

**Evaluation of the Impact of Local Protocol of King Salman Specialized Hospital-KSA of Management of Renal Disease patients requiring Immunosuppressive Therapy Afflicted by Acute COVID 19 Infection – An Observational Study**

**ABSTRACT**

Context:

The new coronavirus disease 2019 (COVID-19) infection emerged in Wuhan city, China, in December 2019. COVID-19 could be associated with high morbidity and mortality in kidney transplant recipients.

Aims:

We aimed to observe the effect of modification of the immunosuppressive regimen in response to the severity of COVID-19 infection on the outcome of renal disease patients and to study factors affecting their mortality.

Methods and Material:

The study was conducted on eighteen patients who were admitted to the King Salman Specialized hospital (KSSH), a COVID-19 isolation center, in Hail city in KSA from February to October 2021. Of them, sixteen patients had kidney transplantation who were maintained on immunosuppression protocols. The other two patients had immune-mediated nephritis maintained on immunosuppression. Locally agreed protocol, regarding immunosuppressive protocol, the antiviral used as well as the used anticoagulant, was planned to be followed considering international guidelines for COVID 19 infection in immunosuppressed patients and Saudi MOH guidelines for the management of COVID 19 infection. Demographic data, associated comorbidities, baseline x-ray, and routine laboratory data were recorded. Patients' outcomes were also noted.

Results:

The studied eighteen patients (13 males and 5 females) had ages ranging from 23 - 60 years. and were divided into two groups; nine patients did not need admission to ICU (group 1) and the other group comprised

nine patients admitted to ICU (group 2) for deterioration of the chest condition to be able to achieve the target oxygen saturation. Of the sixteen transplanted patients, two of them presented with isolated gastrointestinal symptoms, and fourteen patients were presented with COVID-19 pneumonia

The four cases who received vaccination were not admitted to ICU. The frequency of mortality was much higher in group 2. Additionally, the highest level of TLC, CRP, and serum phosphorus was higher in group 2; furthermore, the lowest blood platelet, serum albumin levels and the lowest lymphocytic count were lower in the same group. Moreover, LDH at admission and the lowest D-dimer were higher in cases with ICU admission.

The highest and at discharge levels of CRP and LDH were higher in the deceased group while, the highest serum albumin was higher in the survived group.

#### Conclusions:

Appropriately early discontinuation of antiproliferative drugs of COVID 19 infection in renal immunosuppressed patients and the use higher doses of systemic steroids mainly dexamethasone were associated with better prognosis. Furthermore, discontinuation of antiproliferative drugs did not cause deterioration of kidney function. The inflammatory markers including CRP, LDH as well as low serum albumin, and high D-dimer were related to mortality in severe cases of COVID 19 infection. Isolated GI symptoms without the presence of respiratory symptoms have been observed in patients with COVID-19 and could be treated safely with symptomatic management.

***Keywords: COVID 19 infection, Kidney transplant patients, immunosuppressed patients, antiproliferative drugs, isolated gastrointestinal symptoms***

## 1. INTRODUCTION

The new coronavirus disease 2019 (COVID-19) infection, which emerged in Wuhan city, China, in December 2019, has close genomic structural similarities with the severe acute respiratory syndrome coronavirus (SARS-CoV) that caused the SARS pandemic in 2003 and the middle east respiratory syndrome coronavirus (MERS-CoV) that caused (MERS) epidemic in 2012 (Lu et al, 2020 and Wu et al, 2020). After that, it spread rapidly throughout the world, WHO declared this novel coronavirus a public health emergency of international concern (World Health Organization. Public Health Emergency of International Concern (PHEIC) WHO. Published online 2020:1–10). At the time of data collection, on February 1, 2021, infections related to

COVID-19 affected people from 210 countries were 103018643 reported cases worldwide and 368329 cases in KSA (Maggiore et al, 2020, Wang et al, 2020). The risk factors related to the outcomes of SARS-CoV-2 infections included old age, male gender, obesity, and associated co-morbidities (Aly et al, 2020).

COVID-19 could be associated with high morbidity and mortality in kidney transplant recipients. However, risk factors for COVID-19 disease in patients with kidney transplants remain poorly defined. Solid organ transplant recipients may be at increased risk for COVID-19 as they are immunosuppressed and are less likely to have an effective immune response to vaccination (Kantauskaite et al, 2022). According to the Scientific Registry of Transplant Recipients, currently 86% of renal transplant recipients receive MMF as part of their immunosuppressive regimen, most frequently in combinations with prednisone and tacrolimus (OPTN/SRTR Annual Report. Immunosuppression use for maintenance by regimen prior to discharge, 1997–2006 Recipients with kidney transplants. 2007. [accessed September 9, 2008]). MMF is an inhibitor of inosine-5-monophosphate and is able to preferentially inhibit B-cell and T-cell function (Ritter and Pirofski, 2009). Moreover, The Combined Immunosuppressive and Anti-inflammatory Effects of Dexamethasone were known (Li et al, 2017).

Treatment of COVID-19 particularly in solid organ transplant recipients is empirical and debatable, exclusively the adjustment of the immunosuppressants. Certain questions rushed about renal transplant recipients being infected by COVID-19 – does the infection will develop a poorer prognosis compared to those without an immunosuppressive agent? However, there are limited studies available comparing this population with the general population when infected with COVID 19 regarding clinical symptoms, and laboratory data as well as disease severity and clinical outcomes.

## 2. SUBJECTS AND METHODS

The study was conducted on eighteen patients who were admitted to the King Salman Specialized hospital (KSSH), a COVID-19 isolation center, in Hail city in KSA during the period of February to October 2021. Of them, sixteen patients had kidney transplantation and were maintained on immunosuppression protocol (OPTN/SRTR Annual Report. Immunosuppression use for maintenance by regimen prior to discharge, 1997–2006 Recipients with kidney transplants. 2007. [accessed September 9, 2008]) including calcineurin inhibitors (tacrolimus or cyclosporine), antiproliferative agents (mycophenolate mofetil {MMF} or azathioprine), and a small dose of oral prednisolone. The other two patients had immune-mediated nephritis maintained on immunosuppression. Locally agreed protocol, regarding immunosuppressive protocol, the antiviral used as well as the used anticoagulant, was planned between the treating team; Nephrology, Chest, and ICU consultants to be followed considering international guidelines for COVID 19 infection in immunosuppressed patients and Saudi MOH guidelines for the management of COVID 19 infection (MOH protocol, 21 Jan 2021). This management usually includes antiviral drugs, systemic steroids (dexamethasone 6-10 mg intravenously), anticoagulants, and antibiotics. Management of the studied patients was shared between nephrology, chest, and ICU consultants, according to the international guidelines for infection in immunosuppressed patients (Barlow et al, 2021). Soon after diagnosis, the immunosuppressive protocol was changed with strict instructions to discontinue the antiproliferative drugs, starting intravenous steroids by doses that were increased according to the severity of the chest condition or with an increased need for oxygen therapy, and continuing Tacrolimus with regular measurement of its trough level.

The antiviral therapy was used according to the severity of COVID 19 infection as follows: in mild cases with normal liver function, favipiravir 1800 mg twice for one day then 800 mg BID for 7-10 days, was given; while in severe and critical cases, a loading dose of Remdisivir 200 mg IV then 100 mg once daily for 5 days was used. Enoxaparin (LMWH)40 mg once daily was used as an anticoagulant in low-risk patients and 40 mg twice daily in high-risk patients. Unfractionated heparin (UFH) was used in cases with renal impairment. All the 18 cases were allowed to receive their routine medications for any associated comorbidities during their hospital stay unless contraindicated.

Demographic data, associated comorbidities, and routine laboratory data in addition to the D-dimer, serum ferritin, LDH as well as C-reactive protein of the studied patients were recorded. Imaging of the chest was done through baseline chest x-ray then follow up every 4-7 days and to be done urgently if there was any deterioration, while to be performed daily in cases admitted to ICU. CT chest was done in patients with a prolonged course to exclude post-COVID fibrosis. The protocol of management of every case was described. Patients' outcomes; namely, ICU admission, length of hospital stay, and mortality were also noted. When serial laboratory data were available, the highest and the lowest values, in addition to those at admission and at discharge were selected for statistical analysis.

