The Correlation of Renal Functions with The Severity of COVID-19 in Erbil City

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ABSTRACT

Background and objective: It is well known that infection with SARS-CoV-2 (COVID-19) has pulmonary and extra-pulmonary manifestations including renal system. Understanding the bidirectional impact and correlation between severity of COVID-19 and renal function impairment is crucial in managing the complications of COVID-19 and drug prescription accordingly. This study aimed to assess impairment in renal function at mild, moderate and sever cases of covid-19.

Methods: A study focused on COVID-19 cases was carried out in Erbil, Iraq. The sample consisted of 253 individuals who tested positive for the virus through PCR (135 females and 118 males) aged 18 or older and were obtained through convenience sampling from various clinics and hospitals in the city. The data collection took place from July 1, 2020 to October 2021 and involved gathering the medical history, physical examination results, laboratory tests, and imaging of the cases to assess their health status, the severity of their illness, and their renal function.

Results: The patient's gender did not play a major role in the intensity of COVID-19 illness ($p=0.744$), however, factors such as smoking, hypertension, and diabetes were found to be significant contributors ($p<0.0001$). The kidney function measurement, GFR, revealed a significant difference among all groups ($p<0.0001$) and showed a strong negative relationship with CRP ($r=-0.751$, $p<0.001$) and a moderate positive connection with SpO2 ($r=0.646$, $p<0.001$).

Conclusion: The severity of COVID-19 was found to have a strong negative correlation with kidney function, which was represented by GFR.

Keywords: COVID-19, GFR, CRP, Erbil city.

دراسة العلاقة بين وظائف الكلية مع شدة مرض الكوفيد-١٩ في مدينة اربيل

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الخلاصة

الخلفية و الاهداف : من المعلوم ان الإصابة بعدوى الكوفيد-١٩ لها عوارض رئوية و غير رئوية. ان معرفة التاثير الثنائي الجوانب و العلاقة بين شدة الإصابة بمرض الكوفيد -١٩ و شدة تدهور عمل الكلى ضروري في معالجة مضاعفات العدوى و وصف الادوية و العلاجات المناسبة .

طرق البحث: تم إجراء دراسة عرضية في مدينة اربيل في العراق و تم جمع البيانات من ٢٥٣ حالة إصابة بفيروس مرض الكرونا و تم التاكد من خلال فحوصات PCR و كانوا (١٣٥ إناث و ١١٨ ذكور) بعمر ١٨ عاما و اكثر و ذلك باستخدام طرق احصائية مناسبة لجمع العينات من مختلف عيادات و مستشفيات مدينة اربيل. كانت فترة الدراسة من اليوم الاول لشهر حزيران ٢٠٢٠ إلى نهاية شهر اكتوبر ٢٠٢١ . تم جمع معلومات التاريخ المرضي و الفحص السريري و المختبري و التصوير الشعاعي للبحث و إجراء تقيم شدة المرض و معرفة وظائف الكلية.

النتائج: لم يكن جنس المريض عاملا مهما في تحديد شدة مرض COVID-19 (p=0.744) في حين كان التدخين ارتفاع الضغط الشرياني و مرض السكري عوامل مهمة .(p<0.0001) ان مؤشر وظيفة الكلية GFR أظهر فرقا عالي الاهمية بين كل المجموعات (p<0.0001)
و كان لل GFR علاقة سلبية قوية مع ال CRP (r=0.751, p<0.001) و علاقة ايجابية متوسطة مع ال SpO2 (r=0.646 , p=<0.001) .
الاستنتاج: كانت هناك علاقة سلبية قوية بين و ظيفة الكلية متمثلة بال GFR و شدة مرض الكوفيد -١٩.

الكلمات المفتاحية : كوفيد-١٩ ، مدينة اربيل ، GFR ، CRP .

INTRODUCTION

As of the time of the study, it has been over three years since the initial identification of COVID-19. It is widely recognized that the virus affects not only the respiratory system but also other systems in the human body, with the kidneys being a significant target of the disease [1-4].

The main reason why COVID-19 affects the kidneys is because the virus can attach to the ACE-II receptor, which is abundant in kidney tissue and is the main point of entry for the SARS-CoV-2 virus [5,6] . Additionally, the virus's genetic material (RNA) has been discovered in the kidneys and urine of infected individuals, pointing to the kidneys as a significant target of the virus [7].

