a “High-risk” Zone

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**Background.** Data on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seroprevalence in kidney transplant recipients (KTRs) remain rare. We sought to shed further light on this issue by conducting a single-center study in a kidney transplant center located in one of the France's highest risk zone (Grand Est) for coronavirus disease 2019 (Covid-19) during the initial disease outbreak. **Methods.** To this aim, we used a survey approach coupled with systematic investigation of SARS-CoV-2 serology in a cohort of 1390 KTRs. **Results.** SARS-CoV-2 serologies were available for 780 survey respondents, among whom 48 had anti-SARS-CoV-2 antibodies (total seroprevalence: 6.2%). Thirty-five of the 48 seropositive KTRs had previously received a diagnosis of Covid-19, whereas the remaining 13 patients were not known to be infected (8 asymptomatic cases). Specifically, 18.7% of seropositive KTRs and 1.1% of the entire cohort were asymptomatic. Household exposure was found to markedly increase the risk of SARS-CoV-2 transmission. **Conclusions.** Our findings demonstrate that the overall SARS-CoV-2 seroprevalence in KTRs living in one of the France's highest risk zone for Covid-19 during the first French lockdown was as low as 6.3%. Rapid and strict implementation of protective measures could have significantly mitigated virus spread even in an area of high virus circulation.

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## INTRODUCTION

As of the beginning of 2020, solid organ transplant recipients have been immensely impacted by the coronavirus disease 2019 (Covid-19) pandemic.<sup>1–3</sup> In this scenario, population-based surveys of anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies can provide valuable insights into the dynamics and control of infection rates and are paramount to understand the course of the pandemic.<sup>4</sup> Unfortunately, SARS-CoV-2 testing during the initial wave of Covid-19 was limited by shortage of reagents and screening kits. This issue, coupled with the potential

occurrence of asymptomatic infections, may have lead to underestimating the real prevalence of the disease.<sup>5,6</sup>

There are efforts underway to gain further insight into the seroprevalence of anti-SARS-CoV-2 antibodies to assess the potential achievement of herd immunity. However, published serologic surveys conducted between January 2020 and July 2020 have shown a consistently low seroprevalence across continents—including Europe (Switzerland, 10.8%<sup>4</sup>; Spain, 4.6%<sup>5</sup>; United Kingdom, 8.2%<sup>6</sup>; Italy, 11%<sup>7</sup>; Belgium, 6.9%<sup>8</sup>; Germany, 0.97%<sup>9</sup>; France, 3.1%–10%<sup>10</sup>; and Iceland, 0.8%),<sup>11</sup>

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management, data collection, and critical revision of the article. S.F.K. was in charge of laboratory testing and critically revised the article. All authors approved the final version of the article.

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Asia (China, 3.2%–3.8%),<sup>12</sup> and America (Canada, 0.55%<sup>13</sup>; United States, 1%–6.9%).<sup>14,15</sup> Another issue is that the rate of asymptomatic infections—which was initially calculated based on pilot reports from China and passengers on the Diamond Princess cruise ship<sup>16</sup>—is markedly higher than that initially believed (40%–45% versus 15%–18%, respectively).<sup>17</sup>

Attempts to better understand the seroprevalence of anti-SARS-CoV-2 antibodies in specific clinical settings are currently ongoing. Because reliable data on SARS-CoV-2 seroprevalence in immunosuppressed kidney transplant recipients (KTRs) remain scarce, we sought to shed further light on this issue by conducting a single-center study in a kidney transplant center located in one of the France's highest risk zone (Grand Est) for Covid-19 during the first French lockdown. Specifically, the purpose of this study was 2-fold, that is, to examine the seroprevalence of anti-SARS-CoV-2 antibodies in our KTR population and to identify the rate of asymptomatic Covid-19 infections in this sample of immunosuppressed patients. To achieve these goals, we used a survey approach coupled with systematic investigation of SARS-CoV-2 serology.