#### Statistical Analysis:

After the collection of data, they were analyzed using the statistical package of social science (SPSS, IBM) software version 24. Categorical data were expressed as numbers and percentages and were analyzed by Fisher-exact tests. Scale data were expressed as means  $\pm$  SD or medians (IQR) and minimum & maximum as appropriate. Normality was tested using the Shapiro Wilkinson test. Parametric data were analyzed using the independent sample T-test, while the Mann-Whitney test was used to analyze non-parametric data as appropriate. P value was considered significant if it was  $< 0.05$ .

### 3. RESULTS

The studied eighteen patients had ages ranging from 23 - 60 years. They were 13 males and 5 females. The studied patients were divided into two groups; nine patients did not need admission to ICU (group 1) and the other group comprised nine patients admitted to ICU (group 2). Days of hospital stay ranged from 6-48 days. Fifty percent of the total studied group, six males and three females, were admitted to ICU because of deterioration of the chest condition while reaching to use an oxygen supply of up to 15 liters through a non-rebreathing face mask to achieve oxygen saturation of around 90 percent for the need to receive oxygen supply through high flow nasal cannula or non-invasive ventilation to be able to achieve the target oxygen saturation. The duration of transplantation of the studied sixteen transplanted patients ranged from 1.5 - 20 years. Two of them were presented by gastrointestinal symptoms and fourteen patients were presented with COVID-19 pneumonia.

Descriptive data of the studied group were shown in Tables (1-a, b) while, Tables 2-a, b and c showed comparisons between cases with and without ICU admission. The four cases that received vaccination were not admitted to ICU. Days of hospital admission were statistically significantly lower in patients admitted to ICU and the frequency of mortality was much higher in the same group. The highest level of TLC, CRP, and serum phosphorus was higher in group 2, furthermore, the lowest blood hemoglobin, the lowest platelet, and serum albumin levels were lower in the same group. Moreover, LDH at admission and the lowest D-dimer were higher in cases with ICU admission. Tables 3-a, b, and c showed comparisons between ICU cases according to fatality. Serum creatinine, blood urea nitrogen, and serum phosphorus were comparable on admission in all cases that admitted to ICU either passed away or were discharged alive. The previous parameters were higher at discharge in the expired group. The highest and at discharge levels of CRP and LDH were higher in the deceased group. In the reverse, the highest level of hemoglobin and serum albumin was higher in the survived group. Tables 4-a, b, and c showed descriptive, fate, management, and laboratory parameters of each case.

CASE number eight and twelve; renal transplant patients with COVID 19 infection presented by gastrointestinal symptoms; fever, abdominal pain, nausea and diarrhea. The two cases admitted to the hospital, showed COVID 19 swab positive. They had oxygen saturation more than 95% on room air and continued on their home medications with no intake of antiviral drugs, no change of immunosuppressive protocol, symptomatic management and multivitamins with hospital stay 6 and 7 days respectively.

Case number 14: she was a lupus female patient maintained on MMF and 15 mg prednisolone. She insisted to receive MMF from her immunosuppressive home medications (prescribed and received from her primary transplant center) with an increased dose of steroid to 10 mg dexamethasone till deterioration happened, at that time she was convinced to discontinue MMF but further deterioration had happened, she was artificially ventilated, had deteriorated renal function and started continuous renal replacement therapy (CRRT) for 72 hours and she received oral antiviral. Unfortunately, she passed away. Dexamethasone was given to 8 survivor patients at the dose of 10 mg and to 3 survivors at the dose of 6 mg while hydrocortisone was given to one survivor.

#### Case scenarios

#### ICU survivors (cases 1, 5, 9, 11, and 15)

Five cases were admitted to ICU with a severe presentation. Case 1, 52 years old Saudi male patient had hypertension, diabetes mellitus, chronic kidney disease, and renal transplantation three years ago. He presented to the emergency department with shortness of breath and fever and had been found with a COVID-19 positive swab. The patient was admitted directly to ICU due to respiratory distress, high oxygen requirement, and a picture of ARDS clinically and radiologically. non-invasive ventilation was started alternating with a high-flow nasal cannula. Case 5, and 9 were admitted first to the isolation ward as they were stable initially. However, after a few days, they were deteriorated with increased oxygen requirement and admitted to the intensive care unit to start non-invasive ventilation. Case 11; 51 y old female patient, known to be hypertensive, with a history of kidney transplant 8 years ago, admitted On 21 July with history of fever, cough for 2 days. On arrival, all vitals were stable apart from low blood pressure. The patient had a patch on her right lung in Chest x-ray, she was on room air; however, there was metabolic acidosis, with high creatinine 243. Also, there was electrolyte disturbance. After correction of electrolytes, acidosis, and low blood pressure, and starting our COVID 19 protocol, the patient was discharged 7 days after admission. However, on the 11th of August, the patient was readmitted to the intensive care unit by extensive pneumonia, shortness of breath, tachypnea, and desaturation. Non-invasive ventilation was started; the COVID swab was repeated and was still positive. In all cases, dexamethasone 10 mg IV was added. Discontinuation of MMF, and prednisolone, tacrolimus was continued with measuring trough level regularly. When gradual weaning from non-invasive ventilation happened and oxygen supply through a non-rebreathing mask started, then, the patient transferred back to the isolation ward until discharge. The patients were discharged with the following immunosuppressive protocol; prednisolone 40 mg once daily then, withdrawal by 5 mg weekly till 5 mg/day, and restarted MMF when prednisolone dose was 20 mg daily. Case 15; A 53y old male patient who was a known case of ANCA negative vasculitis, HTN, with positive COVID swab, complaining of shortness of breath and cough, admitted on 14th of August on 15 L O2 via non-rebreathing face mask; SPO2 was 89-90%. Non-invasive ventilation was initiated alternating with a high-flow nasal cannula. MRSA screen was positive for staph aureus, intravenous linezolid was started. Gradual weaning from O2 was done, on 13 September, and the patient was discharged on 2 L O2. The case 15 patient was maintained on 75 mg azathioprine and prednisolone that held and replaced by dexamethasone 10 mg intravenously till discharged on prednisolone 40 mg once daily with withdrawal by 5 mg weekly till 5 mg and restarted azathioprine when prednisolone 20 mg daily.

#### ICU mortality cases (Case 3, 7, 10):

Three cases of renal transplants passed away in the intensive care unit. One patient (case 3) was admitted first to the ward for 2 days, and then shifted to ICU due to deterioration of chest condition, with tachypnea, hypoxia SPO2 on 15L non-rebreathing face mask 90 - 91%. The other 2 cases (cases 7, and 10) were admitted directly to the intensive care unit due to respiratory distress, refractory hypoxemia, and picture suggesting adult respiratory distress syndrome on presentation. Our COVID 19 protocol was started in all cases. MMF was planned to be stopped in all cases but unfortunately, two of the three cases insisted to receive MMF

from immunosuppressive home medications (prescribed and received from her primary transplant center) for 2-3 day still they became convened to stop it. Dexamethasone 10 mg intravenously was added. All three patients deteriorated with no response to non-rebreathing ventilation and a high-flow nasal cannula. So, the endotracheal tube was inserted with deterioration of the general condition of the three cases. Septic shock had complicated the course. Tacrolimus was discontinued after the Multidisciplinary meeting decision in the 3 cases; however. Kidney function tests deteriorated after the discontinuation of tacrolimus but not to the level necessitating renal replacement therapy. After few days, the patients expired.

Less severe cases (cases 2, 4,6, 13, 16, 17, 18):

Those patients presented with cough, fever, and shortness of breath. Two of them (case 2, 9) were maintaining required oxygen saturation on room air. Other cases were initially maintained on 2-4 L O<sub>2</sub>, most of them had a stationary course. However, for case 18, he was presented late with high O<sub>2</sub> requirements. In all, our protocol for COVID 19 was started, and adjustment of immunosuppressive therapy was done. They were not admitted to the intensive care unit and were discharged home after improvement. In all cases, Remdesivir and dexamethasone 10 mg intravenously were added. MMF and prednisolone were held, and tacrolimus was continued by measuring trough level regularly. With the improvement of the patients, gradual weaning from oxygen was started, and discharged on prednisolone 40 mg once daily with withdrawal by 5 mg weekly till 5 mg and restarted MMF when prednisolone 20 mg daily.

