

## Restarting living donor kidney transplant during COVID-19: a single center experience



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### ABSTRACT

**Background:** The decision to declare COVID-19 a pandemic in March 2020 turned the situation into a medical emergency that also affected the care and program for kidney transplants. Since it enhances patients' quality of life, kidney transplantation has been the only effective therapy option for people with end-stage renal disease (ESRD). While kidney transplants are extremely beneficial, there is still a significant risk of COVID-19 infection, particularly for recipients who must take immunosuppressive medications following the procedure.

**Purpose:** This study aimed to evaluate kidney transplant procedures in Dr. Sardjito General Hospital before and during the pandemic based on recipients' and donors' characteristics and laboratory findings such as creatinine and urine time.

**Patients and methods:** This study is designed as cross-sectional analytic research to evaluate 30 patients who underwent kidney transplants in Dr. Sardjito General Hospital before (April 2019-2020) and during (April 2020-2021) the COVID-19 era. Data analyses were carried out using SPSS version 25.0 and were served with simple charts and tables.

**Results:** There was a decrement in kidney transplant procedures before (n=16) and during (n=14) COVID-19. The recipients that underwent the most transplantation before the pandemic were 20-29 years old, while during the pandemic were 40-49 years old. There is no significant difference in length-of-stay before ( $12.0 \pm 4.17$  days) and during ( $9.29 \pm 3.73$  days) COVID-19 ( $p=0,077$ ). Laboratory findings such as creatinine of pre-transplantation ( $9.47 \pm 4.05$ ;  $7.81 \pm 6.00$ ) and 3 months post-transplantation ( $1,55 \pm 0,78$ ;  $1,15 \pm 0,67$ ) also did not show significant changes ( $p=0,153$ ) as well as urine time ( $245.60 \pm 225.55$ ;  $428.38 \pm 657.70$ ;  $p=0.321$ ).

**Conclusion:** In the COVID-19 era and prior, kidney transplant procedures declined at Dr. Sardjito General Hospital. There are no significant variations in duration of stay, creatinine levels before and three months after transplantation, or urine frequency. Overall, transplant results were comparable before and after the COVID-19 era.

**Keywords:** kidney transplantation, COVID-19, pandemic.

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### INTRODUCTION

SARS-CoV-2 is a virus belonging to the Coronaviridae family with flu-like symptoms and the potential for death. The virus primarily attacks the respiratory tract and can manifest with various symptoms, such as fever, cough, shortness of breath, tracheitis, bronchitis, and pneumonia, and can manifest in the digestive tract.<sup>1</sup>

Indonesia's first case of COVID-19 was declared on March 6, 2020. Based on data from the Indonesian government, there were 6,168,342 million confirmed positive cases; since the first case, the death rate reached 156,902 as of July 24, 2022.<sup>2</sup> The statement regarding the decision of COVID-19 as a pandemic in March 2020 became a public health emergency, including those related to the surgical process, one of which was in the

case of kidney transplantation, which in the process included patient evaluation, organ procurement and perseverance, surgery and post-transplant care, and management of immunosuppression on recipients.<sup>3</sup> There is no absolute indication for kidney transplantation; however, kidney transplantation is the definitive therapy in patients with end-stage renal disease (ESRD). About 13% of adults worldwide suffer from chronic kidney disease (CKD), while in Indonesia, according to Indonesian Ministry of Health the prevalence of CKD reaches 713,783 cases.<sup>4</sup>

Kidney transplant recipients have a high risk of suffering from severe to critical COVID-19 due to chronic immunosuppression and other coexisting conditions, furthermore, they have a significant risk of graft dysfunction and

death. Due to the immunosuppressed state after transplantation, recipients are more susceptible to viral infections and pneumonia. Strong information regarding the epidemiology, clinical, and management of COVID-19 in kidney transplant recipients is lacking and unclear.<sup>5,6</sup> Compared to other countries, kidney transplantation in Indonesia is still far behind, presumably due to the weak support of kidney transplant regulations in Indonesia, such as the absence of specific regulations on kidney transplants and donor bodies in the form of technical guidelines and regulatory guidelines for their implementation.<sup>7</sup>

In this study, researchers wanted to evaluate the impact of COVID-19 on the surgical process, especially in the urological surgery department of the kidney transplant at Dr. Sardjito General Hospital

Yogyakarta during the pre and after the release of the latest recommendations in the pandemic era. From this evaluation, the researcher hopes that this research can be a valuable resource for developing better recommendations in Indonesia's urology field.

