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A Comparison Study of Coronavirus Disease 2019 Outcomes in Hospitalized Kidney Transplant Recipients

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Abstract

Background. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can infect any human host, but kidney transplant recipients (KTR) are considered more susceptible based on previous experience with other viral infections. We evaluated rates of hospital complications between SARS-CoV-2 positive KTR and comparator groups.

Methods. We extracted data from the electronic health record on hospitalized patients with SARS-CoV-2 testing at six hospitals from March 4th through September 9th, 2020. We compared outcomes between SARS-CoV-2 positive KTR and controls: SARS-CoV-2 positive non-KTR, SARS-CoV-2 negative KTR and SARS-CoV-2 negative non-KTR.

Results. Of 31,540 inpatients, 3213 tested positive for SARS-CoV-2. There were 32 SARS-CoV-2 positive and 224 SARS-CoV-2 negative KTR. SARS-CoV-2 positive KTR had higher ferritin levels *[1412 (748,1749) vs. 553 (256,1035), p<0.01]* compared to SARS-CoV-2 positive non-KTR. SARS-CoV-2 positive KTR had higher rates of ventilation *(34% vs. 14%, p<0.01; vs. 9%, p<0.01; vs. 5%, p<0.01)*, vasopressor use *(41% vs. 16%, p<0.01; vs. 17%, p<0.01; vs. 12%, p<0.01)* and acute kidney injury (AKI) *(47% vs. 15%, p<0.01; vs. 23%, p<0.01; vs. 10%, p<0.01)* compared to SARS-CoV-2 positive non-KTR, SARS-CoV-2 negative KTR, and SARS-CoV-2 negative non-KTR, respectively. SARS-CoV-2 positive KTR continued to have increased odds of ventilation, vasopressor use and AKI compared to SARS-CoV-2 positive non-KTR independent of Elixhauser score, Black race and baseline eGFR. Mortality was not significantly different between SARS-CoV-2 positive KTR and non-KTR, but there was a notable trend towards higher mortality in SARS-CoV-2 positive KTR *(25% vs. 16%, p=0.15, respectively)*.

Conclusion. Hospitalized SARS-CoV-2 positive KTR had a high rate of mortality and hospital complications such as requiring ventilation, vasopressor use, and AKI. Additionally they had higher odds of hospital complications compared to SARS-CoV-2 positive non-KTR after adjusting for Elixhauser score, Black race and baseline eGFR. Future studies with larger sample size of KTR need to validate our findings.

Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its associated disease (coronavirus disease 2019) was first identified in the Wuhan district of China in December, 2019 and was declared a global pandemic by the World Health Organization on March 11, 2020. The current case count has exceeded 21 million worldwide with more than 760,000 deaths.[1] The United States of America has emerged as the country with the highest number of infections in the world with more than 5.2 million cases at this time.[1] While it is believed that this virus can infect any potential human host, the kidney transplant recipient (KTR) population is considered more susceptible to severe infection based on their ongoing treatment with immunosuppression and previous experience with other viral infections.[2, 3]For instance, it has been shown that influenza in transplant recipients has been associated with high rates of medical complications and even mortality.[3] Similarly, multiple other respiratory viral infections have also been shown to have worse outcomes in transplant recipients as compared to the general population.[2] On the other hand, it has been observed that the hyper-inflammatory phase in the setting of SARS-CoV-2 infection is associated with significant clinical deterioration and poor outcomes.[4, 5] Therefore, it is hypothesized that transplant recipients taking immunosuppression may be protected from this hyper inflammatory phase of coronavirus disease 2019.[6-10] However, research studies from the Brescia Task force, Columbia Transplant Center, the Post-Transplant Glomerular Diseases international consortium and other centers have reported case fatality rates in SARS-CoV-2 positive transplant recipients in the range of 24-35%, which is significantly higher than the estimated case fatality rates in the general population.[9, 11-15] The rates of AKI have varied from 33-52% with 20-25% of these requiring renal replacement therapy.[11,13,15] Yet, these published studies did not have a control group or extrapolated comparative data from the wider population database (historical controls).[11-15]

Recently published literature from the STOP-COVID investigators and the Henry Ford group have provided more insight by comparing outcomes in SARS-CoV-2 positive Solid Organ Transplant (SOT) patients and SARS-CoV-2 positive non-SOT controls.[16, 17] Both groups reported similar mortality in the comparison groups, however the former focused only on critically ill SOT patients whereas the latter included all inpatient SOT patients. Both studies did not include a comparator group of transplant recipients who tested negative for SARS-CoV-2. A control group of kidney transplant recipients who tested negative for SARS-CoV-2 would allow us to understand the attributable risk of the adverse outcomes that would be associated with coronavirus disease 2019. There remains a need to investigate the differences in coronavirus disease 2019 outcomes in all hospitalized KTR in comparison to other control groups within the same hospital system and the same time frame to ensure exposure to similar treatment protocols. In an effort to address this gap in knowledge, we present the outcomes of inpatient SARS-CoV-2 positive KTR and contemporaneous control

groups from the same institution including SARS-CoV-2 positive non-KTR, SARS-CoV-2 negative KTR and SARS-CoV-2 negative non-KTR.

Methods

We used the Electronic Health Record (EHR) data between March 4th, 2010 to September 9th, 2020 from six hospitals within the Yale New Haven Health System (YNHHS). We identified adult inpatients who were at least 18 years of age, and who were tested for SARS-CoV-2 via nasopharyngeal RNA PCR swab 14 days preceding hospitalization and up to the date of discharge. Using the International Classification of Disease-10 (ICD-10) codes, we identified patients who were KTR within our dataset with code Z94.0.[18] SARS-CoV-2 positivity was defined as the first nucleic acid detection via the SARS Cov-2 RNA nasopharyngeal swab.