## MATERIALS AND METHODS

All KTRs included in the study—who had been transplanted at the Department of Nephrology, Strasbourg University Hospital (Grand Est, France) before March 6, 2020—that is, before the first French lockdown (mandated on March 17, 2020)—were asked to undergo SARS-CoV-2 serology either in a private laboratory facility or in our center. Only patients with a functioning graft were deemed eligible. While different ELISA (ELISA) kits were used for serology testing (see Supplementary List S1, SDC, <http://links.lww.com/TP/C199>), all of them were formally

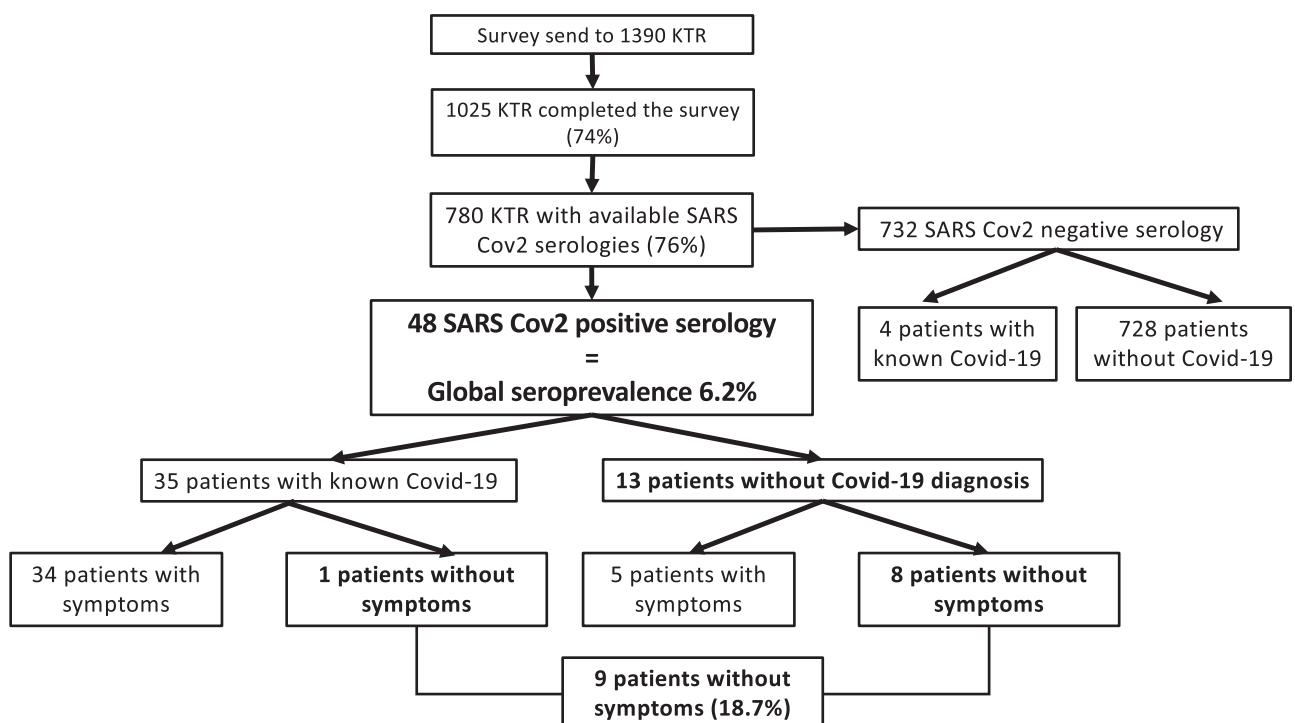
approved by French health authorities after validation of their performance.<sup>18</sup> Acquisition of data on anti-SARS-CoV-2 antibodies terminated on September 15, 2020. In parallel, the following survey (see Supplementary Survey S1, SDC, <http://links.lww.com/TP/C199>) was sent by either email or postal service on June and August 2020:

1. Did you experience infectious symptoms between January and June 2020 and, if yes, of what type?
2. Did you have contact with a Covid-19 confirmed case and, if yes, was the contact person within your household or not?
3. Did you undergo nasopharyngeal swab testing and, if yes, what were the laboratory results?