## MATERIAL AND METHODS

This cross-sectional study with a retrospective analytic design was carried out in Dr. Sardjito General Hospital to evaluate the characteristics of patients who underwent kidney transplantation before and during the COVID-19 pandemic. We included 30 patients who underwent kidney transplantation from April 2019 to April 2021 and excluded patients outside of April 2019 to April 2021. We obtained the data for age, gender, biological relation of recipients and donor, and laboratory findings such as creatinine, urine time and ischemic time using the patient's medical record from the period before the pandemic from April 2019 to April 2020 and during the pandemic from April 2020 to April 2021. The data obtained were then processed using SPSS version 25.0 and Microsoft Excel. Descriptive statistical components, such as percentages, averages and standard deviations, were used to describe the data and then presented in tables and charts.

## RESULTS

Thirty kidney transplant surgeries were carried out in Dr. Sardjito General Hospital before and during the COVID-19 pandemic. A year before the epidemic, there were 16 kidney transplant surgeries, compared to 14 during the pandemic. According to Table 1's findings, the mean recipient age was 40 years old a year prior to the pandemic, with the highest prevalence occurring in the 20–29 age group (n=6, 37.5%), while the mean recipient age during the pandemic was 38 years old, with the highest prevalence occurring in the 40–49 age group (n=6, 42.9%). In the year prior to the pandemic, the mean donor age was 39 years old, with the highest prevalence occurring in the 30–39-year-old age group (n=6, 37.5%), while during the pandemic, the mean donor age was 42 years old, with

the highest prevalence occurring in the 40–49-year-old age group (n=6, 42.9%). Males made up the majority of recipients and donors both before and after the pandemic. A year before the pandemic, the recipient and donor's biological relationships were primarily unrelated (n=9, 56.25%). Similarly, the receiver and donor's biological relationship during the pandemic was largely unconnected (n=11, 78.6%).

According to Table 2, the average length of post-operative hospitalization for kidney transplant patients one year prior to the pandemic was 12.0±4.17 days, but it decreased to 9.29±3.73days during the pandemic. The patient's typical pre-transplant creatinine level was 9.47±4.05 mg/dL a year prior to the pandemic, but it dropped to 7.81±6.00 mg/dL during the epidemic. A year before the pandemic, the patient's 3-month post-transplant mean creatinine was 1.55 mg/dL, which also reduced to 1.15 mg/dL during the epidemic. Patients' mean 1<sup>st</sup> warm ischemic time decreased to 271.14±180.88 seconds during the epidemic from 274.67±206.34 seconds a year prior. Patients' mean cold ischemia times ranged

from 1919.47±806.67 seconds a year prior to the pandemic to 1572.64±624.272 seconds. The patients' mean 2nd warm ischemic time was 3284.47±808.323 seconds a year prior to the pandemic and 3284.47±808.323 seconds during the pandemic. Patients' mean total ischemia time reduced to 4672.14±959.954 seconds during the pandemic from 5478.60±1497.350 seconds on average a year earlier. Patients' mean pee times ranged from 245.60±225.55 seconds a year prior to the pandemic to 428.38±657.70 seconds. Even though each variable's mean fell, the drop was not statistically significant (p-value > 0.05).

## DISCUSSION

The transplant procedure has recently become challenging for surgeons and doctors due to the absence of information on kidney transplants during the COVID-19 pandemic. In this study, activity in the surgical protocol for kidney transplantation at Dr. Sardjito General Hospital is compared between the pre-COVID-19 (April 2019 to 2020) and COVID-19 eras (April 2020 to 2021).

**Table 1. Age, gender, and biological relation characteristic of kidney transplant procedure a year before pandemic and during pandemic in Dr. Sardjito General Hospital.**

Variable	n (%)	
	A Year Before COVID-19 (Mean = 40 years old)	During COVID-19 (Mean = 38 years old)
<b>Recipient's Age</b>		
20-29	6 (37.5)	4 (28.6)
30-39	2 (12.5)	2 (14.2)
40-49	2 (12.5)	6 (42.9)
50-59	4 (25)	2 (14.2)
60-69	2 (12.5)	0
<b>Recipient's Gender</b>		
Male	13 (81.25)	11 (78.6)
Female	3 (18.75)	3 (21.4)
<b>Donor's Age</b>	(Mean = 39 years old)	(Mean = 42 years old)
20-29	3 (18.75)	2 (14.2)
30-39	6 (37.5)	3 (21.4)
40-49	3 (18.75)	6 (42.9)
50-59	3 (18.75)	2 (14.2)
60-69	1 (6.25)	1 (7.1)
<b>Donor's Gender</b>		
Male	9 (56.25)	8 (57.1)
Female	7 (43.75)	6 (42.9)
<b>Biological Relation</b>		
Related	7 (43.75)	3 (21.4)
Unrelated	9 (56.25)	11 (78.6)