**Table (1): Descriptive data of the studied group**

		<b>n</b>	<b>%</b>
<b>Sex</b>	<i>Female/ Male</i>	5/13	27.8/72.2
<b>COVID 19 presentation</b>	<i>chest symptoms</i>	16	88.9
	<i>GIT symptoms</i>	2	11.1
<b>DM</b>		8/18	44.4
<b>HTN</b>		13/18	72.2
<b>IHD</b>		2/18	11.1
<b>Fate of the patient</b>	<i>Improved</i>	14	77.8
	<i>Died</i>	4	22.2
<b>Antiviral drugs used</b>	<i>no antiviral taken</i>	4	22.2
	<i>Oral antiviral</i>	6	33.3
	<i>IV antiviral</i>	5	27.8
	<i>oral and iv antiviral</i>	3	16.7
<b>Anticoagulant used</b>	<i>LMWH</i>	16	88.9
	<i>UFH</i>	2	11.1
<b>COVID 19 swab at discharge</b>	<i>Negative</i>	11	61.1
	<i>Positive</i>	7	38.9
<b>Transplantation/Nephritis</b>		16/2	88.9/11.1
<b>Previous COVID Vaccination</b>	<i>No</i>	13	76.5
	<i>One dose</i>	3	17.6
	<i>Two doses</i>	1	5.9

**Table 2-a: Comparison between cases with and without ICU admission:**

		<b>ICU Admission</b>				<b>p</b>
		<b>Group 1</b>		<b>Group 2</b>		
		<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	
<b>Sex</b>	Female	2	22.2%	3	33.3%	<b>1.000</b>
	Male	7	77.8%	6	66.7%	
<b>Covid Presentation</b>	Chest symptoms	7	77.8%	9	100.0%	<b>0.471</b>
	GIT symptoms	2	22.2%	0	0.0%	
<b>DM</b>	Yes	4/9	44.4%	4/9	44.4%	<b>1.000</b>
<b>HTN</b>	Yes	7/9	77.8%	6/9	66.7%	<b>1.000</b>
<b>IHD</b>	Yes	1/9	11.1%	1/9	11.1%	<b>1.000</b>
<b>Kidney Transplantation</b>	Yes	9/9	100.0%	7/9	77.8%	<b>0.471</b>

<b>Fate of the Patient</b>	Improved	9	100.0%	5	55.6%	<b>0.082</b>
	Died	0	0.0%	4	44.4%	
<b>Renal function Deterioration</b>	Stable	8	88.9%	5	55.6%	<b>0.294</b>
	Deterioration without need for RRT	1	11.1%	3	33.3%	
	Need for RRT	0	0.0%	1	11.1%	
<b>Antiviral drugs used</b>	No drug taken	2	22.2%	2	22.2%	<b>0.389</b>
	Oral	4	44.4%	2	22.2%	
	IV	3	33.3%	2	22.2%	
	Oral and iv	0	0.0%	3	33.3%	
<b>A anticoagulant used</b>	Heparin	1	11.1%	1	11.1%	<b>1.000</b>
	Clexan	8	88.9%	8	88.9%	
<b>Covid 19 swab at Discharge</b>	Negative	5	55.6%	6	66.7%	<b>1.000</b>
	Positive	4	44.4%	3	33.3%	
<b>CKD</b>	With kidney transplant	9	100.0%	7	77.8%	<b>0.471</b>
	With autoimmune disease.	0	0.0%	2	22.2%	
<b>Vaccination</b>	No dose	5	55.6%	9	100.0%	<b>0.135</b>
	One dose	3	33.3%	0	0.0%	
	Two doses	1	11.1%	0	0.0%	

\*p value was measured using Fisher-Exact test

**Table 2-b: Comparison between cases with and without ICU admission**

	n	Mean±SD	Median (Q1-Q3)	p
<b>Duration of Kidney Transplantation</b>	9	9.83±6.61	10.00 (3.0-16.0)	0.262
	7	8.71±7.06	7.0 (3.0-17.0)	
<b>Days of hospital stay</b>	9	10.67±4.00	11.00 (7.00-13.50)	0.010
	9	25.67±13.40	25.00 (15.00-37.00)	
<b>Weight kg</b>	9	85.17±19.02	82.00 (75.00-89.00)	0.605
	9	80.28±20.29	85.00 (62.50-95.50)	
<b>BMI</b>	9	30.23±8.19	29.73 (24.23-34.23)	0.648
	9	28.66±5.93	29.76 (22.96-32.76)	

\*P value was computed using T test

\*First row represent group 1 \*Second row represent group 2

**Table (2-c): Comparisons between with group1 and group 2**

	n	Mean	SD	Median	IQ		p
					Q1	Q3	
<b>Hb at admission</b>	8	13.04±2.3		12.5	11.67	15.57	0.963
	9	12.97±2.78		13.7	10	15.1	
<b>Hb the lowest</b>	8	10.78±3.15		11.55	8.77	13.6	0.021
	9	7.45±2.14		8.7	5.4	9.25	
<b>TLC the highest</b>	8	9.8±3.1		10.6	7.7	12.3	0.056
	9	16.3±8.4		17.4	8.9	22.6	

<b>TLC the lowest</b>	8	5.1±2.0	4.6	3.4	6.8	0.106
	9	3.7±1.4	3.7	2.4	4.8	
	9	173.0±66.4	174.0	132.5	212.0	
<b>Platelet the highest</b>	8	354.1±193.5	303.0	210.8	535.3	0.638
	9	319.3±94.6	298.0	218.0	423.0	
<b>Platelet the lowest</b>	8	222.8±159.7	188.5	123.8	223.8	0.08
	9	121.4±28.1	125.0	108.0	142.5	
<b>Lymph number at admission</b>	9	0.6±0.3	0.5	0.4	0.9	0.986
	8	0.6±0.2	0.6	0.5	0.8	
<b>Lymph number at discharge</b>	8	0.6±0.4	0.5	0.4	0.6	0.536
	9	0.7±0.5	0.7	0.3	1.2	
<b>Lymph number the highest</b>	8	0.8±0.3	0.8	0.5	0.9	0.323
	9	1.0±0.4	1.1	0.6	1.3	
<b>Lymph number the lowest</b>	8	0.35±0.19	0.33	0.21	0.53	0.360
	9	0.28±0.24	0.18	0.14	0.46	
<b>D.dimer at admission</b>	7	0.9±0.8	0.4	0.2	1.6	0.9
	9	0.9±0.7	0.6	0.5	1.5	
<b>D.dimer the highest</b>	3	1.3±1.7	0.5	0.2		0.278
	9	13.0±17.1	6.6	1.8	19.9	
<b>D.dimer the lowest</b>	3	0.2±0.1	0.2	0.1		0.059
	9	0.7±0.4	0.6	0.4	1.0	
<b>CRP at admission</b>	5	3.1±2.9	1.9	1.1	5.6	0.194
	9	10.5±11.7	6.7	3.9	11.7	
<b>CRP at discharge</b>	2	3.2±2.9	3.2	1.1		0.291
	7	17.4±16.7	9.9	3.0	37.9	
<b>CRP the highest</b>	2	5.0±4.3	5.0	1.9		<b>0.018</b>
	7	24.8±14.5	18.6	11.3	39.7	
<b>LDH at admission</b>	2	158.5±71.4	158.5	108.0		<b>0.054</b>
	9	316.7±93.6	320.0	225.0	395.0	
<b>S. ferritin at admission</b>	3	971.4±694.4	1002.0	262.3		0.382
	5	602.0±435.8	376.2	303.5	1013.5	
<b>INR the highest</b>	8	1.6±1.1	1.2	1.1	1.4	0.258
	5	1.2±0.1	1.2	1.1	1.4	
<b>Creatinine the highest</b>	9	164.9±82.0	137.0	116.4	195.2	0.197
	9	271.4±222.6	210.6	119.5	315.0	
<b>Creatinine the lowest</b>	9	106.3±37.1	104.1	78.7	111.0	0.86
	9	101.7±68.4	81.0	61.1	125.1	
<b>BUN the highest</b>	9	14.5±6.8	16.5	7.5	17.8	0.136
	9	22.0±12.7	16.4	9.8	35.0	
<b>BUN the lowest</b>	9	8.5±4.8	6.5	4.8	12.8	0.982
	9	8.4±5.2	5.3	4.4	14.1	