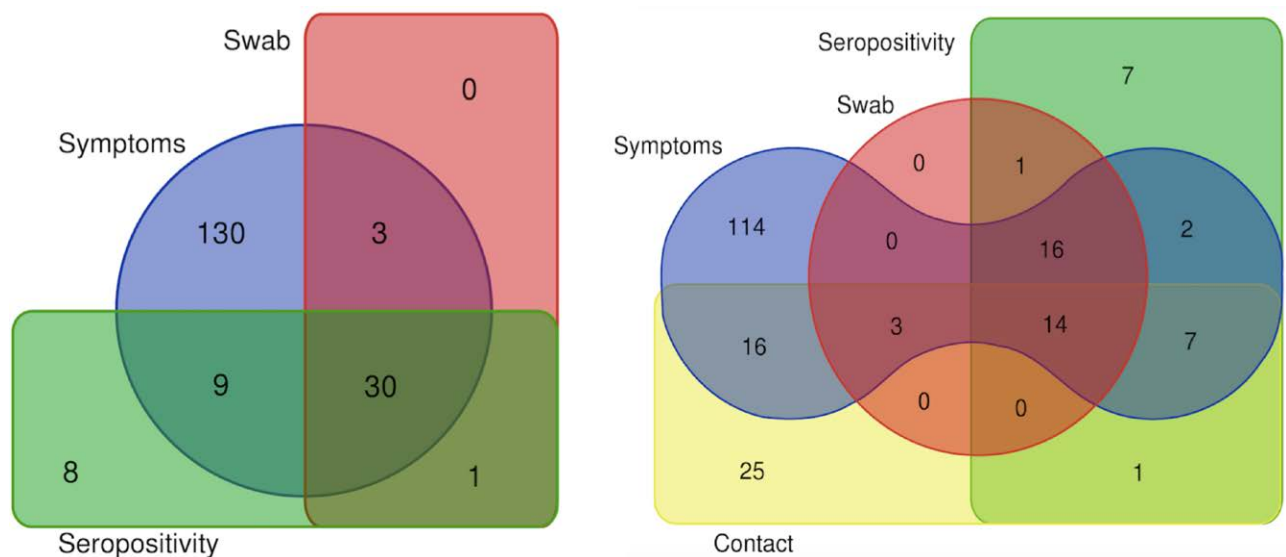
The study was approved by the local institutional review board (approval number: DC-2013-1990).

## RESULTS

Of the 1390 KTRs who received the survey, 1025 returned the questionnaire (response rate: 74%). Findings concerning infection symptoms and contact tracing are summarized in Figure S1 (SDC, <http://links.lww.com/TP/C199>). Results of SARS-CoV-2 serology were available for 780 respondents (76%; Figure 1), among whom 48 had anti-SARS-CoV-2 antibodies (total seroprevalence: 6.2%). Of the 48 seropositive KTRs, 9 did not experience infection symptoms (prevalence of asymptomatic Covid-19: 18.7%). Thirty-five of the 48 seropositive KTRs (73%) had previously received a diagnosis of Covid-19. Of them, 31 had positive reverse transcription polymerase chain reaction (RT-PCR) testing of nasopharyngeal swabs and 2 presented typical lung CT imaging findings. The remaining 2 cases had highly suggestive clinical symptoms (eg, anosmia/ageusia) or reported a household contact with a



**FIGURE 1.** Flow of kidney transplant recipients through the study. Covid-19, coronavirus disease 2019; KTR, kidney transplant recipient; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.



**FIGURE 2.** Venn diagrams summarizing the reciprocal interrelations between clinical symptoms, contact with a confirmed case of Covid-19, positive RT-PCR testing of nasopharyngeal swabs, and results of SARS-CoV-2 serology. A, Interrelations between clinical symptoms, positive RT-PCR testing of nasopharyngeal swabs, and SARS-CoV-2 serology. B, Interrelations between clinical symptoms, contact with a confirmed case of Covid-19, positive RT-PCR testing of nasopharyngeal swabs, and SARS-CoV-2 serology. Covid-19, coronavirus disease 2019; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

confirmed case. Four patients with a confirmed diagnosis of Covid-19 had negative serology testing. Among the 38 patients who were diagnosed with Covid-19, 7 were managed at home, 21 were hospitalized in a conventional unit, and 10 were directly admitted or subsequently transferred into an intensive care unit.

Thus, the seroprevalence among KTRs with known Covid-19 was 89.7% (35/39; Figure 1). We identified 13 patients (1.7% of the entire cohort) who had a positive SARS-CoV-2 serology in the absence of known disease. Of them, 5 reported infection symptoms between the end of January and April 2020. Notably, 4 of these 5 patients had a contact with a known Covid-19 case. The remaining 8 cases remained asymptomatic during the 6 mo before the termination of the survey. Of these 5 KTRs, only 1 reported a contact with a known Covid-19 case during an outpatient visit. Based on these findings, the frequency of completely asymptomatic Covid-19 in our cohort of KTRs was 1.1% (9/780).