**Table 2. Length of stay and laboratory parameters of kidney transplant procedure a year before pandemic and during pandemic in Dr. Sardjito General Hospital.**

Variable	mean±SD		p-value
	A Year Before COVID-19	During COVID-19	
LOS Post-operation (days)	12.0±4.17	9.29±3.73	0.077
Cr Pre-transplantation (mg/dL)	9.47±4.05	7.81±6.00	0.387
Cr 3 Months Post-transplantation (mg/dL)	1.55±0.78	1.15±0.67	0.153
WIT 1 (seconds)	274.67±206.34	271.14±180.88	0.961
CIT (seconds)	1919.47±806.67	1572.64±624.272	0.209
WIT 2 (seconds)	3284.47±808.323	2828.36±517.09	0.084
Total Ischemic Time (seconds)	5478.60±1497.350	4672.14±959.954	0.098
Urine Time (seconds)	245.60±225.55	428.38±657.70	0.321

**Abbreviations:** LOS, length of stay; Cr, Creatinine; WIT, warm ischemic time; CIT, cold ischemic time.

### **Kidney Transplantation During COVID-19 Pandemic**

Although only 2 patients from before (n=16) compared to during the pandemic (n=14) underwent kidney transplant procedures less frequently overall. Like other nations, the United States also saw a 72% delay in living donor kidney transplant programs and a 76% drop in dead donor transplants.<sup>8,9</sup> According to the Italian survey, there has been a significant decrease in transplant procedures at every transplant facility nationwide, particularly in regions with a high percentage of positive COVID-19 patients.<sup>10</sup> The COVID-19 rate in Yogyakarta Special Region is relatively high, coming in sixth out of all Indonesian provinces.<sup>2</sup> This decrease occurred presumably because recipients preferred to delay until the lockdown regulation was over. In exchange, recipients were willing to continue dialysis, which was considered safer for that period.<sup>11</sup> The temporary delay in transplantation with living donors is supported by recommendations from around the world, especially for areas and cities with a high prevalence of COVID-19 and for recipients over 60 years of age.<sup>12</sup>

Fewer kidney transplant operations were performed during the COVID-19 pandemic. The doctor's judgment, the patient's decision, and other circumstances can all affect whether or not a kidney transplant is performed during the COVID-19 epidemic. The drop in kidney transplants during the pandemic can be attributed to the fluctuating surgical schedule of urology surgeons and the community's perception of the risks of COVID-19 which made people afraid to enter the hospital. Although it is well known that kidney transplantation can

improve patients' quality of life, it is thought that, at the time, the COVID-19 transmission and mortality risks did not outweigh the advantages of the transplant operation.

### **Risk of COVID-19 Infection in Kidney Transplant Recipients**

After a kidney transplant, infection is a frequent consequence, and respiratory tract infection is one of the most typical illnesses. The prognosis for transplant patients is typically worse than that of the general population. Furthermore, acute rejection in transplant recipients can be predicted by the molecular cross-reactivity of respiratory virus infections.<sup>1</sup> A prior study conducted during the 2009 influenza A pandemic revealed a correlation between the incidence of influenza A in the months immediately following kidney donation (H1N1).<sup>13</sup>

Immunosuppressive medications are required during and after kidney transplant procedures to lower the likelihood that transplanted organs will be rejected by suppressing the patient's immune response. However, their side effects during a pandemic can increase the risk of recipients contracting COVID-19 infection and, in the worst cases, result in severe illness or even death.<sup>11,14</sup>

According to a study on recipients of kidney transplants who tested positive for COVID-19, the treatment of COVID-19 involves reducing immunosuppressive medications (withdrawal of mycophenolate in 96% of cases and tacrolimus in 62.5%) as well as a combination of hydroxychloroquine, antivirals, and steroids. Interestingly, five of the eight patients who received

tocilizumab, an anti-IL-6 antibody, exhibited improvement.<sup>12</sup> Tocilizumab has also been used as a therapy for kidney transplant patients affected by COVID-19 since the pandemic's beginning.<sup>15</sup> Recent protocols for kidney transplantation during the pandemic indicate the need to reduce immunosuppressive therapy in symptomatic and asymptomatic patients.