<b>K the highest</b>	9	5.4±1.1	5.2	4.5	6.1	0.885
	9	5.5±0.4	5.6	5.1	5.7	
<b>K the lowest</b>	9	3.8±0.5	3.5	3.4	4.3	0.707
	9	4.0±1.2	4.0	3.1	4.2	
<b>Phosphorus the highest</b>	7	1.2±0.2	1.2	1.0	1.3	<b>0.007</b>
	9	1.8±0.6	2.0	1.3	2.3	
<b>Phosphorus the lowest</b>	7	0.8±0.2	0.8	0.6	0.9	0.736
	9	0.8±0.4	0.6	0.5	1.1	
<b>Ca at admission</b>	8	2.1±0.2	2.1	2.0	2.3	<b>0.033</b>
	9	2.0±0.1	2.0	1.9	2.1	
<b>Ca at discharge</b>	9	2.1±0.2	2.2	2.0	2.2	0.547
	9	2.1±0.2	2.1	2.0	2.2	
<b>Ca the highest</b>	8	2.0±0.2	2.0	1.8	2.1	0.092
	9	1.7±0.3	1.8	1.5	1.9	
<b>Albumin the highest</b>	8	32.1±7.6	29.4	25.6	41.2	0.975
	9	32.2±4.6	33.0	29.0	35.5	
<b>Albumin the lowest</b>	8	25.3±3.8	25.6	22.0	26.7	<b>0.035</b>
	9	21.9±2.2	22.4	20.0	23.5	

P value was measured using T test or Mann-Whitney test as appropriate.

\*First row represent group 1 \*Second row represent group 2

**Table 3-a: Comparisons between ICU cases according to fatality**

		Outcome of the patients				P
		Survived		Died		
		n	%	n	%	
<b>DM</b>	No	3	60.0%	2	50.0%	1
	Yes	2	40.0%	2	50.0%	
<b>HTN</b>	No	1	20.0%	2	50.0%	0.524
	Yes	4	80.0%	2	50.0%	
<b>IHD</b>	No	5	100.0%	3	75.0%	0.444
	Yes	0	0.0%	1	25.0%	
<b>Mode of death</b>	0	5	100.0%	0	0.0%	0.008
	With no indication to dialysis	0	0.0%	3	75.0%	
	With indication to dialysis	0	0.0%	1	25.0%	
<b>State of kidney function</b>	Stable	5	100.0%	1	25.0%	0.286
	With deteriorated kidney function	0	0%	2	50.0%	
	deterioration up to dialysis (Started CRRT)	0	0.0%	1	25.0%	
<b>Antiviral drugs used</b>	No drug taken	1	20.0%	1	25.0%	0.524
	Oral	0	0.0%	2	50.0%	
	IV	2	40.0%	0	0.0%	
	Oral and iv	2	40.0%	1	25.0%	

<b>Anticoagulant used</b>	Clexane	5	100.0%	3	75.0%	0.444
	Heparin	0	0.0%	1	25.0%	
<b>Covid 19 swab at discharge</b>	0	4	80.0%	2	50.0%	0.524
	1	1	20.0%	2	50.0%	
<b>CKD with</b>	Transplant	4	80.0%	3	75.0%	1
	autoimmune disease.	1	20.0%	1	25.0%	

P value was computed by Fisher-Exact test

**Table (3-b): Comparisons between ICU cases according to fatality**

<b>Fate of the patient</b>					<b>P</b>
<b>Age Mean±SD</b>	Improved	5		43.6±12.8	0.232
	Died	4		53.3±7.9	
<b>Duration of Kidney Transplantation Mean±SD</b>	Improved	4		5.0±2.9	0.11
	Died	3		13.7±8.5	
<b>Days of hospital stay Mean±SD</b>	Improved	5		31.6±15.5	0.147
	Died	4		18.3±5.3	
<b>Days of ICU Admission Mean±SD</b>	Improved	5		7.6±4.7	0.093
	Died	4		15.8±7.9	
<b>weight/kg Mean±SD</b>	Improved	5		77.7±26.8	0.696
	Died	4		83.5±10.7	
<b>Hb at discharge Mean±SD</b>	Improved	5		12.3±2.9	0.054
	Died	4		8.65±1.25	
<b>Hb the lowest Mean±SD</b>	Improved	5		6.9±2.4	0.624
	Died	4		8.1±1.95	
<b>TLC the worst high Mean±SD</b>	Improved	5		14.2±6.3	0.417
	Died	4		19.1±10.8	
<b>TLC the worst low Mean±SD</b>	Improved	5		3.9±0.9	0.660
	Died	4		3.4±2.0	
<b>Platelet at admission Median (Q1-Q3/ Min-Max)</b>	Improved	5	15.00 (127.5-271.0)	124.0-384.0	0.413
	Died	4	144.0 (148.0-195.75)	140.0-202.00	
<b>Platelet the lowest Mean±SD</b>	Improved	5		130.8±19.6	0.294
	Died	4		109.8±35.6	
<b>Lymph number at admission Mean±SD</b>	Improved	4		0.7±0.3	0.651
	Died	4		0.6±0.1	
<b>Lymph number at discharge Mean±SD</b>	Improved	5		0.9±0.4	0.215
	Died	4		0.5±0.4	
<b>Lymph number the highest Mean±SD</b>	Improved	5		1.1±0.4	0.433
	Died	4		0.8±0.4	
<b>Lymph number the lowest Mean±SD</b>	Improved	5		0.4±0.3	0.128
	Died	4		0.1±0.1	
<b>CRP at admission Mean±SD</b>	Improved	5		12.1±16.0	0.681
	Died	4		8.5±3.8	
<b>CRP at discharge Mean±SD</b>	Improved	4		7.8±8.1	0.072
	Died	3		30.1±17.6	

<b>CRP the highest</b> Mean±SD	Improved	4	20.5±13.2		0.414
	Died	3	30.5±16.8		
<b>LDH at admission</b> Mean±SD	Improved	5	306.0±96.2		0.729
	Died	4	330.0±103.0		
<b>LDH at discharge</b> Mean±SD	Improved	5	241.4±46.1		0.01
	Died	3	465.0±127.5		
<b>LDH the highest</b> Mean±SD	Improved	5	321.6±75.0		0.036
	Died	3	572.7±193.3		
<b>LDH the lowest</b> Mean±SD	Improved	5	215.6±38.1		0.036
	Died	3	343.7±99.6		
<b>S. ferritin at admission</b> Mean±SD	Improved	2	1013.5±433.5		0.06
	Died	3	327.7±60.4		
<b>S. ferritin at discharge</b> Mean±SD	Improved	1	1116.9		0.801
	Died	3	901.6±650.6		
<b>S. ferritin the highest</b> Mean±SD	Improved	2	1087.5±328.8		0.97
	Died	3	1070.3±507.2		
<b>S. ferritin the lowest</b> Mean±SD	Improved	2	912.0±289.8		0.180
	Died	3	298.4±110.4		
<b>INR the highest</b> Mean±SD	Improved	5	1.5±0.3		0.474
	Died	3	2.3±1.7		
<b>Creatinine at admission</b> Mean±SD	Improved	5	151.4±74.9		0.954
	Died	4	147.7±81.3		
<b>Creatinine at discharge</b> Mean±SD	Improved	5	98.4±37.9		0.193
	Died	4	365.6±319.4		
<b>Creatinine the highest</b> Mean±SD	Improved	5	174.3±89.7		0.154
	Died	4	392.8±293.4		
<b>Creatinine the lowest</b> Median (Q1-Q3)/ Min-Max	Improved	5	9.89 (47.64-125.07)	41.03-159.48	0.462
	Died	4	70.9 (71.25-218.01)	68.0-261.07	
<b>BUN at admission</b> Mean±SD	Improved	5	7.6±3.5		0.981
	Died	4	7.7±5.2		
<b>BUN at discharge</b> Mean±SD	Improved	5	8.3±5.0		0.003
	Died	4	31.6±10.8		
<b>BUN the highest</b> Mean±SD	Improved	5	14.3±8.4		0.028
	Died	4	31.7±10.6		
<b>BUN the lowest</b> Median (Q1-Q3)/ Min-Max	Improved	5	84.91 (3.27-10.77)	2.58-16.47	0.190
	Died	4	4.92 (6.23-14.52)	5.25-14.91	
<b>K the highest</b> Mean±SD	Improved	5	5.5±0.5		0.959
	Died	4	5.5±0.3		
<b>K the lowest</b> Mean±SD	Improved	5	4.4±1.4		0.288
	Died	4	3.5±0.7		
<b>K at discharge</b> Median (Q1-Q3)/ Min-Max	Improved	5	4.09 (3.55-4.52)	3.42-4.70	0.063
	Died	4	5.59 (4.62-5.68)	4.30-5.70	
<b>Mg at admission</b> Mean±SD	Improved	5	0.7±0.2		0.355
	Died	4	0.6±0.1		
<b>Mg at discharge</b> Mean±SD	Improved	5	0.8±0.2		0.037
	Died	4	1.0±0.1		