This study was approved by the Yale human investigation committee (HIC #2000027733) and operated under a waiver of informed consent and was deemed minimal risk as medical record research. This study adhered to the Declaration of Helsinki.

Baseline characteristics, vital signs and laboratory measurements

Covariates of interest were extracted from the EHR and included data on demographics, comorbidities, biochemical data and vital signs. We calculated the Elixhauser comorbidity score using a validated administrative coding system.[19] Given the longitudinal nature of our study design, and repeated measurements per observation, we summarized inpatient continuous variables (such as vital signs, and lab measurements) as the median of all available measurements per patient. Therefore the median (interquartile) values presented in this study represent the median of the medians.

Operational definitions of outcomes

Our primary outcomes were intensive care unit (ICU) admission, use of mechanical ventilation, use of vasopressors, development of acute kidney injury (AKI) and inpatient mortality during index hospitalization. ICU admission was defined by manual mapping of location data for patients and was independently validated through chart review. Ventilator use was defined by a procedure order placed for a patient consistent with ventilation orders and vasopressors were defined by manual mapping of medications from the pharmacy formulary consistent with this class of medication. Medication use was defined as “yes” if participant was ever exposed to the medication at index hospitalization. Hospital mortality was defined by structured discharge disposition data from the health record and was also validated with chart review. We defined AKI using KDIGO (Kidney Disease: Improving Global Outcomes) criteria as follows ≥0.3 mg/dL or 50% increase in creatinine from baseline. Baseline creatinine was defined as the median of the last 3 creatinine values obtained 7 to 365 days before hospital admission.

Statistical Analysis

Continuous variables were reported as median (interquartile range, IQR), and categorical variables were reported as frequencies, n (%). Differences in clinical and demographic characteristics were evaluated by the Kruskal-Wallis test or Chi-square test for continuous or categorical variables, respectively. We used logistic regression models to assess the associations between KTR who were SARS-CoV-2 positive with the primary outcomes of intensive care unit (ICU) admission, ventilator use, vasopressor use, development of AKI and hospital mortality. The odds ratios and 95% confidence intervals of both the univariable and multivariable models (adjusting for Elixhauser comorbidity score, Black race and baseline eGFR) are reported. All inference testing was two-sided with an alpha of 0.05. We constructed three logistic regression models. The first model evaluated associations between KTR status and outcomes among SARS-CoV-2 positive patients. The second model evaluated associations between SARS-CoV-2 status and outcomes among KTR. Finally, the third model evaluated the associations between SARS-CoV-2 positive KTR and outcomes compared to SARS-CoV-2 negative non-KTR. All models were adjusted for Elixhauser comorbidity score, Black race and baseline eGFR. Analyses were conducted in SAS, version 9.4 (SAS Institute Inc).

Results

Baseline Characteristics

Overall we included 31,540 patients, among whom 3213 (10%) tested positive for SARS-CoV-2 and 28,327 (90%) tested negative for SARS-CoV-2. Among those who tested positive for SARS-CoV-2, 32 (1%) were KTR, and among those who tested negative, 224 (0.8%) were KTR (**Figure 1**). The median (IQR) age of all patients tested for SARS-CoV-2 was 60 (38, 74) years. Females made up 58% (18,135 out of 31,540) of the cohort, and 17% (5,302 out of 31,540) were black. The median Elixhauser comorbidity score was 4 (1,8) with 28% (8,743 out of 31,540) having diabetes, 55% (17,398 out of 31,540) with hypertension, 32% (10,001 out of 31,540) with chronic pulmonary disease, and 28% (8685 out of 31,540) with obesity. SARS-CoV-2 positive KTR had higher rates of black participants, diabetes, stroke and longer length of hospital stay as compared to all other control groups including SARS-CoV-2 positive non-KTR, and SARS-CoV-2 negative KTR and non-KTR (**Table 1**). Furthermore, SARS-CoV-2 positive KTR had a similar level of comorbidity to other KTR who were SARS-CoV-2 negative, but they had a significantly higher level of comorbidity as measured by Elixhauser score as compared to all non-KTR who were both SARS-CoV-2 positive and negative.

Distribution of vital signs and biochemical data

SARS-CoV-2 positive KTR had significantly higher peak blood pressures as compared to all other control groups (**Table S1**). On biochemical analysis, SARS-CoV-2 positive KTR had significantly higher median blood urea nitrogen [40.8 (24.5, 56) *vs.*

17.5 (12, 28), p<0.001] and creatinine [2.1 (1.3, 2.7) *vs.* 0.9 (0.7, 1.2), p<0.001] during their hospitalization as compared to SARS-CoV-2 positive non-KTR. SARS-CoV-2 positive KTR also had metabolic derangements associated with kidney dysfunction such as lower bicarbonate [21.5 (19.5, 23.5) *vs.* 24 (22, 26), p<0.001] as compared to non-KTR who were SARS-CoV-2 positive (**Table 2**). Furthermore, SARS-CoV-2 positive KTR had significantly lower median absolute lymphocyte count [0.7 (0.5, 1) *vs.* 1.2 (0.8, 1.5), p<0.001] as shown in **Table 2**, and higher ferritin [1412 (747.5, 1748.5) *vs.* 553 (256, 1035), p<0.001] as compared to SARS-CoV-2 positive non-KTR (**Figure 2** and **Table 2**). Ferritin remained significantly higher in the SARS-CoV-2 positive KTR group as compared to non-KTR after adjusting for Elixhauser score (**Table S2**). C-reactive protein, high sensitivity c-reactive protein, and d-dimer levels were not significantly different between SARS-CoV-2 positive KTR and non-KTR, although there was a trend towards higher d-dimer levels in the SARS-CoV-2 positive KTR group.