### **Post-operative Hospitalization and Laboratory Parameters**

The present study showed that the typical length of post-operative hospitalization for kidney transplant patients reduced from 12 days to 9 days a year before and during the COVID-19 pandemic. This result is consistent with a meta-analysis study that demonstrates efforts to improve productivity and innovation in the perioperative management of kidney transplant procedures with an improved recovery pathway that can reduce post-operative hospitalization by an average of 2.35 days.<sup>16</sup>

Elevated creatinine is a hallmark of renal allograft rejection, although not specific. Decreased immunosuppression in kidney transplant recipients with COVID-19 may lead to an increased risk of rejection. It is important to investigate further other potential causes that cause an increase in creatinine.<sup>17</sup> In this study, the mean pre-transplant and 3-month post-transplant creatinine a year before the pandemic decreased when compared with the time during pandemic from 9.57 mg/dL to 7.81 mg/dL and 1.55 mg/dL to 1.15 mg/dL. It can be concluded that the kidney transplant procedure performed in this study did not show any rejection reaction based on the creatinine marker, however,

in order to improve the analysis of this data in the future, a multi-center study of pre and post covid era renal transplantation procedure need to be done.

## CONCLUSION

There was a decrement of kidney transplant procedure in Dr. Sardjito General Hospital within before and during the COVID-19 era. No significant differences were found within length-of-stay, creatinine pre and 3 months post-transplantation, and urine time. Overall, transplant outcomes have remained similar before and during the COVID-19 era.

## ETHICAL CONSIDERATIONS

The study was approved and declared ethical by the Ethics Committee of the Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada. Ethics committee approval number: KE/FK/1233/EC/2022.

## CONFLICT OF INTEREST

The author reports no conflicts of interest in this work.

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## AUTHOR CONTRIBUTIONS

MFZ designed the study and performed the measurements. TG was involved in planning and supervising the work.

MFZ processed the experimental data, performed the analysis, and drafted the manuscript. TG aided in interpreting the results and worked on the manuscript. All authors discussed the results and commented on the manuscript

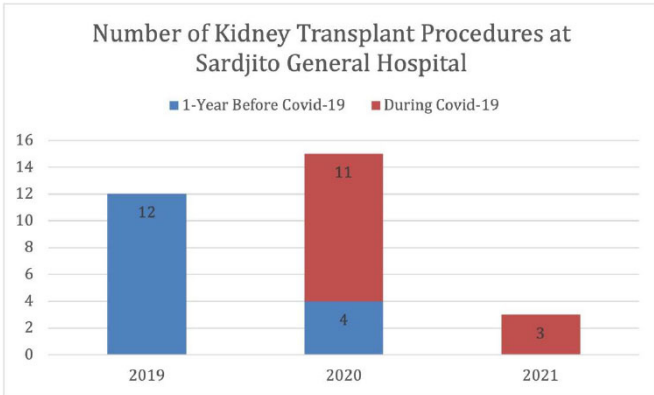
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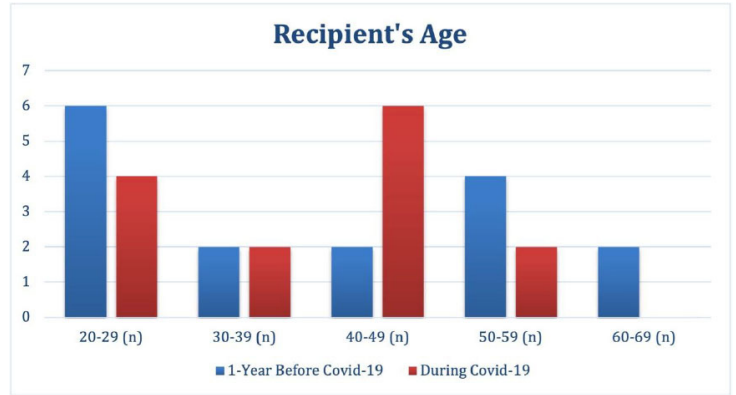