<b>Mg the worst high</b> Median (Q1-Q3)/ Min-Max	Improved	5	0.98 (0.97-1.17)	0.95-1.31	0.413
	Died	4	1.11 (0.98-1.29)	0.95-1.33	
<b>PO4 at admission</b> Median (Q1-Q3)/ Min-Max	Improved	5	0.96 (0.84-1.38)	0.81-1.74	0.905
	Died	4	1.04 (0.74-1.38)	0.71-1.43	
<b>PO4 the highest</b> Mean±SD	Improved	5	1.5±0.4		0.01
	Died	4	2.3±0.3		
<b>Phosphorus the lowest</b> Mean±SD	Improved	5	0.8±0.3		0.799
	Died	4	0.8±0.4		
<b>Ca the highest</b> Mean±SD	Improved	5	2.3±0.1		0.17
	Died	4	2.1±0.1		
<b>Ca the lowest</b> Mean±SD	Improved	5	1.8±0.2		0.2
	Died	4	1.6±0.4		
<b>Ca at discharge</b> Median (Q1-Q3)/ Min-Max	Improved	5	2.16 (2.15-2.25)	2.13-2.26	0.016
	Died	4	2.01 (1.65-2.04)	1.54-2.04	
<b>Albumin the highest</b> Mean±SD	Improved	5	34.7±2.9		0.066
	Died	4	29.1±4.8		
<b>Albumin the lowest</b> Mean±SD	Improved	5	23.2±0.8		0.097
	Died	4	20.3±2.5		
<b>BMI</b> Mean±SD	Improved	5	26.8±6.5		0.311
	Died	4	31.0±4.9		

P value was measured using T-test and Mann-Whitney test as appropriate

**Table (4-a): clinical and the protocol of management of individual cases**

	Gender	Age	Duration of Kid Tran	Total Length of stay	ICU	ICU Length of stay	Fate of the patient	Immunosuppressive protocol during	The antiviral used	BMI	anti-coagulant	LATE PRESENTATION TO THE HOSPITAL
Case 1	Male	52	3.0	46	Yes	15	Improved	dexamethazone 6 mg then 10 mg +tacrolimus	IV	34.29	Enoxaparin	
Case 2	Male	37	2.0	7	No		Improved	hydrocortisone 50mg/12 hours +tacrolimus	IV	26.12	Enoxaparin	After 2 days
Case 3	Female	51	17.0	14	Yes	12	Died	dexsmesathone 10 after 5 days of admission to icu hydrocortisone 80mg /12 hours +tacrolimus stopped in the last 3 days	Oral + IV	37.50	Enoxaparin	After 5 days
Case 4	Female	40	10.0	14	No		Improved	hydrocortisone 50mg /6h then dexamethasone 6mg 3 days	IV	22.34	Enoxaparin	
Case 5	Male	39	7.0	11	Yes	6	Improved	dexamethazone 6mg +tacrolimus	IV	31.02	Enoxaparin	
Case 6	Male	50	6.0	13	No		Improved	dexamethazone 6mg +tacrolimus	oral	47.75	Enoxaparin	
Case 7	Male	59	4.0	17	Yes	15	Died	MMF for 3 days, dexamethazone 6mg then 10 mg then 6 mg +tacrolimus.	Oral	25.71	Enoxaparin	After 4 days
Case 8*	Male	51	4.0	6	No		Improved	No change in the immunosuppressive drugs	No	20.31	UFH	
Case 9	Male	23	2.0	25	Yes	3	Improved	dexamethazone 10 mg+tacrolimus	No	20.20	Enoxaparin	
Case 10	Male	60	20.0	26	Yes	27	Died	dexamethazone 6 for 2 day dexta 10 for 10 d ,hydrocortisone 50/6h +tacrolimus stopped in the last week	No	29.76	Enoxaparin	
Case 11	Female	51	8.0	48	Yes	5	Improved	dexamethazone 6mg then	Oral +	19.86	Enoxaparin	

								10 mg+ tacrolimus	IV				
<b>Case 12*</b>	Male	47	15.0	7	No		Improved	No o change in the immunosuppressive drugs	No	26.12	Enoxaparin		
<b>Case 13</b>	Male	41	18.0	18	No		Improved	dexa methazone 6mg then 10 mg+tacrolimus	Oral	35.25	Enoxaparin		
<b>Case 14^</b>	Female	43		16	Yes	9	Died	prednisolone 60mg, dexa 10, MMF for 3 days	1	31.22	UFH	After 5 days	
<b>Case 15^</b>	Male	53		28	Yes	9	Improved	dexamesathone 10	Oral + IV	28.41	Enoxaparin		
<b>Case 16</b>	Male	38	16.0	8	No		Improved	dexamethazone 10mg +tacrolimus	Oral	31.25	Enoxaparin		
<b>Case 17</b>	Female	39	1.5	11	No		Improved	dexamethazone 10mg + tacrolimus	IV	33.20	Enoxaparin		
<b>Case 18</b>	Male	44	16.0	12	No		Improved	dexamethazone10mg +tacrolimus	Oral	29.73	Enoxaparin		

\*Those cases are presented with GIT symptoms

^ Cases with autoimmune disease

**Table 4-b: Laboratory data of selected individual cases**

	<b>D.dimer at admission</b>	<b>D.dimer The highest</b>	<b>CRP at admission</b>	<b>LDH at admission</b>	<b>HB on admission g/dl</b>	<b>TLC (the highest)</b>	<b>TLC the Lowest</b>	<b>PLT (the lowest)</b>	<b>Lymph count (the lowest)</b>	<b>D.Dimer (the lowest)</b>	<b>INR (the highest)</b>	<b>Albumin (at admission)</b>	<b>LDH (the highest)</b>	<b>CRP (the highest)</b>
<b>Case-1</b>	3.36	3.36	0.332	364	13.8	19.02	5.15	131	1.8	0.26	1.93	31	364	12.4
<b>Case-2</b>	0.22	.22	1.31		13.8					0.19	1.11	35.8		
<b>Case-3</b>	7.85	7.85	11.3	453	12.5	17.42	4.49	125	0.5	0.5	1.52	21.7	721	11.3
<b>Case-4</b>			8.05		14.8	12.77	4.52	193	3.1		1.27	27.5		8.05
<b>Case-5</b>	16.22	16.22	3.74	248	15.8	8.56	4.30	124	9.8	0.59	1.13	29	248	
<b>Case-6</b>			1.9		9.2	10.87	7.39	111	4.1		1.18	26		1.9
<b>Case-7</b>	23.6	23.60	4.01	320	12.1	22.71	5.59	114	0.7	0.084	1.2	30	354	37.9
<b>Case-8</b>					12.2	6.7	4.75	233	3.9		1.45	25		
<b>Case-9</b>	6.62	6.62	5.25	180	9.2	9.33	3.72	153	2.3	0.95	1.25	39	256	18.6
<b>Case-10</b>	54	54.00	12.1	345	14.9	30.9	1.44	59	0.4	1.06	4.27	23.5	643	42.4
<b>Case-11</b>	1.8	1.80	39.7	312	11.1	11.29	2.72	102	6	1.19	1.57	24	314	39.7
<b>Case-12</b>			3.24		15.9	3.85	3.60	196	17.3			34		
<b>Case-13</b>	3.19	3.19			12.3	12.85	5.01	184	1	0.088	1.16	24		
<b>Case-14</b>	1.8	1.80	6.66	202	8.9	5.22	2.06	141	5.4	0.84		27		
<b>Case-15</b>	1.7	1.70	11.3	426	14.6	22.56	3.61	144	1	0.61	1.5	22.4	426	11.3