Rates of hospital complications

The overall rates of intensive care unit admissions during the index hospitalization, ventilation, vasopressor use, acute kidney injury and death were 20% (6287 out of 31,540), 6% (1,850 out of 31,540), 12% (3,799 out of 31,540), 9% (2882 out of 31,540) and 4% (1317 out of 31,540), respectively. SARS-CoV-2 positive KTR had significantly higher rates of ventilation, vasopressor use and acute kidney injury compared to all other control groups as shown in **Table 3**. SARS-CoV-2 positive KTR also had significantly higher rates of hospital mortality (25%) as compared to SARS-CoV-2 negative KTR (2%) and SARS-CoV-2 negative non-KTR (3%), but not compared to SARS-CoV-2 positive non-KTR (16%, p=0.15). Additionally, SARS-CoV-2 positive KTR had about 3 times the odds of requiring mechanical ventilation as compared to SARS-CoV-2 positive non-KTR [Odds ratio: 3.31 (95% CI: 1.59, 6.89)] independent of Elixhauser comorbidity score, Black race and baseline eGFR as shown in **Figure 3**. SARS-CoV-2 positive KTR also had 2.3 times the odds of requiring vasopressors [2.32 (1.12, 4.80)] and 2.5 times the odds of developing AKI [2.48 (1.17, 5.29)] independent of Elixhauser score, Black race and baseline eGFR. The relationship between SARS-CoV-2 infection and the outcomes of vasopressor use and mechanical ventilation are significantly modified by kidney transplant status as shown by the interaction p-values in **Table 3**. Similar associations were identified when comparing the outcomes of mechanical ventilation, vasopressor use and AKI in SARS-CoV-2 positive KTR with SARS-CoV-2 negative KTR and non-KTR (**Tables S3** and **S4**). In addition mortality rates were significantly higher in SARS-CoV-2 positive KTR as compared to SARS-CoV-2 negative KTR and SARS-CoV-2 negative non-KTR after adjusting for Elixhauser comorbidity score, Black race and baseline eGFR (**Tables S3** and **S4**).

Distribution of coronavirus disease 2019 related pharmacotherapy and immunosuppressive medications

There were some differences in the management of SARS-CoV-2 positive patients between KTR and non-KTR, with more KTR patients receiving hydroxychloroquine and tocilizumab than non-KTR, with a trend towards higher use of methylprednisolone

(**Table 4**). Additionally, among KTR there were some differences in immunosuppression use with significantly lower use of mycophenolate in SARS-CoV-2 positive KTR compared to SARS-CoV-2 negative KTR as shown in **Table 5.** Details of type and timeline of kidney transplantation as well as induction therapy in SARS-CoV-2 positive KTR is provided in **Table S5**. We also compared Tacrolimus levels in kidney transplant recipients who are SARS-CoV-2 positive with and without hospital complications (**Table S6**) and we identified that there were lower median Tacrolimus levels in recipients with hospital complications.

Discussion

In this study we evaluated hospital outcomes in SARS-CoV-2 positive KTR. We identified that SARS-CoV-2 positive KTR had a higher risk of hospital complications such as mechanical ventilation, vasopressor use and development of AKI as compared to other SARS-CoV-2 positive and SARS-CoV-2 negative patients. Hospitalized SARS-CoV-2 positive KTR had a high rate of mortality at 25%. There was a higher rate of mortality in SARS-CoV-2 positive KTR as compared to SARS-CoV-2 negative KTR and non-KTR. Although there was no significant difference in mortality between SARS-CoV-2 positive KTR (25%) and SARS-CoV-2 positive non-KTR (16%), there was a notable trend towards higher mortality in SARS-CoV-2 positive KTR. Our results add to the existing body of literature showing that SARS-CoV-2 positive KTR have more hospital complications as compared to non-KTR infected with SARS-CoV-2, but our findings also identified that these complications are independent of comorbidities, Black race and baseline eGFR, and remain higher in comparison to SARS-CoV-2 negative KTR and non-KTR.[9, 11-15]

Our study further explored differences in lab measurements and vital signs between SARS-CoV-2 positive KTR and SARS-CoV-2 positive non-KTR as well as SARS-CoV-2 negative patients. SARS-CoV-2 positive KTR portrayed a more severe clinical profile with higher blood pressures, more severe metabolic acidosis, and lower kidney function. Furthermore, SARS-CoV-2 positive KTR had more severe elevations in inflammatory markers such as ferritin. Although elevations in ferritin may be confounded by pre-existing history of anemia in KTR, these elevations remained significant even after adjusting for level of comorbidity. The elevations in ferritin and a trend of higher levels of d-dimer offer further support against the notion that chronic treatment with immunosuppressive medications may attenuate the inflammatory phase associated with SARS-CoV-2 infection.[20-22]

To our knowledge this study is first to utilize multiple comparison groups with a large sample size from the same institution and the same time frame. Our cohort included patients from 6 hospitals, both community level and academic level hospitals, which enhance the generalizability of our findings to different inpatient settings. Additionally, all SARS-CoV-2 positive patients were systematically treated with a standard protocol for using anti-viral drugs, IL-6 inhibitors and other potential treatments thus making them more comparable for assessing outcomes. Despite these standard protocols, there was a higher use of hydroxychloroquine

and tocilizumab in KTR, which likely reflects the severity of illness in SARS-CoV-2 positive KTR. Furthermore, we identified a notable trend towards higher mortality in SARS-CoV-2 positive KTR (25%) as compared to SARS-CoV-2 positive non-KTR (16%), in spite of the trend towards higher use of corticosteroids, which has been shown to decrease mortality in patients with severe respiratory illness secondary to coronavirus disease 2019 in the RECOVERY (Randomized Evaluation of COVid-19 thERapY) trial.[23] Our study timeline also captures both the ascending and peak time periods of the coronavirus pandemic, and therefore our hospital complications and mortality rates more accurately reflect the temporal changes associated with coronavirus disease 2019. Furthermore, we evaluated our hospital complications and mortality outcomes independent of Elixhauser comorbidity score, Black race and baseline eGFR.[19] The Elixhauser score has previously been validated and was significantly associated with in-hospital mortality and health service measures associated with burden of illness in prior studies.[19, 24]