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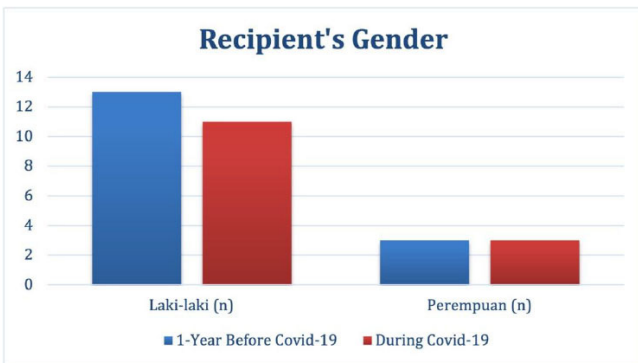




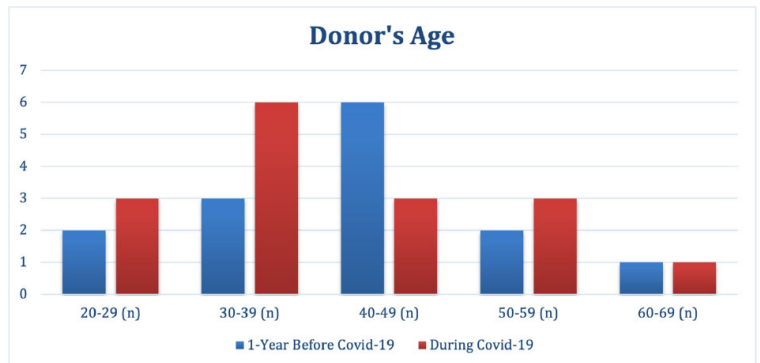
**Figure 1.** Number of kidney transplant procedure a year before pandemic and during pandemic at Dr. Sardjito General Hospital.



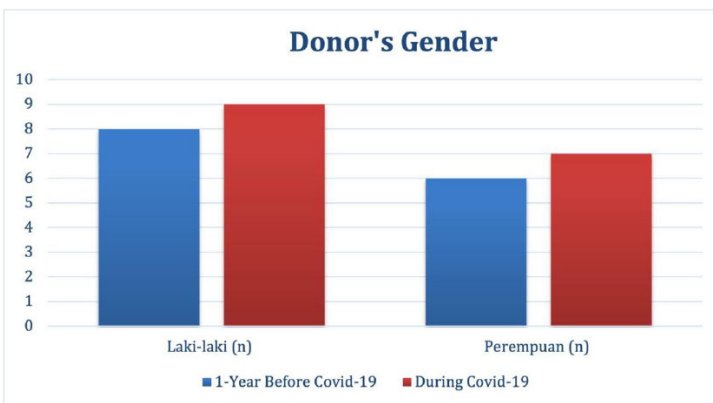
**Figure 2.** Recipient's age characteristic of kidney transplant procedure a year before pandemic and during pandemic at Dr. Sardjito General Hospital.



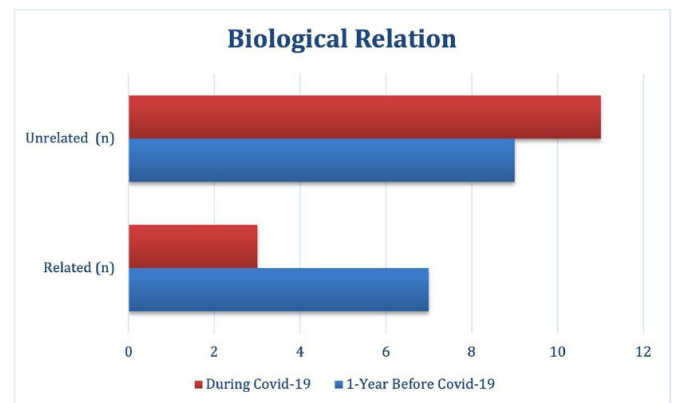
**Figure 3.** Recipient's gender characteristic of kidney transplant procedure a year before pandemic and during pandemic at Dr. Sardjito General Hospital.