<i>Case-16</i>					12.7	10.59	8.72	604	6.7			25.2		
<i>Case-17</i>	0.45	.45	0.807	209	14	10.57	3.34	117	2.7	0.33		40		
<i>Case-18</i>		3.36		108	14.6	10.57	3.34	144	3			32		

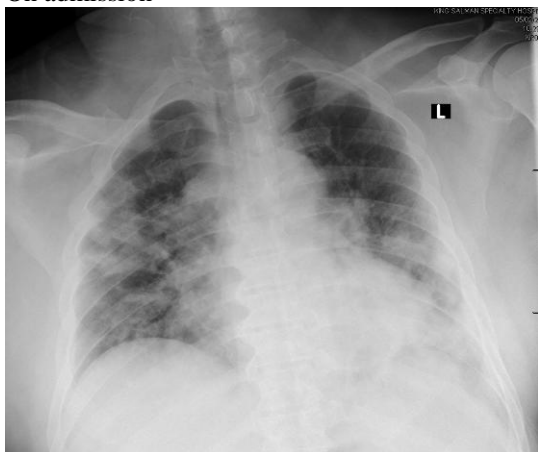
**Table (4-c): Electrolyte presentation of the individual cases**

	<i>Creatinine</i>		<i>BUN</i>		<i>Ca</i>		<i>Po4</i>		<i>Mg</i>		<i>K</i>	
	<i>on admission</i>	<i>on discharge</i>	<i>on admission</i>	<i>on discharge</i>	<i>on admission</i>	<i>on discharge</i>	<i>on admission</i>	<i>on discharge</i>	<i>on admission</i>	<i>on discharge</i>	<i>on admission</i>	<i>on discharge</i>
<i>Case-1</i>	106	73.13	5.69	4.27	2.01	2.16	1.02	1.11	0.7	0.72	4.58	4.7
<i>Case-2</i>	97.89	91.46	4.82	7.51	2.27	2.21	1.15	1.3	0.91	0.67	4.32	5.15
<i>Case-3</i>	135.23	198.29	7.32	36.13	1.88	1.98	0.71	1.62	0.66	1.17	4.22	4.3
<i>Case-4</i>	74.73	92.75	3.15	7.04	1.97	1.75	0.63	0.99	0.61	0.71	5.71	5.12
<i>Case-5</i>	93.91	79.14	4.13	6.45	2.09	2.26	0.96	0.89	0.63	0.56	4.36	4.09
<i>Case-6</i>	115	90	13.22	9.44	2.26	2.13	1.04	1.22	0.94	0.73	4.5	4.73
<i>Case-7</i>	126.55	105.69	6.1	15.95	2.12	2.03	1.24	1.38	0.66	1.09	5.3	5.6
<i>Case-8</i>	195.3	231.55	22.01	20.42	1.86	1.96	1.28	0.85	0.75	0.67	3.68	4.24
<i>Case-9</i>	222	159.48	9.99	16.47	1.95	2.24	1.74	1.31	0.89	0.98	4.57	4.34
<i>Case-10</i>	68	334.99	2.44	33.92	1.89	1.54	0.84	2.36	0.5	0.91	3.72	5.57
<i>Case-11</i>	243.71	69.22	12.59	4.92	2.03	2.13	0.81	0.73	0.55	0.78	3.54	3.42
<i>Case-12</i>	117.03	115	6.27	4.93		2.02			0.73		3.81	3.54
<i>Case-13</i>	231.84	104.12	18.15	14.26	2.03	2.21	1.24	1.34	0.82	0.82	7.56	4.25
<i>Case-14</i>	261.07	823.4	14.91	40.42	1.81	2.04	1.43	2.72	0.75	0.95	4.25	5.7
<i>Case-15</i>	91.62	110.78	5.7	9.14	1.9	2.16	0.87	1.09	0.89	0.87	3.65	3.68
<i>Case-16</i>	103.88	111.9	12.49	11.4	2.24	2.24			0.59	0.73	4.34	4.62
<i>Case-17</i>	106.19	114	6.46	17.2	2.08	2.15	0.5	0.71	0.61	0.71	3.35	4.41
<i>Case-18</i>	106.19	114	6.46	17.2	2.17	2.4	0.72	0.83	0.61	0.96	3.47	4.29