It is important to note that our findings differed from two recently published studies with comparator groups. We identified that transplant status in the setting of SARS-CoV-2 infection is linked to worse hospital outcomes, but not mortality, whereas Chaudhry *et al*. found no difference between solid organ transplant recipients and non-recipients with regard to a composite outcome of ICU care, mechanical ventilation and all-cause mortality. [17] The variability in our findings is likely due to differences in sample size and cohort characteristics. Chaudhry *et al*. reported on 100 patients in the control group who were non-transplant recipients infected with SARS-CoV-2 among whom 80% were black as compared to only 26% in our control group of 3181 SARS-CoV-2 infected non-transplant recipients. However, in our cohort, even after adjusting for Black race, SARS-CoV-2 positive KTR still had higher odds of hospital complications. Our findings are also in contrast to the recently published work by the STOP-COVID investigators, which did not find differences in outcomes between SARS-CoV-2 positive transplant and non-transplant recipients.[15] This is also partly due to our cohort differences, as we did not limit our cohort to ICU patients. This may be a key difference as the subset of non-KTR patients that are admitted to the ICU are substantially sicker than patients managed on the medical wards, which is evident in our mortality rate of 16% in SARS-CoV-2 positive non-KTR compared to a rate of 43% in SARS-CoV-2 positive non-transplant recipients as reported by Molnar *et al*. [15]

A large variable that separates kidney transplant patients from the general population is the use of immunosuppression. In spite of multiple publications, the role of immunosuppression in the clinical course of coronavirus disease 2019 has remained unclear.[7, 8] While on one hand due to immunosuppression KTR are theoretically at higher risk of acquiring this infection and also having a less favorable course, on the other hand immunosuppression could play a protective role against the inflammatory phase of this disease.[6-9] In our cohort we could not identify a trend towards less inflammation in KTR patients infected with SARS-CoV-2. In fact, KTR had higher levels of ferritin as compared to non-KTR infected with SARS-CoV-2. Although some in-vitro studies suggest a

potential anti-viral effect of cyclosporine, tacrolimus and mycophenolate,[25] there have been no human trials to support this potential benefit. Our findings suggest that transplant status is linked to higher hospital complications, which may be due to immunosuppression, but this question was not answered by our study.[20, 26] Furthermore, we identified lower median Tacrolimus levels in SARS-COV-2 positive KTR who required ventilation, vasopressor use, and ICU admission. However, it is likely that clinicians stopped or lowered immunosuppression dosing in patients with more severe clinical presentation.

Our KTR population infected with SARS-CoV-2 had a lower rate of mycophenolate use compared to other KTR who were SARS-CoV-2 negative. The clinical relevance of this difference in immunosuppression and impact on outcomes remains unclear. It is also important to note that these differences in immunosuppression are heavily influenced by clinical judgment. Immunosuppression management within the Yale New Haven Health System typically included the removal of the anti-metabolite/secondary agent and the calcineurin inhibitor/primary agent was adjusted based on the severity of the illness in SARS-CoV-2 infected patients. Steroids were routinely continued and the use of methylprednisolone was based on the severity of lung involvement and was decided on in conjunction with the intensive care and infectious disease clinicians. Hence, the role of immunosuppression in coronavirus disease 2019 outcomes needs to be interpreted with caution as it may be a marker of the severity of illness and more reflective of clinical management rather than offer insight into the causal pathway of coronavirus disease 2019 outcomes in KTR. Furthermore, our data was limited in capturing cumulative dose of immunosuppression as our definition of medication use was based on any exposure of immunosuppression while inpatient.

We also found a significantly higher incidence of liver disease in the SARS-CoV-2 KTR compared to both the SARS-CoV-2 negative cohorts. Whether liver disease is a risk factor for Coronavirus disease 2019 is uncertain based on the current literature[27] and this finding may be reflective of underlying non alcoholic fatty acid liver disease in the setting of significantly higher incidence of diabetes in the SARS-CoV-2 positive KTR.

Our findings need to be interpreted in the context of our study's limitations. Although we have a large sample size, with multiple comparison groups, our study is still limited to a single geographical location and hence our results may only be generalizable to other populations with similar demographics. Given the smaller number of participants with KTR and SARS-CoV-2 infection from a single hospital network, we were limited in how many confounders we could adjust for in our associative analyses and therefore our identified associations need to be validated in a larger multicenter cohort of SARS-CoV-2 positive KTR. We used Elixhauser score in our multivariable model, which is limited by the use of ICD-codes to calculate the comorbidity score. Additionally, we identified patients who were tested for SARS-CoV-2 anywhere from 14 days prior to admission to time of discharge. This may

have included asymptomatic patients getting tested for discharge planning or prior to surgery, which may have decreased the severity of illness in our cohort. Nonetheless, we would expect this bias to non-differentially affect all groups.

In conclusion, hospitalized SARS-CoV-2 positive KTR had a high rate of mortality and hospital complications. Additionally, SARS-CoV-2 positive KTR had higher rates of hospital complications compared to SARS-CoV-2 positive non-KTR independent of the level of comorbidities, Black race and baseline eGFR. Although these findings need to be validated in larger studies, they may help inform discussions between KTR and their physicians regarding the severity of coronavirus illness in the kidney transplant population.