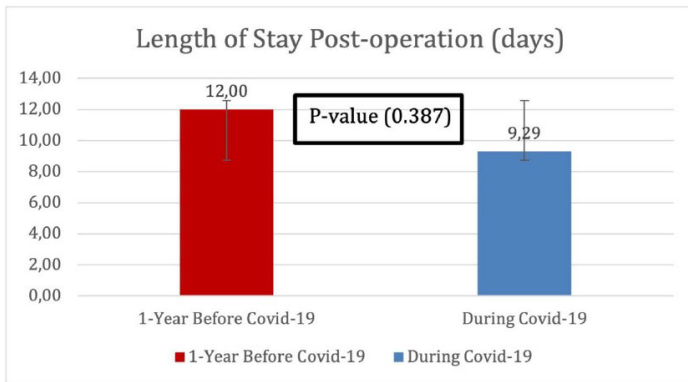
**Figure 4.** Donor's age characteristic of kidney transplant procedure a year before pandemic and during pandemic at Dr. Sardjito General Hospital.



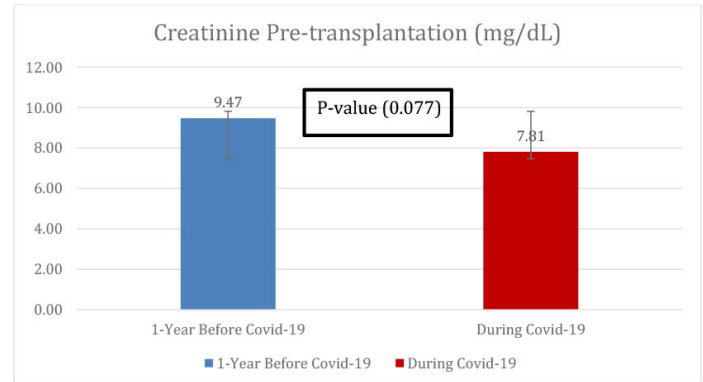
**Figure 5.** Donor's gender characteristic of kidney transplant procedure a year before pandemic and during pandemic at Dr. Sardjito General Hospital.



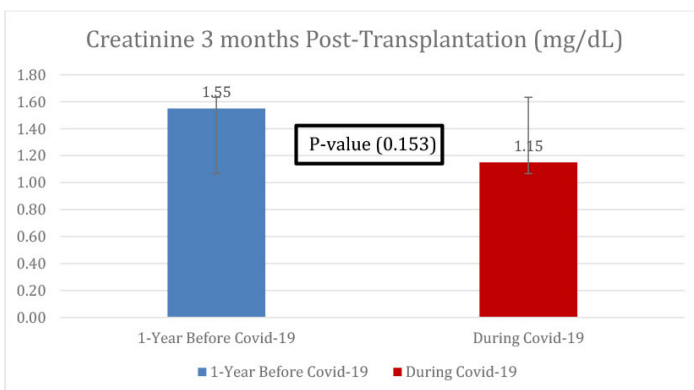
**Figure 6.** Biological relation characteristic of kidney transplant procedure a year before pandemic and during pandemic at Dr. Sardjito General Hospital.



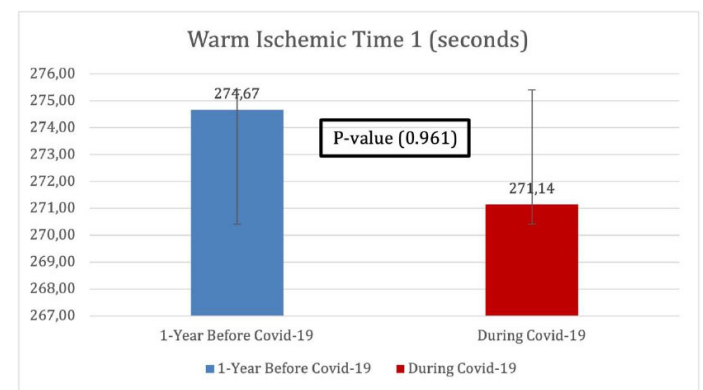
**Figure 7.** Length of stay post-operation characteristic of kidney transplant procedure a year before pandemic and during pandemic at Dr. Sardjito General Hospital.



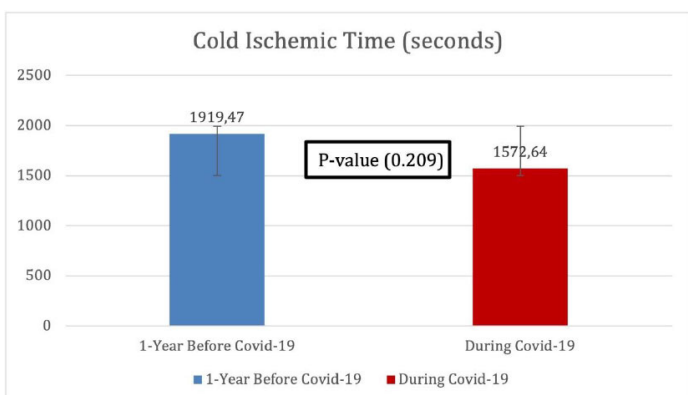
**Figure 8.** Creatinine pre-transplantation characteristic of kidney transplant procedure a year before pandemic and during pandemic at Dr. Sardjito General Hospital.