The reciprocal interrelations between self-reported symptoms, contact tracing, positive RT-PCR testing of nasopharyngeal swabs, and positivity for anti-SARS-CoV-2 antibodies in the 780 study patients are summarized in Figure 2. The prevalence of anti-SARS-CoV-2 antibodies was higher in symptomatic than in asymptomatic patients (23% versus 1.5%, respectively) and in those who had a contact with a known Covid-19 case compared with those who did not (33% versus 3.6%, respectively; Table 1). As expected, the seroprevalence was higher for patients who reported a household contact (44%) than for those with a known no-household contact (eg, friends, relatives, colleagues, or other patients; 22%).

The sensitivity and specificity of different infection symptoms for diagnosing Covid-19 in our cohort of KTRs during the ongoing Covid-19 pandemic are shown in Table S1 (SDC, <http://links.lww.com/TP/C199>). While fever and diarrhea had the highest sensitivity for a diagnosis

of Covid-19, the maximum positive predictive value was observed for ageusia/anosmia.

## DISCUSSION

Our findings demonstrate that the overall SARS-CoV-2 seroprevalence in KTRs living in one of the France's highest risk zone for Covid-19 during the first French lockdown was as low as 6.3%. While this study specifically focused on an immunocompromised population, it also served to compare the frequency of anti-SARS-CoV-2 antibodies with that reported for French immunocompetent subjects. In this regard, the following adjusted seroprevalence estimates

**TABLE 1.**

**Results of SARS-CoV-2 serology according to presence or absence of symptoms, history of contact with a confirmed case, and results of RT-PCR testing of nasopharyngeal swabs**

	Positive serology (n = 48)	Negative serology (n = 732)
Symptoms (n = 780)		
Yes	39 (23%)	133 (77%)
No <sup>a</sup>	9 (1.5%)	599 (98.5%)
Contact with a confirmed case <sup>b</sup> (n = 779)		
Yes	22 (33%)	44 (67%)
No	26 (3.6%)	687 (96.4%)
RT-PCR testing (n = 152)		
Positive	31 (91%)	3 (9%)
Negative <sup>c</sup>	7 (5.9%)	111 (94.1%)

Data are summarized as counts (percentages).

<sup>a</sup>Including 1 case of known Covid-19 diagnosed by nasopharyngeal swab.

<sup>b</sup>Unknown data, n = 1.

<sup>c</sup>Including 5 cases diagnosed with Covid-19 based on CT findings or typical clinical symptoms coupled with contact with a confirmed case.

Covid-19, coronavirus disease 2019; CT, computed tomography; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

have been recently published: 10.0% for Ile de France, 9.0% for Grand Est (the same region in which our study was conducted), and 3.1% for Nouvelle Aquitaine<sup>10</sup>—with the first 2 areas being zones of high SARS-CoV-2 circulation. These results suggest that SARS-CoV-2 seroprevalence may be lower for KTRs compared with the general French population. It is not possible, however, to conclude whether the frequency of anti-SARS-CoV-2 antibodies in immunocompromised hosts is invariably lower than that of immunocompetent subjects because the reported seroprevalence for the general population vary widely between 0.9% (in a nationwide study from Iceland)<sup>11</sup> and 11% (in some high-risk areas in Italy).<sup>7</sup>

Further clarification of SARS-CoV-2 seroprevalence in specific clinical populations can also assist in our understanding of antibody response against the virus. For example, a recent United States nationwide study reported a mean seroprevalence of 8% in patients undergoing dialysis—albeit with marked geographic differences (from 1.9% in Missouri to 33.6% in New York City).<sup>19</sup> Dialysis patients are at increased risk for Covid-19 because they need to visit a healthcare facility 3 times per wk. Other studies conducted in New York City and London reported a global seroprevalence of respectively 16.6% and 10.3% in KTRs—which is significantly higher than that observed in the present investigation.<sup>20,21</sup> This can be explained by the lower frequency of symptomatic cases of Covid-19 in our cohort (versus 132 cases out of 1475 KTRs reported in the US study)<sup>20</sup> and the lower population density in France.