Disclosures

D. Moledina reports a patent to Systems and Methods to Diagnose Acute Interstitial Nephritis pending. E. Marin reports Consultancy Agreements: Natera, Veloxis; Scientific Advisor or Membership: *Kidney360* Review board; Other Interests/Relationships: Member: ASN, AST. F. Wilson reports Consultancy Agreements: Translational Catalyst, LLC; Ownership Interest: Owner of Efference, LLC; Scientific Advisor or Membership: Editorial Board - American Journal of Kidney Disease; Editorial Board - Clinical Journal of the American Society of Nephrology; Other Interests/Relationships: Board of Directors - Gaylord Health Care; Medical Commentator - Medscape. All remaining authors have nothing to disclose.

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Table S3. Associations between SARS-CoV-2 positive KTR and hospital complications as compared to SARS-CoV-2 negative KTR

Table S4 Associations between SARS-CoV-2 positive KTR and hospital complications as compared to SARS-CoV-2 negative non-KTR

Table S5 Type and timeline of kidney transplantation and induction therapy in SARS-CoV-2 positive kidney transplant recipients

Table S6: Comparison of Tacrolimus levels in kidney transplant recipients who are SARS-CoV-2 positive with and without outcomes

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Figure Legends

Figure 1. Study flow diagram

Figure 2. Distribution of ferritin among SARS-CoV-2 positive patients

SARS-CoV-2 positive KTR (represented in dark red) have significantly higher Ferritin levels compared to SARS-CoV-2 positive non-KTR (represented in light red). The above boxplot shows the mean, represented by the 'X'; median, represented by the horizontal line inside the box; interquartile range represented by the outer bounds of the box; minimum and maximum data points excluding outliers, represented by the whiskers.

Figure 3. Forest plot of the odds ratio of hospital complications in SARS-CoV-2 positive KTR as compared to SARS-CoV-2 positive non-KTR

The above forest plot shows that SARS-CoV-2 positive KTR have significantly higher odds of mechanical ventilation, vasopressor use and acute kidney injury (AKI) independent of Elixhauser score, Black race and baseline eGFR. The squares represent the odds ratio and the lines represent the 95% confidence intervals. Significant associations are represented in red and non-significant associations are in black. The x-axis uses a logarithmic scale to the base of 10. The above associations are the unadjusted analyses and the bottom associations are adjusted for Elixhauser score, Black race and baseline eGFR.

Table 1. Baseline characteristics

Baseline Characteristics	**Cases**	**Controls**			**P-values**		
	SARS-CoV-2 **+/KTR** N=32	SARS-CoV-2 **+/Non-KTR** N=3181	SARS-CoV-2 **-/KTR** N=224	SARS-CoV-2 **-/Non-KTR** N=28103	P^1	P^2	P^3
Age	61.5 (55.5,65.5)	65 (51,79)	59.5 (47,67)	59 (37,74)	0.184	0.228	0.441
Female	14 (44%)	1611 (51%)	107 (48%)	16403 (58%)	0.438	0.670	0.094
Black	18 (56%)	825 (26%)	53 (24%)	4406 (16%)	<.001	<.001	<.001
BMI (kg/m^2)	28.2 (23.8,30.7)	28.5 (24.4,33.9)	27.9 (23.3,32.3)	28.3 (24.2,33.3)	0.434	0.927	0.581
Obesity	13 (41%)	1033 (32%)	87 (39%)	7552 (27%)	0.328	0.846	0.080
CHF	15 (47%)	697 (22%)	83 (37%)	5680 (20%)	0.001	0.285	<.001
Alcohol Abuse	3 (9%)	287 (9%)	20 (9%)	3700 (13%)	0.945	0.934	0.526
CPD	10 (31%)	1028 (32%)	69 (31%)	8894 (32%)	0.898	0.959	0.961
Baseline eGFR	37.4 (29.1, 58.1)	76.8 (51.6, 98.1)	31.5 (12.9, 53.5)	79.6 (56.3, 100.3)	<.001	0.068	<.001
Diabetes Mellitus	25 (78%)	1254 (39%)	129 (58%)	7335 (26%)	<.001	0.026	<.001
Hypertension	31 (97%)	2050 (64%)	218 (97%)	15099 (54%)	<.001	0.884	<.001
Liver Disease	12 (38%)	343 (11%)	68 (30%)	3846 (14%)	<.001	0.415	<.001
Malignancy	3 (9%)	360 (11%)	39 (17%)	4347 (15%)	0.730	0.251	0.341
Stroke	7 (22%)	207 (7%)	19 (8%)	1659 (6%)	0.001	0.019	<.001
Elixhauser Score	10 (8,13.5)	5 (2,9)	10 (7,13)	4 (1,8)	<.001	0.330	<.001
Length of Hospital Stay	10.2 (6.6, 25.7)	7.9 (4.1, 14.9)	4.8 (3.2, 8.2)	3.3 (2.1, 6.1)	0.011	<.001	<.001

BMI, body mass index; CHF, congestive heart failure; CPD, chronic pulmonary disease; KTR, kidney transplant recipient.
P-values were obtained using the Kruskal Wallis test. Values in red represent statistically significant differences.
P^1 tests the difference between SARS-CoV-2 positive KTR and SARS-CoV-2 positive non-KTR, P^2 tests the difference between SARS-CoV-2 positive KTR and SARS-CoV-2 negative KTR, P^3 tests the difference between SARS-CoV-2 positive KTR and SARS-CoV-2 negative non-KTR.