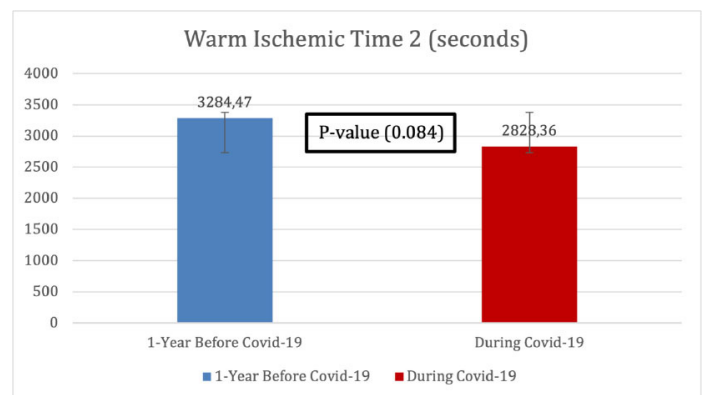
**Figure 9.** Creatinine 3 months post-transplantation characteristic of kidney transplant procedure a year before pandemic and during pandemic at Dr. Sardjito General Hospital.



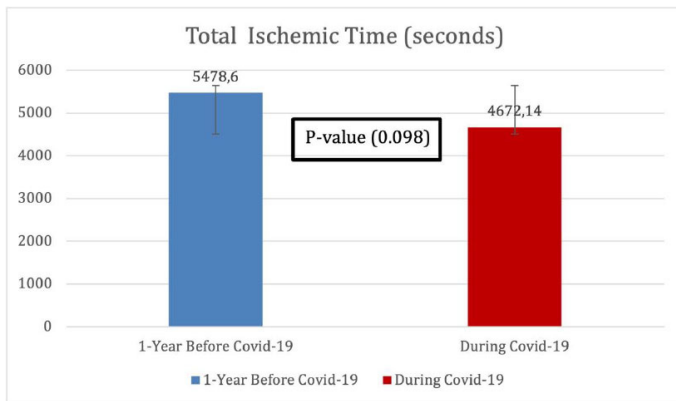
**Figure 10.** Warm ischemic time 1 characteristic of kidney transplant procedure a year before pandemic and during pandemic at Dr. Sardjito General Hospital.



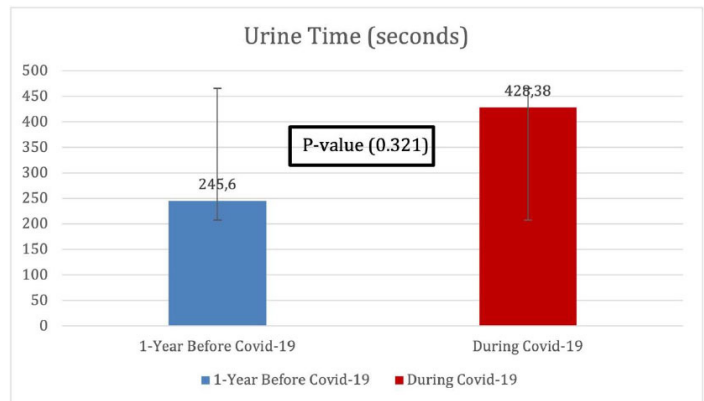
**Figure 11.** Cold ischemic time characteristic of kidney transplant procedure a year before pandemic and during pandemic at Dr. Sardjito General Hospital.



**Figure 12.** Warm ischemic time 2 characteristic of kidney transplant procedure a year before pandemic and during pandemic at Dr. Sardjito General Hospital.



**Figure 13.** Total ischemic time characteristic of kidney transplant procedure a year before pandemic and during pandemic at Dr. Sardjito General Hospital.



**Figure 14.** Urine time characteristic of kidney transplant procedure a year before pandemic and during pandemic at Dr. Sardjito General Hospital.