COVID-19 can cause kidney damage through two primary mechanisms: direct and indirect. The direct mechanism occurs when the virus directly infects renal tissue by binding to ACE II receptors, which are present in the kidneys, leading to damage of intrinsic renal cells and affecting both the bladder and the kidneys. The indirect mechanism is more complex, it results from systemic effects, such as acute tubular injury, collapsing glomerulopathy and systemic hemodynamic instability, which can cause a decline in renal function [8,9] . According to Jia et al in 2020 these indirect mechanisms can be the reasons behind the decline in renal function [10] .

Furthermore, Claudio Ronco and Thiago Reis conducted studies on systemic hemodynamic instability in relation to COVID-19 patients, and their findings indicate that pre-renal azotemia, which is a type of kidney dysfunction caused by a loss of volume or dehydration, is a leading pathophysiological pathway for the acute decline in renal function seen in these patients. Their studies focused on understanding the mechanisms of this type of azotemia and its impact on the kidneys in the context of COVID-19 [11] .

Additionally, the use of broad-spectrum antimicrobial drugs in high doses has also been linked to interstitial nephritis, which can further contribute to the damage of the kidneys during COVID-19 infections [12] . In addition to the impact of pre-renal azotemia and the use of broad-spectrum antibiotics, age and preexisting medical conditions (comorbidities) have been shown to further worsen kidney function in COVID-19 patients [13] .

METHODS

A research study was performed in Erbil, Iraq over the time period from July 1st, 2020 to the end of October 2021. The study was designed as a cross-sectional study.

Study Population: To conduct the study, information on patients was gathered from daily clinic COVID-19 cases and other hospitals in Erbil that were treating COVID-19 patients. A comprehensive approach was used to collect data on the patients' health status, illness severity, and renal function. This included taking a full medical history, performing a physical examination, conducting clinical examinations, and laboratory tests, and using imaging techniques.

Inclusion criteria: All mild, moderate and severe newly diagnosed male and female cases of covid-19 cases confirmed by RT-PCR test that ages 18 years and above with no previous history of any chronic kidney illnesses were included in this study.

Exclusion criteria: This study excluded individuals with critical COVID-19 cases, those under 18 years old, prior documented SARS-CoV-2 infection or vaccination, a history of chronic kidney disease, and confirmed cases of acute or chronic renal disease with a GFR below 15 ml/min.

Estimation of Glomerular filtration rate (GFR): The estimated level of GFR was calculated using MDRD GFR Calculator : Cockroft-Gault equation: eGFR= {(140-age) X BW(Kg)} / {72 X Serum creatinine}. The result is multiplied by 85 in female [14].

Statistics:

Data were analyzed using SPSS version 25. The different results of the groups were analyzed by Tukey's test. Pearson's Test was used to find out correlation between and among different parameters.

Ethical Consideration

Written consent was obtained from all participants, and additional data was obtained from the patient's medical records. The study was reviewed and approved by the Research Ethics Committee of the College of Medicine at Hawler Medical University.

RESULTS

In this study, a total of 253 cases of COVID-19 of varying severity were included along with 200 apparently healthy persons regarded as a control group for statistical analysis. The mean age of the different groups (control group = 46.63 ± 16.5, mild = 45.84 ± 14.7, moderate = 43.03 ± 14.4, and severe = 50.24 ± 14.9) did not show a statistically significant difference between the control and severe groups. However, there was a statistically significant difference between the mild and moderate groups (as seen in Table 1).

Table 1 The mean age and BMI distribution of among studied samples of control and covid-19 patients.

Parameter	Control (n=200)	Mild (n=142)	Moderate (n=70)	Sever (n=41)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Age	46.63 ± 16.5 ab	45.84 ± 14.7 a	43.03 ± 14.4 b	50.24 ± 14.9 ab
BMI	21.7 ± 1.9 a	23.8 ±3.6 B	26.2 ± 4.4 c	24.8 ± 4.4 b

Different letters, a, b, c and d, indicate the significance of the data.

The BMI among different groups was (control = 21.7 ± 1.9, mild =23.8 ±3.6, moderate = 26.2 ± 4.4, sever = 24.8 ± 4.4) (Table 1).