On analyzing the occurrence of asymptomatic Covid-19 in our sample, we found that KTRs comprised less asymptomatic cases than those observed in the general population. Specifically, 18.7% of seropositive KTRs and 1.1% of the entire cohort were asymptomatic. A recent review of 16 studies involving patients with positive RT-PCR testing of nasopharyngeal swabs reported a 40%–45% rate of asymptomatic SARS-CoV-2 infection (range, 30.8%–87.9%).<sup>17</sup> A multicohort analysis conducted by Carrat et al<sup>7</sup> showed that anti-SARS-CoV-2 antibodies are present in 3.7% of French asymptomatic patients. The results reported by Azzi et al<sup>20</sup> in a transplant population from New York City revealed that asymptomatic patients had a seroprevalence of 6.5%. Prompt implementation of protective measures (eg, social distancing and use of facial masks) in our KTRs could have significantly mitigated virus spread (even in a high-risk zone) and likely had an effect on the observed seroprevalence rate.

In our study, the presence of anti-SARS-CoV-2 antibodies appeared to be associated with a clinical diagnosis of Covid-19, a contact with a known Covid-19 case (especially within the household), and the presence of infection symptoms like fever and ageusia/anosmia. Household exposure is known to markedly increase the risk of SARS-CoV-2 transmission. In a study conducted in Iceland, Gudbjartsson et al<sup>11</sup> observed that subjects with household exposure had a 5.2-fold increased likelihood of being seropositive than those with other exposure types. We found that, of our KTRs who reported a household contact with a known Covid-19 case, 34% had anti-SARS-CoV-2 antibodies. Because a similar frequency was described in the Spanish serosurvey (37.4%),<sup>2</sup> we believe that active prevention and control measures to limit virus spread should be vigorously implemented for the KTR population.

There are several limitations to this study. First, serological testing was not conducted in a centralized laboratory; however, all of the ELISA kits used for serology were formally approved by French health authorities and displayed good performances.<sup>18</sup> Second, anti-SARS-CoV-2 antibodies were searched after a median of 3 mo from symptom onset, and a limited number of KTRs were tested between 6 and 8 mo. On analyzing the dynamics of serological response in healthcare personnel, Patel et al<sup>22</sup> found that 58% of subjects had antibodies below the detection threshold at 60 d from appearance of symptoms. Thus, the cross-sectional nature of our study could be associated with a bias related to the transient nature of antibodies. Even so, 72.4% of our KTRs were found to display anti-SARS-CoV-2 immunoglobulin G up to 6 mo after symptomatic Covid-19.<sup>23</sup> Third, sole reliance on serology for estimating the rates of SARS-CoV-2 infection in our population has inherent caveats. Indeed, it has been demonstrated that some patients, particularly those with a household contact with a known Covid-19 case, could develop T-cell immunity without simultaneous humoral protection.<sup>24</sup> It is also possible that patients with previous exposure to seasonal coronaviruses could have developed cross-reactive T-cell immunity against SARS-CoV-2, which can make them more likely to have pauci- or asymptomatic infections without an accompanying humoral response.<sup>25,26</sup> Fourth, it would have been interesting to measure neutralizing antibodies, which are probably the most effective in conferring protective immunity against the virus. Thus, implementation of Covid T cell and neutralizing antibodies detection tests could help clarify the global response of our patients against SARS-CoV-2. Unfortunately, these high-end assays are expensive and time consuming, ultimately being unsuitable for routine use in a large number of patients. Finally, a key prerequisite for inclusion in the study was the ability to respond to the survey; thus, patients who died of Covid-19 were not represented in our report. In general, the mortality rate from the disease in our KTRs approached 20%.

Despite these limitations, our findings indicate that KTRs with Covid-19 are capable of developing an effective humoral response against SARS-CoV-2. Although the study was conducted in one of the France's highest risk zone for Covid-19 during the first French lockdown, the overall seroprevalence was as low as 6.3%. Moreover, we found that asymptomatic cases of Covid-19 among KTRs were uncommon (1.1% of the entire cohort and 18.7% of seropositive KTRs). Further research is needed to examine more rigorously the hypothesis of protection conferred by anti-SARS-CoV-2 neutralizing antibodies, as well as to clarify the potential occurrence of specific cellular immunity.

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