Table 2. Distribution of laboratory measurements among all groups

	Cases	**Controls**			**P-values**		
Median Laboratory Measurements	SARS-CoV-2 **+/KTR** N=32	SARS-CoV-2 **+/Non-KTR** N=3181	SARS-CoV-2 **-/KTR** N=224	SARS-CoV-2 **-/Non-KTR** N=28103	P^1	P^2	P^3
	Basic Metabolic Panel						
Sodium, meq/L	141 (138.8,142)	139 (137,141)	137.8 (135.5,140)	139 (136.5,140.5)	0.012	<.001	0.001
Potassium, meq/L	4.4 (3.9,4.6)	4 (3.8,4.3)	4.3 (3.9,4.6)	4 (3.8,4.3)	0.001	0.861	<.001
Chloride, meq/L	105.3 (102,107.8)	102.5 (100,105.5)	103 (99,106)	104 (101,106)	0.007	0.029	0.069
Bicarbonate, meq/L	21.5 (19.5,23.5)	24 (22,26)	21.8 (19.3,23)	24 (22,26)	<.001	0.832	<.001
BUN, mg/dL	40.8 (24.5,56)	17.5 (12,28)	34.8 (21,52)	15.5 (11,23)	<.001	0.413	<.001
Creatinine, mg/dL	2.1 (1.3,2.7)	0.9 (0.7,1.2)	2 (1.3,4.5)	0.9 (0.7,1.2)	<.001	0.304	<.001
Albumin, g/dL	3 (2.8,3.4)	3.2 (2.9,3.6)	3.5 (3.1,4)	3.5 (3.1,4)	0.153	<.001	<.001
	Complete Blood Count						
WBC, k/uL	5.7 (4.4, 8.1)	6.5 (4.9, 9.0)	7.6 (5.3, 10.9)	9.0 (6.8, 11.5)	0.205	0.049	<.001
Hemoglobin, g/dL	10.5 (8.6,12.2)	12 (10.4,13.3)	10.2 (8.8,11.8)	11.7 (10.2,13.1)	<.001	0.929	0.001
Platelets, k/uL	190.8 (161,248)	226 (173.5,293)	184 (132.8,232)	213 (167,265.5)	0.014	0.561	0.115
ALC, k/uL	0.7 (0.5,1)	1.2 (0.8,1.5)	0.7 (0.3,1.2)	1.5 (1.1,2)	<.001	0.520	<.001
ANC, k/uL	4.3 (2.6,6.1)	4.4 (3,6.7)	6 (3.9,8.8)	6.3 (4.4,8.7)	0.592	0.027	0.001
	Inflammatory Markers						
Ferritin, ng/mL	1412 (747.5,1748.5)	553 (256,1035)			<.001		
CRP, mg/dL	4.3 (1.6,11)	6.1 (1.9,11)			0.750		
hsCRP, mg/L	45.3 (14.3,92.3)	44.6 (13,86.3)			0.889		
D-dimer, ug/mL	1.7 (1,2.8)	1.2 (0.7,2.5)			0.074		

ALC, absolute lymphocyte count; ANC, absolute neutrophil count; BUN, blood urea nitrogen; CRP, c-reactive protein; hsCRP, high sensitivity c-reactive protein; KTR, kidney transplant recipients.

P-values were obtained using the Kruskal Wallis test. Values in red represent statistically significant differences.

P^1 tests the difference between SARS-CoV-2 positive KTR and SARS-CoV-2 positive non-KTR, P^2 tests the difference between SARS-CoV-2 positive KTR and SARS-CoV-2 negative KTR, P^3 tests the difference between SARS-CoV-2 positive KTR and SARS-CoV-2 negative non-KTR.

Table 3. Distribution of hospital complications among SARS-CoV-2 tested patients.

		Cases	**Controls**			**P-values**			
Hospital Complications	**Total** N=31540	SARS-CoV-2 **+/ KTR** N=32	SARS-CoV-2 **+/ Non-KTR** N=3181	SARS-CoV-2 **-/ KTR** N=224	SARS-CoV-2 **-/ Non-KTR** N=28103	P^1	P^2	P^3	$P^{Interaction}$
ICU admission	6287 (20%)	11 (34%)	766 (24%)	55 (25%)	5455 (19%)	0.176	0.235	0.033	0.372
Ventilation	1850 (6%)	11 (34%)	437 (14%)	20 (9%)	1382 (5%)	<.001	<.001	<.001	0.045
Vasopressor Use	3799 (12%)	13 (41%)	503 (16%)	37 (17%)	3246 (12%)	<.001	0.001	<.001	0.010
Acute kidney injury	2882 (9%)	15 (47%)	458 (15%)	51 (23%)	2358 (10%)	<.001	0.004	<.001	0.072
Inpatient Mortality	1317 (4%)	8 (25%)	498 (16%)	5 (2%)	806 (3%)	0.149	<.001	<.001	0.115

ICU, intensive care unit; KTR, kidney transplant recipient

P-values were obtained using the Kruskal Wallis test. Values in red represent statistically significant differences.

P^1 tests the difference between SARS-CoV-2 positive KTR and SARS-CoV-2 positive non-KTR, P^2 tests the difference between SARS-CoV-2 positive KTR and SARS-CoV-2 negative KTR, P^3 tests the difference between SARS-CoV-2 positive KTR and SARS-CoV-2 negative non-KTR, and $P^{Interaction}$ tests the interaction between SARS-CoV-2 and KTR status (a significant interaction p-value can be interpreted as the relationship between SARS-CoV-2 infection and outcome is significantly modified by kidney transplant status).

Table 4. Distribution of Coronavirus Disease 2019 Treatment

Treatment	Total N=3213	SARS-CoV-2 positive		P-value
		KTR N=32	Non-KTR N=3181	
Hydroxychloroquine	2136 (66%)	27 (84%)	2109 (66%)	0.031
Tocilizumab	1275 (40%)	21 (66%)	1254 (39%)	0.003
Methylprednisolone	611 (19%)	10 (31%)	601 (19%)	0.076
Remdesivir	309 (10%)	2 (6%)	307 (10%)	0.516
Azithromycin	618 (19%)	6 (19%)	612 (19%)	0.944

KTR, kidney transplant recipient
P-values were obtained using the Kruskal Wallis test. Values in red represent statistically significant differences.
Fischer exact test was used for comparison in cells with <5 participants.