The gender of the study participants across different groups did not have a significant impact (p = 0.744). However, the prevalence of smoking, hypertension, and diabetes showed a highly significant difference among the groups (p<0.0001) (as shown in Table 2).

Table 2 The characteristics of sex, smoking, HTN and DM among the different groups.

	Control		Mild		Moderate		Sever		P value
Sex	Male N (%)	Female N (%)	Male N (%)	Female N (%)	Male N (%)	Female N (%)	Male N (%)	Female N (%)	0.744
	97 (48.5)	103 (51.5)	61 (43)	81 (57)	31 (44.3)	39 (55.7)	20 (48.8)	21 (511.2)	
Smoking	Yes N (%)	No N (%)	Yes N (%)	No N (%)	Yes N (%)	No N (%)	Yes N (%)	No N (%)	<0.0001
	12 (6)	188 (94)	19 (13.4)	122 (86.6)	17 (24.2)	53 (75.8)	11 (26.8)	30 (73.2)	
HTN	Yes N (%)	No N (%)	Yes N (%)	No N (%)	Yes N (%)	No N (%)	Yes N (%)	No N (%)	<0.0001
	4 (2)	196 (98)	12 (8.4)	130 (91.6)	9 (12.8)	61 (87.2)	8 (19.5)	33 (79.5)	
DM	Yes N (%)	No N (%)	Yes N (%)	No N (%)	Yes N (%)	No N (%)	Yes N (%)	No N (%)	<0.0001
	2 (1)	199 (99)	10 (7)	132 (93)	17 (24.2)	53 (75.8)	11 (26.8)	30 (73.2)	

The results of the study indicate that there was no statistically significant difference in gender between the COVID-19 cases and the control group. However, there were significant differences in the smoking, hypertension, and diabetes conditions among the groups. When looking at the mean difference in GFR and other inflammatory markers with SpO2% using Tukey's HSD, there was a highly significant difference among all groups. The results for total WBC and CRP showed a significant difference between the control and all other groups, but no significant difference between the mild and moderate groups.

The results for ESR showed a significant difference between the control and all other groups, but no significant difference between the moderate and severe groups (Table 2, Figure 1).

Table 3 The difference in mean of GFR and other inflammatory markers with SpO2% among different groups of Covid-19 cases.

Parameter	Control	Mild	Moderate	Sever
GFR ml/min	103.35 d	88.725 C	81.304 b	52.756 a
Total WBC Cells/cmm	6.472 a	9.775 B	10.617 b	14.707 c
S. Ferritin Ug/L	137.23 a	237.94 B	508.76 c	527.17 c
CRP mg/L	3.439 a	52.007 B	51.157 b	158.024 c
ESR mm/1st Hour	15.83 a	34.87 B	53.84 c	57.83 c
SpO2 %	96.10 c	95.61 C	94.81 c	76.07 a

Within a group of severe COVID-19 cases, there was a highly significant negative correlation (r = -0.751) between GFR and CRP that was statistically very significant ($p < 0.001$), as shown in Figure 2.

Additionally, there was a significant positive correlation (r = +0.646) between GFR and SpO_2% that was statistically very significant ($p < 0.001$) among severe COVID-19 cases, as demonstrated in Figure 3.

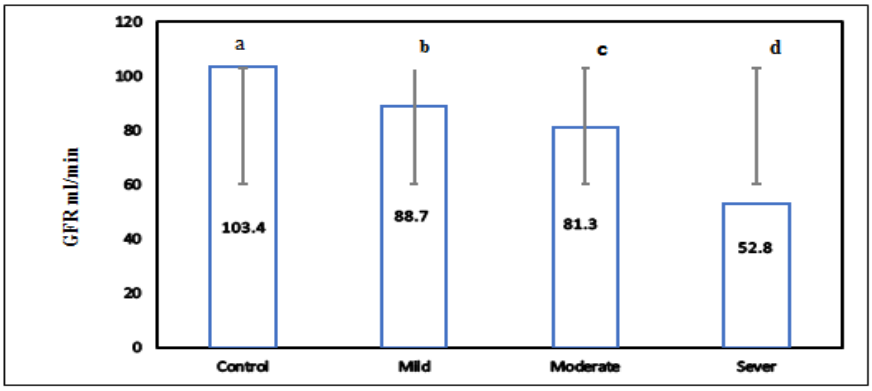

Figure1 Estimation of GFR among different groups of Covid-19 cases.