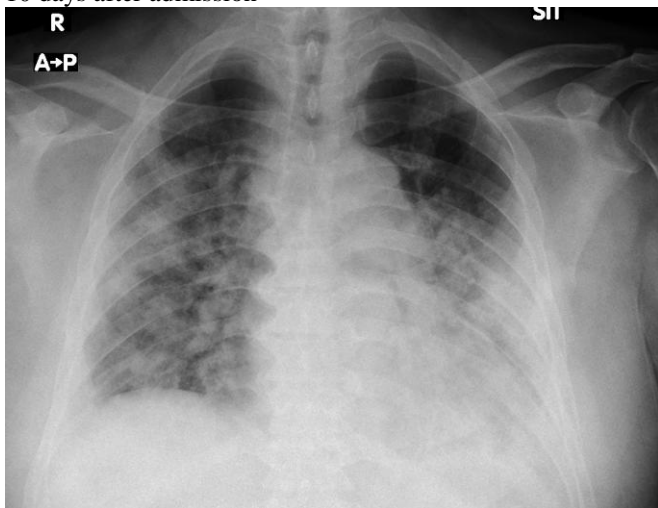
**Fig1 : CHEST IMAGING OF SIX CASES ADMITTED TO INTENSIVE CARE UNIT**

Case 1: one of the ICU survivors

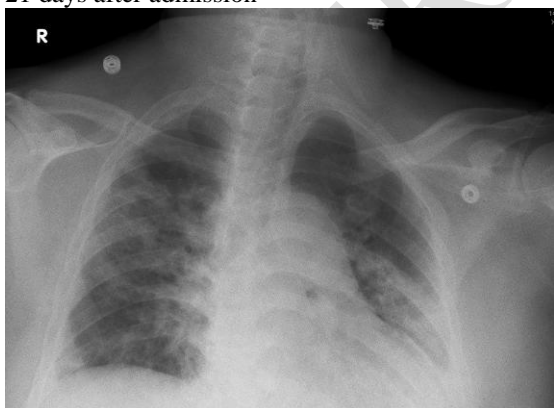
On admission



10 days after admission



21 days after admission

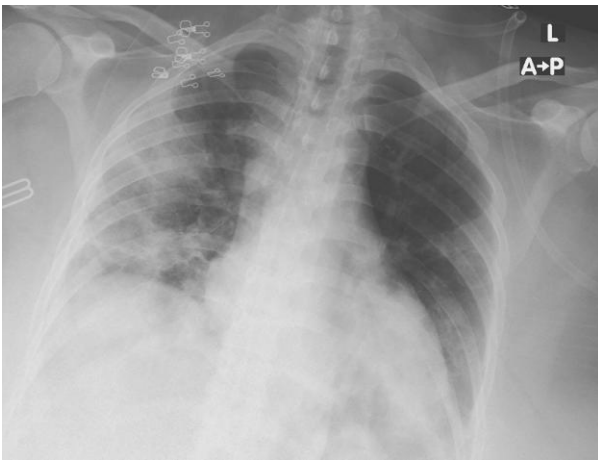


Case 3: Female ICU mortality

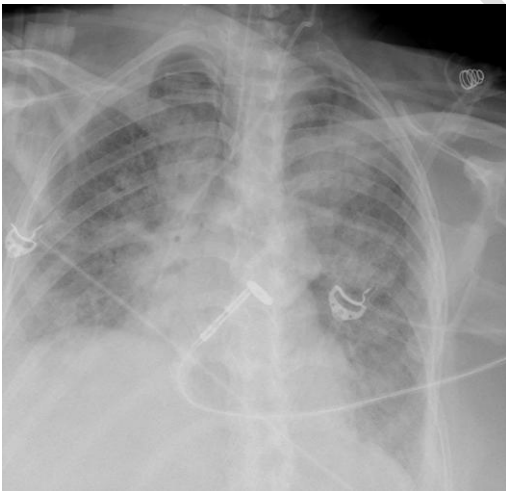
At ADMISSION



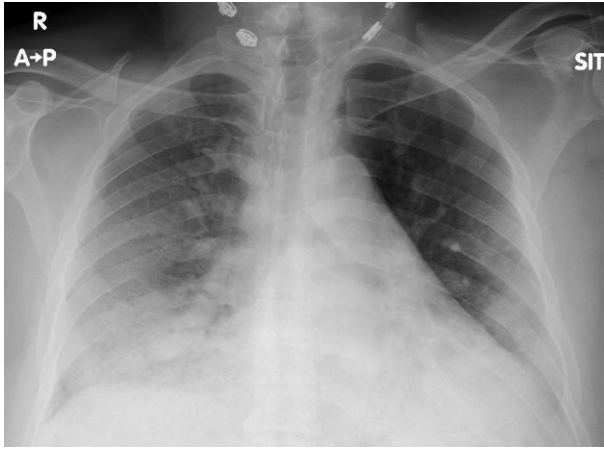
TWO DAYS LATER



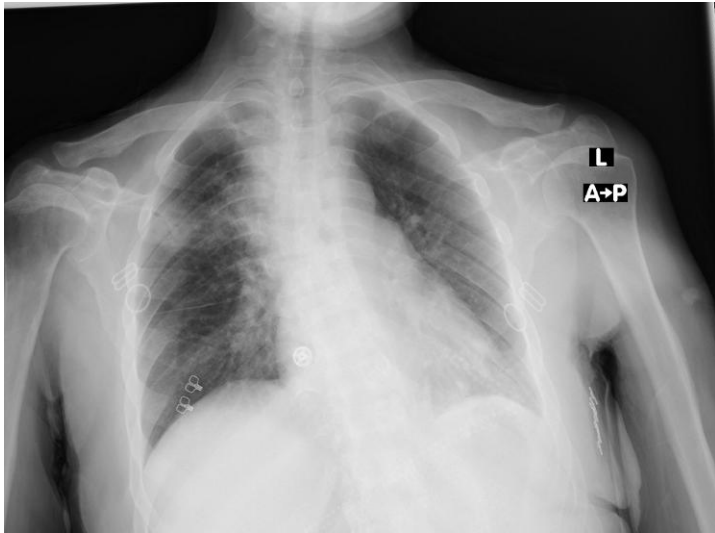
ONE WEEK LATER



Case 10: Male ICU mortality



Case 11: ICU survivor  
ON ADMISSION



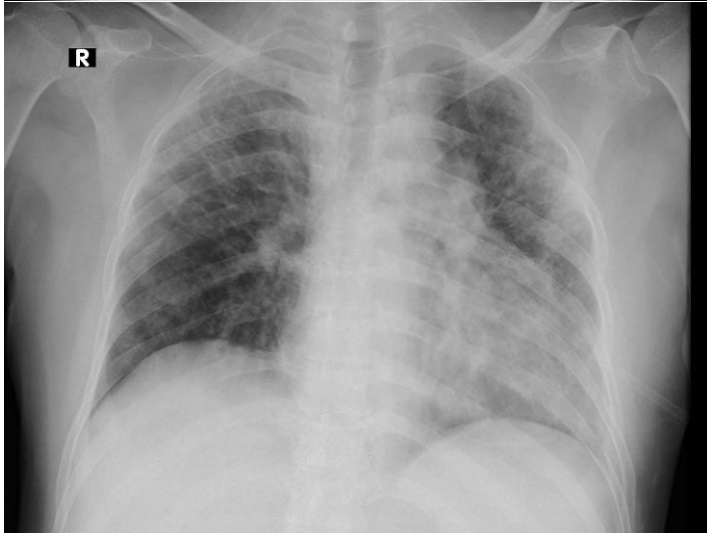
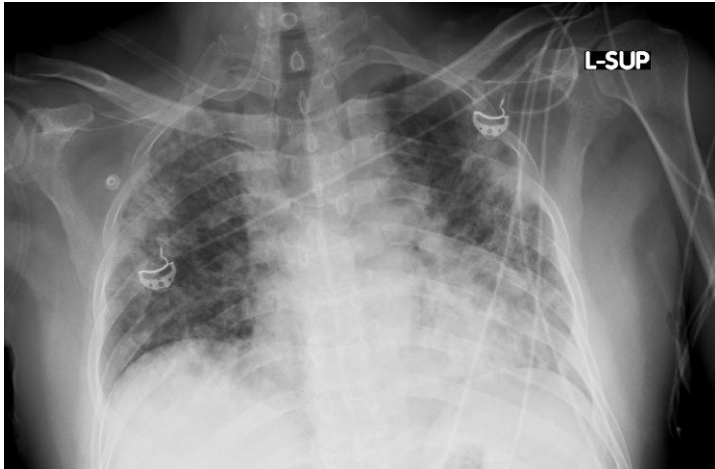
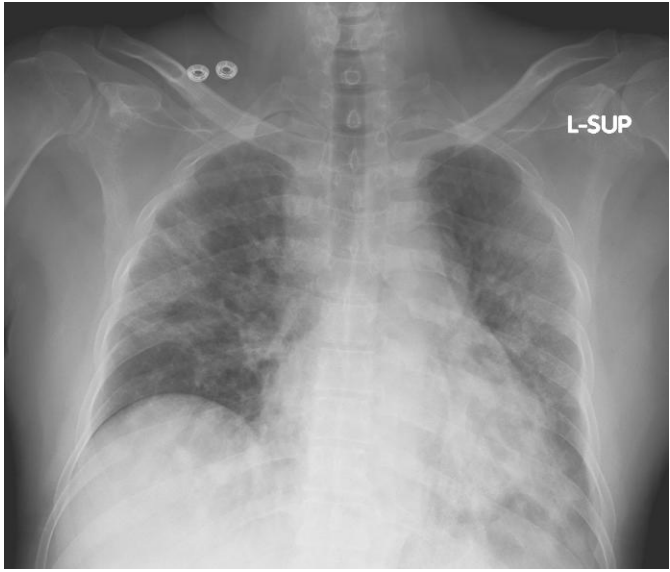
10 DAYS LATER

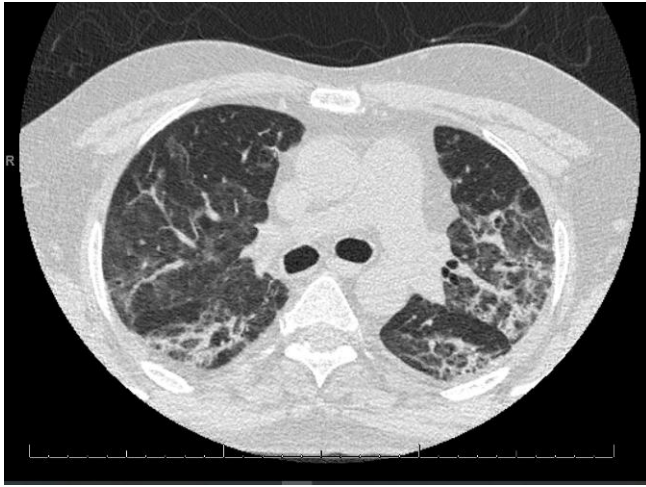


BEFORE DISCHARGE



Case 15: ICU survivor  
Patient with GN





#### 4. Discussion

Renal patients with immunosuppressive protocols are a brittle population due to their immunosuppressed status. However, there has been a limited number of studies existing that compared this population with the general population concerning clinical presentations and laboratory parameters as well as disease severity and clinical outcomes in COVID-19 infection.

We aimed to observe the effect of modification of the immunosuppressive regimen in response to the severity of COVID-19 infection on the outcome of renal disease patients and to study factors affecting their mortality for nine months from February to October 2021.

In the present study, we observed the clinical course of patients suffering from renal diseases or who had been subjected to renal transplantation that was linked to immunosuppression therapy and suffered from COVID-19 infection during the period of February to October 2021. Locally agreed protocol, regarding immunosuppressive protocol, the antiviral used as well as the used anticoagulant, was planned between the treating team; Nephrology, Chest, and ICU consultants to be followed considering international guidelines for COVID 19 infection in immunosuppressed patients and Saudi MOH guidelines for the management of COVID 19 infection (MOH protocol, 21 Jan 2021) (Barlow et al, 2021).