Table 5. Maintenance immunosuppression among kidney transplant recipients with and without SARS-CoV-2 while inpatient

Immunosuppression	**Total** N=256	**Kidney transplant recipients**		**P-value**
		SARS-CoV-2 **Positive** N=32	SARS-CoV-2 **Negative** N=224	
Tacrolimus	195 (76%)	27 (84%)	168 (75%)	0.244
Belatacept	16 (6%)	2 (6%)	14 (6%)	1.00
Cyclosporine	12 (5%)	1 (3%)	11 (5%)	0.655
Sirolimus	7 (3%)	0 (0%)	7 (3%)	0.601
Everolimus	5 (2%)	0 (0%)	5 (2%)	1.00
Mycophenolate	152 (59%)	11 (34%)	141 (63%)	0.002
Azathioprine	14 (5%)	2 (6%)	12 (5%)	0.689
Steroids	219 (86%)	26 (81%)	193 (86%)	0.460

P-values were obtained using the Kruskal Wallis test. Values in red represent statistically significant differences. The Fischer exact test was used for comparison in cells with <5 participants.

Figure 1. Study flow diagram

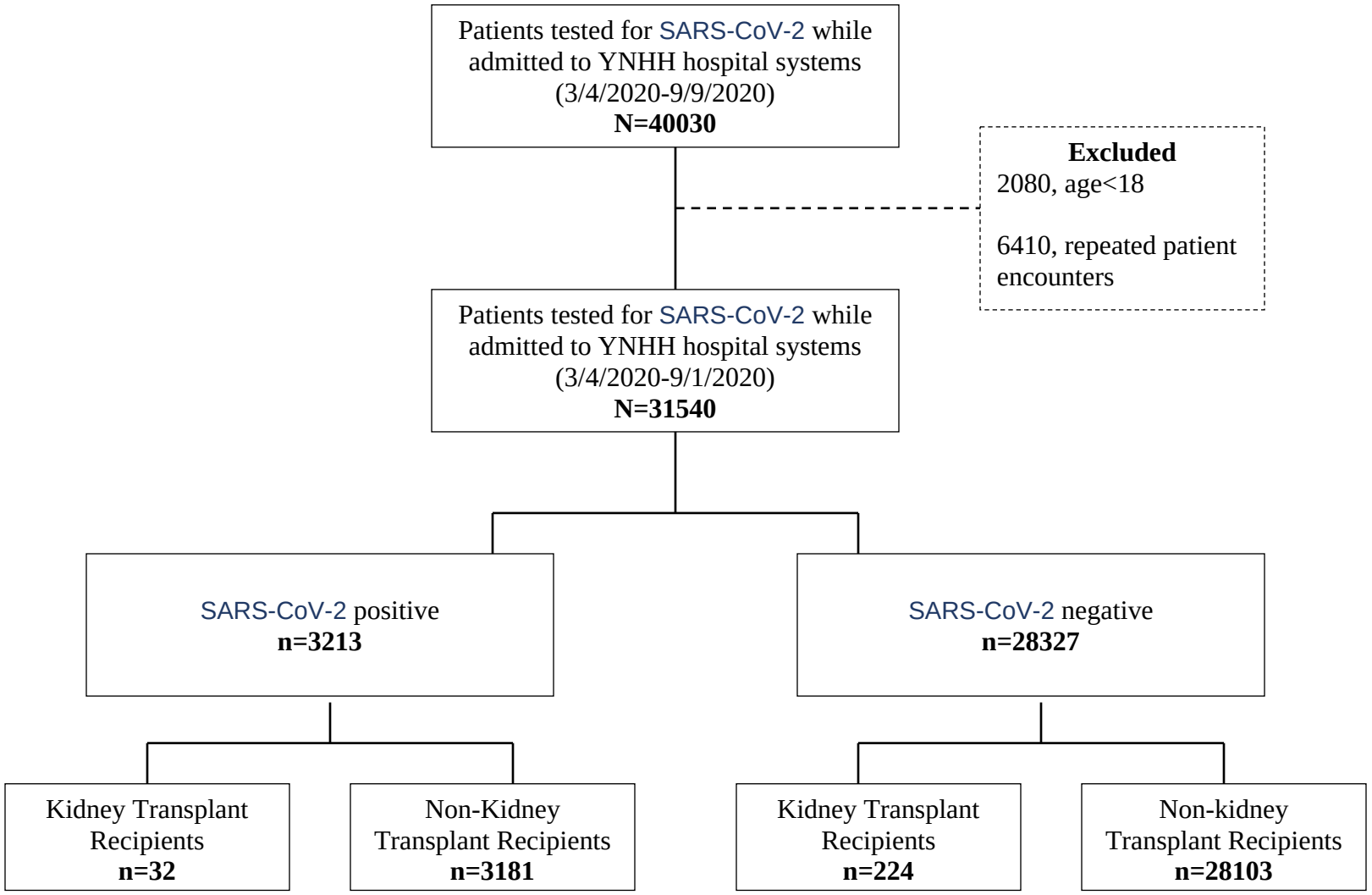
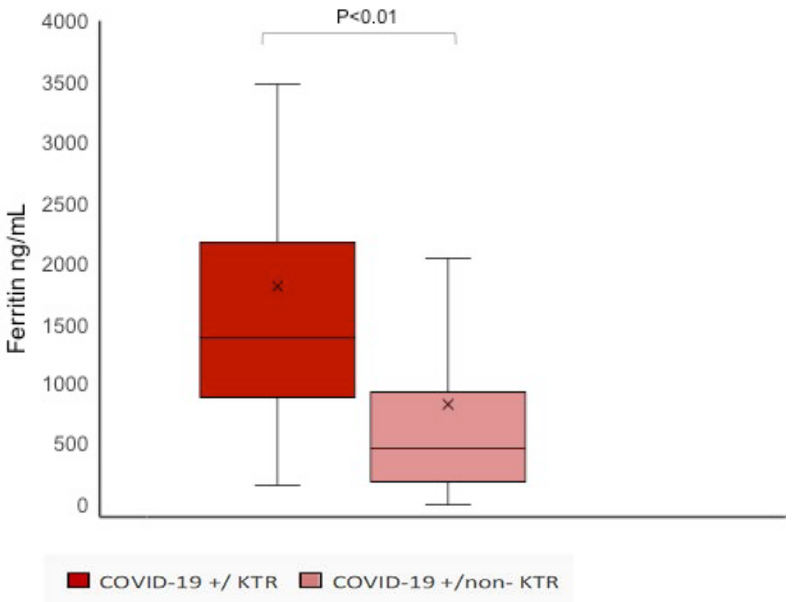
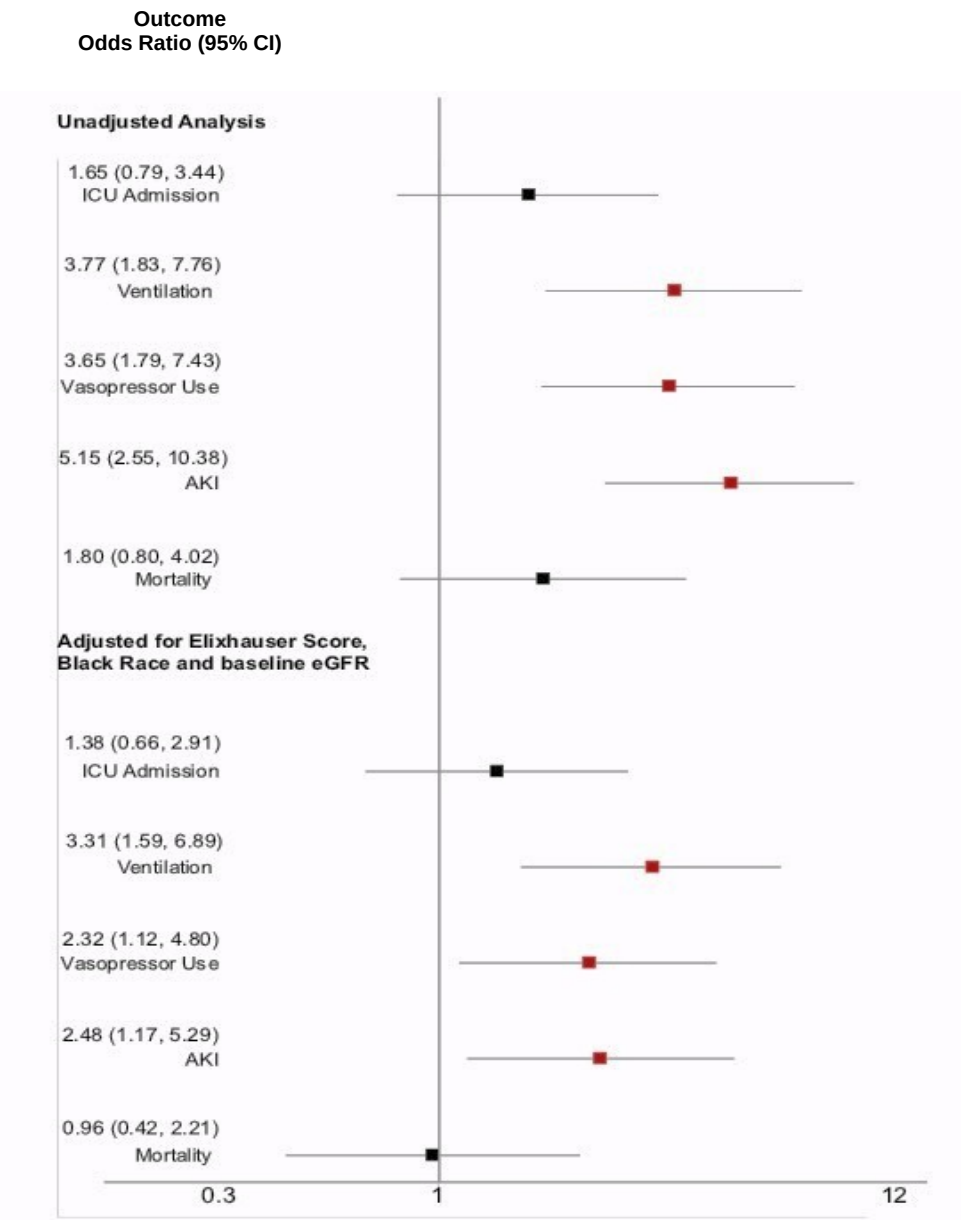


Figure 2. Distribution of ferritin among SARS-CoV-2 positive patients



Legend: SARS-CoV-2 positive KTR (represented in dark red) have significantly higher Ferritin levels compared to SARS-CoV-2 positive non-KTR (represented in light red). The above boxplot shows the mean, represented by the 'X'; median, represented by the horizontal line inside the box; interquartile range represented by the outer bounds of the box; minimum and maximum data points excluding outliers, represented by the whiskers.

Figure 3. Forest plot of the odds ratio of hospital complications in SARS-CoV-2 positive KTR as compared to SARS-CoV-2 positive non-KTR



The Odds Ratio (95% CI) of developing hospital complications in SARS-CoV-2 positive KTR and SARS-CoV-2 positive non-KTR

Legend: The above forest plot shows that SARS-CoV-2 positive KTR have significantly higher odds of mechanical ventilation, vasopressor use and acute kidney injury (AKI) independent of Elixhauser score, Black race and baseline eGFR. The squares represent the odds ratio and the lines represent the 95% confidence intervals. Significant associations are represented in red and non-significant associations are in black. The x-axis uses a logarithmic scale to the base of 10. The above associations are the unadjusted analyses and the bottom associations are adjusted for Elixhauser score, Black race and baseline eGFR.