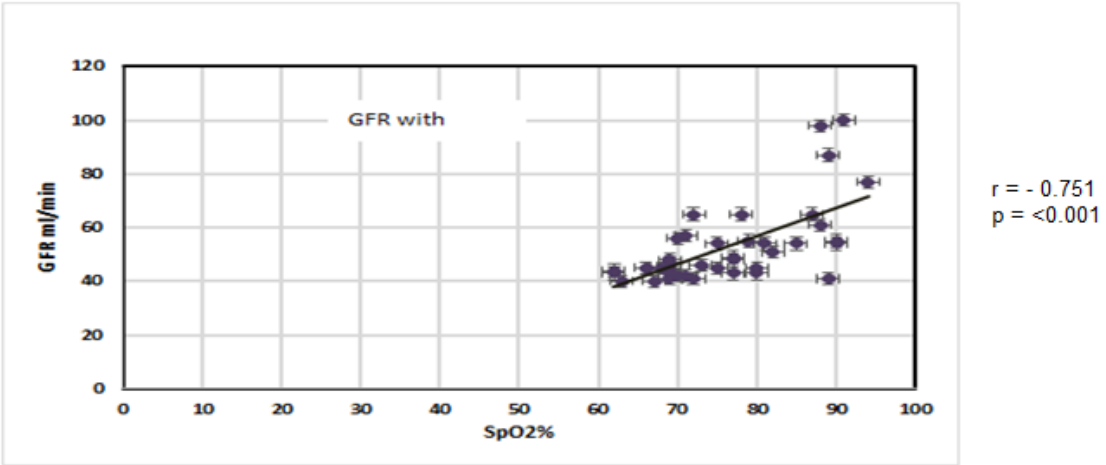

Figure 2 Correlation of GFR with CRP in the group of sever Covid-19 patients.

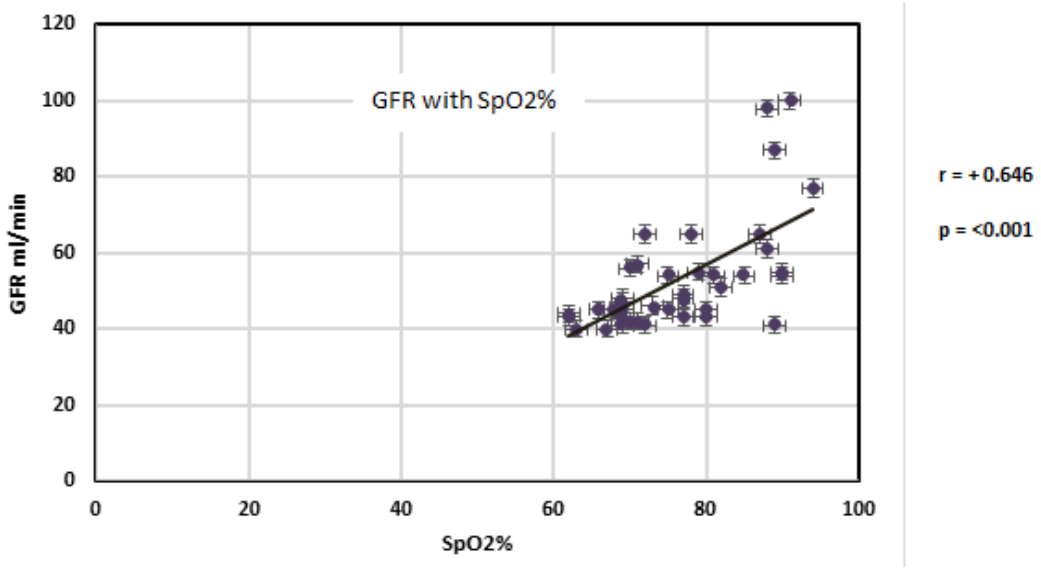

Figure 3 Correlation of GFR with SpO2% in the group of sever Covid-19 patients.