The studied patients were divided into two groups; one group comprised nine patients admitted to ICU and nine patients does not need admission to ICU; there was a further subdivision of the ICU group into deceased and survived groups at discharge.

In the current study, there was a good prognosis for patients who presented early to the hospital and started early cessation of antiproliferative drugs even in patients with severe COVID-19 pneumonia with admission to ICU. This is supported by many researchers who reported that the broad immunosuppressive abilities that make MMF an efficacious drug for transplant and autoimmune diseases might also enhance the risk of infectious complications (Hanvesakul, et al, 2008) (Allison and Eugui, 2005) (Ritter and Pirofski, 2009). Kantauskaite and his colleagues, 2022 found that the strongest predictor for an impaired response to neutralization capacity after SARS-CoV-2 vaccination was MMF treatment as well as higher trough MMF concentrations correlated with lower antibody titers supporting a dose-dependent unfavorable effect of MMF. On the other side, the other immunosuppressive drugs had no significant influence. (Kantauskaite et al, 2022). In another case study 29 years old male presented with a severe infection of COVID19 pneumonia with admitted to ICU; when He was treated with; modified immunosuppressants; discontinuing MMF, unchanged dose of tacrolimus and oral corticosteroids, antibiotics, antiviral and traditional Chinese medicine, he recovered from COVID-19 pneumonia after 29 days of hospitalization and the renal function returned to normal. (Dong et al, 2020). Additionally, in the current study, there was a better prognosis with the use of higher doses of systemic steroids mainly dexamethasone and this was supported by Li and his associates, 2017 who stated that the immunosuppressive and anti-inflammatory effects of Dexamethasone were known and used in certain situations as rheumatoid arthritis (Li et al, 2017). In the current study, tacrolimus was stopped on the deterioration of the chest condition and on mechanically ventilated patients spite of this, the three cases died after a few days. Our finding was not matched with Suryantoro and his colleagues, 2021 who decided to stop the immunosuppressive agents and followed administration of lopinavir/ritonavir, hydroxychloroquine, and dexamethasone which gives a good clinical effect on the patient's condition after being worsened and mechanically ventilated (Suryantoro et

al, 2021). This could be attributed to their use of different antivirals and or their use of hydroxychloroquine in their protocol of management.

In this work, kidney function tests were not affected by the discontinuation of antiproliferative drugs in the whole studied group. This could be attributed to the use of higher systemic steroids with the discontinuation of anti-proliferative drugs. Additionally, kidney function tests were not affected by the use of antiviral medications which were Favipiravir and/or remdesivir. This is partially supported by Wang and his associates, 2020 who found that intravenous remdesivir was adequately tolerated in seriously ill patients with COVID-19 (Wang et al, 2020). However, Hassanipour and his colleagues, 2021 found that the mortality rate in the Favipiravir group was approximately 23% lower than in their control group, but this finding is not statistically significant (Hassanipour et al 2021).

Gayam and his associates, 2020 reported that COVID-19 primarily manifests as lung infection and had significant extrapulmonary complications affecting most organ systems, including the gastrointestinal tract and myalgia which were the main presentation among African-Americans hospitalized in patients with COVID-19 infection. (Gayam et al, 2020). In the current work, there was a better scenario in COVID-19 patients who presented with isolated gastrointestinal manifestations even though, they did not receive antiviral or change their immunosuppressive protocol. This is reinforced by some authors who found that a small group of patients presented with isolated gastrointestinal symptoms and did not develop fever or respiratory symptoms later. Therefore, COVID-19 infection could be considered for patients presenting with primarily gastrointestinal manifestations. (An et al, 2020) (Holshue et al, 2020) (Groff et al, 2021). On the contrary, Hegazy, and colleagues, 2021 conveyed that patients with mild symptoms who present with diarrhea and duration of symptoms longer than 12 days are expected to have a worse prognosis (Hegazy et al, 2021). Moreover, Teimaa and his associates, 2022 found that the presence of associated gastrointestinal symptoms in COVID19 infection patients reflected the severity of the infection. (Teimaa et al,2022). In summary, Sulaiman and his colleagues, 2020 reported that the presence of COVID19-related gastrointestinal symptoms alone carried a better prognosis while their presence with respiratory symptoms was associated with higher morbidity and mortality (Sulaiman et al, 2020).

In our study, there was no difference in the severity of COVID-19 infection regarding age, male gender, associated comorbidities, or BMI. This could be explained by all the studied groups were CKD and maintained on immunosuppressive medications making all of them a high-risk group. This finding was not coincident with the SYSTEMATIC REVIEW performed by Ali and colleagues, 2020 who assessed the risk factors related to the outcomes of SARS-CoV-2 infections, which were old age, male gender, obesity, and associated co-morbidities in the form of cardiovascular diseases, diabetes mellitus, chronic kidney disease, liver disease, cerebrovascular diseases and COPD (Ali and colleagues, 2020).

On the other hand, the inflammatory markers in the form of high CRP, and low serum albumin as well as high LDH, high D-dimer, and lower platelet count were more in the severe group that was admitted to ICU particularly, those who passed away in the current study.

Additionally, there was more lymphopenia in the deceased group. This is partially in harmony with Ali and colleagues, 2020 who reported that most of their Laboratory parameters associated with critical COVID-19 disease included lymphopenia, thrombocytopenia, leucocytosis, increased neutrophils, increased C reactive protein and ferritin, increased D dimer, raised ALT and/or AST, decreased albumin, increased cardiac troponin and elevated LDH (Ali et al, 2020). Many authors were partially in accordance with our study; Gayam and his associates, 2020 concluded that Advanced age, higher BMI, elevated serum ferritin, CRP, and D-dimers at the time of presentation are independent predictors of mortality among hospitalized Africa-American patients with COVID-19 infection (Gayam et al, 2020). In the same context, Ahmeidi and his colleagues, 2020 reported that the inflammatory markers, including interleukin-6, D-dimer, neutrophil-to-lymphocyte ratio, and high-sensitivity C-reactive protein levels were found to be indicative of severe COVID-19 infection and mortality. (Ahmeidi et al, 2020). Furthermore, in a meta-analysis conducted by Tian and his colleagues, 2020, they found that baseline cardiometabolic disease and evidence of increased acute inflammation and end-organ damage (cardiac, renal, liver, and hematologic) on admission were associated with an increased risk of mortality due in COVID-19 infection. (Tian et al, 2020). In our study, the laboratory parameters could be helpful indicators of COVID-19 infection severity and could be used as early pointers for the management modification before deterioration.

In this work, it is observed that serum albumin was decreased in all cases admitted to ICU but decreased more significantly in the deceased group, however, serum albumin is an acute phase reactant and its impact on survival in COVID-19 patients need to be studied This is strengthened by Violi et al, 2021 who found that serum albumin was independently associated with mortality, irrespective of adjustment for gender, ICU admission, heart failure, COPD, and CRP levels which denote that serum albumin may be used to identify patients at higher risk of mortality in COVID-19 patients (Violi et al, 2021). Furthermore, the mortality frequency was higher in the current ICU group, this could be explained by the presence of severe COVID19 infection and the development of severe sepsis in the deceased group and this is in agreement with Violi and his colleagues, 2021 who found that nonsurvivors had more prevalence of intensive care unit admission than survivors (Violi et al, 2021).

In this study, the four vaccinated patients had less severe infections with a better prognosis as they did not admit to the intensive care unit and were discharged directly from the isolation ward. This could be supported by Kantauskaite and his colleagues, 2022, who found that after the vaccination, 24.9% of transplant recipients became seropositive, of whom 68% had neutralizing antibodies. However, they found that this immune response was significantly lower compared to the control group (Kantauskaite et al, 2022).

Conclusion:

Appropriately early discontinuation of antiproliferative drugs for COVID-19 infection in renal immunosuppressed patients and the use of higher doses of systemic steroids mainly dexamethasone was associated with better prognosis. Furthermore, discontinuation of antiproliferative drugs did not cause deterioration of kidney function. The inflammatory markers including CRP, LDH as well as low serum albumin, and high D-dimer were related to mortality in severe cases of COVID-19 infection. Isolated GI symptoms without the presence of respiratory symptoms have been observed in patients with COVID-19 and could be treated safely with symptomatic management.

### **Informed consent**

Informed consent was obtained verbally from the study participant.

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