DISCUSSION

The COVID-19 pandemic showed that the virus is not limited to affecting just the lungs, but also other organs such as the kidneys. This study aimed to examine the impact of the virus on kidney function by measuring changes in glomerular filtration rate (GFR) in patients with mild, moderate, and severe cases. However, critically ill patients were not included in the study as it was considered unethical to obtain samples from them without their consent.

The purpose of this study was to gain a deeper insight into the impact of COVID-19 on the kidneys, which could result in the development of new therapies and patient care approaches for those impacted by the virus.

Although COVID-19 affects individuals of all ages [15], the results of this study showed that the average age of severe COVID-19 cases is higher, however, this difference was not statistically significant when compared to mild and moderate cases.

A number of scientific articles showed a strong correlation of the severity of covid-19 and body weight marked by BMI [16,17] which is in contrast to the results of our study. This might be attributed to differences in sample population or sample size.

As for the gender of different groups, there were no statistically significant difference among different groups and it is clear that both sexes are affected with all severity levels and this result is in accordance results obtained by Ambrosino I, et al in 2020 [18].

In this study, a statistically high significant difference ($p < 0.0001$) was found between smokers and non-smokers among different groups and smoking was associated with increase disease severity. Others, found similar results. Smoking increases severity of COVID-19 due to its effects on the respiratory system, which weakens the body's ability to fight off infections and makes it more susceptible to severe illness. Smoking also impairs the immune system and increases inflammation in the body, which can worsen the symptoms of COVID-19 [19,20].

A previous study has already established that concurrent chronic illnesses, such as hypertension and diabetes, can increase the risk of severe forms of COVID-19 [21]. This study provides further evidence of this correlation by showing a statistically significant difference between patients with diabetes and/or hypertension and those without these conditions among all groups in the study.

Extra-pulmonary manifestations of COVID-19 are many and this virus attacks multiple tissues and its destruction is not confined to the respiratory system [22]. The kidneys are regarded as one of the major targets attacked by the virus [5]. Many mechanisms have been assumed leading virtually to decline in renal function with the progress of the disease [13]. The focus of this study was to study this aspect by measuring GFR and comparing this index among groups of different severity. It is was very clear that with increasing severity of the disease, GFR is declining and the difference among all groups is statistically highly significant. Our findings align with the results obtained by Gok et al,2020 and Hirsch et al, 2021 [23,24].

Patients with COVID-19 exhibit high levels of the inflammatory markers. COVID-19 exhibits high levels of inflammatory markers because the virus triggers a strong immune response in the body. This immune response, known as a "cytokine storm," can cause excessive inflammation that can

damage healthy tissue and organs, leading to severe illness. Additionally, the SARS-CoV-2 virus can directly infect and damage cells, triggering further inflammation and exacerbating symptoms [25]. The estimated levels of the inflammatory markers in this study were compared among different groups. Both of ESR and serum ferritin showed statistically highly significant differences when comparing control with either of mild or moderate groups and when comparing moderate with severe cases but there was no statistically significant difference between moderate and severe group.

The inflammatory marker CRP is a reliable index for the severity of many acute conditions including COVID-19, and higher CRP levels are associated with more severe inflammation [26,27].

Results of this study showed a strong, negative correlation between GFR and CRP among the group of severely infected COVID-19 cases, which is statistically highly significant.

The classification of the severity of COVID-19 considers SpO2, or oxygen saturation, as a crucial indicator [28,29] . According to this study, there is a moderate, positive correlation between GFR and SpO2%, which is statistically significant. This is due to the fact that oxygenation is a critical aspect of COVID-19, as it plays a major role in determining the progression of the disease [30].

As a result, the oxygen saturation level was measured in all groups, and the results showed no significant differences among them. However, when comparing any group with the severe group, the results showed highly significant differences in terms of oxygen saturation levels. Oxygen saturation remain not affected till most of the respiratory membrane is affected by the virus [28-30].

CONCLUSION

This study concluded that the impact of COVID-19 on the kidneys, as an extrapulmonary organ, increases as the severity of the disease increases. The study found a strong and statistically significant negative relationship between the level of COVID-19 severity and kidney function, as measured by GFR. This relationship should be considered when managing COVID-19 patients.

Funding and Competing Interests

The author of the study state that they do not have any conflicting interests, and there was no funding involved in the study.

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