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## Long-term renal outcomes in COVID-19 survivors: a cohort study

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#### Abstract

**Introduction.** COVID-19 has been associated with both acute and chronic extrapulmonary complications, including renal dysfunction. Understanding the long-term effects of COVID-19 on renal function is essential for managing recovery in affected individuals.

**Objective.** This study aimed to evaluate the long-term renal outcomes in patients who recovered from COVID-19, focusing on changes in glomerular filtration rate (GFR), blood urea nitrogen (BUN), and serum creatinine levels

Materials & methods. A retrospective cohort study was conducted using data from the Mashhad University of Medical Sciences cohort. The study included patients who had confirmed COVID-19 and a minimum follow-up period of six months post-recovery. Renal function was assessed by measuring the Glomerular Filtration Rate (GFR), Blood Urea Nitrogen (BUN), and serum creatinine levels both at baseline (when COVID-19 was initially diagnosed) and at follow-up. Statistical analysis was performed to explore the associations between renal outcomes and various factors, including gender, the severity of COVID-19, and blood pressure status.

Results. In the study, 55.3% were male, and the mean age of 51.38 ± 13.41. Among the patients, 55.3% were male and 44.7% were female. The difference in mean creatinine level between baseline and follow-up was significant (p < 0.001). The difference in mean GFR between baseline and follow-up was significant (p < 0.001). In men, the mean blood urea nitrogen at the first visit and at the follow-up difference was not statistically significant (p = 0.241). In women, the mean blood urea nitrogen was a statistically significant decrease (p = 0.003). Other parameters, including creatinine and GFR, did not differ significantly in both male and female groups at the time of hospitalization and follow-up.

Conclusion. Overall, the results of this study suggest that COVID-19 can affect kidney function, especially in association with underlying factors such as hypertension and diabetes, and female gender, which may be risk factors for more severe renal complications in patients with COVID-19. The decrease in GFR in patients with hypertension and diabetes highlights the importance of controlling these diseases in patients with COVID-19. Overall, this study showed that COVID-19 can have lasting effects on patients' kidney function.

Keywords: COVID-19; renal function; long-term outcomes; GFR; BUN; creatinine; gender differences

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Authors' contribution: S. Naderi, K. Samadi — study concept, study design development, data analysis, drafting the manuscript; literature review, drafting the manuscript, software; A.A. Zeraati, N. Mahdavifar, A. Kaffash, Z. Jalambadani — data acquisition, data analysis, statistical data processing; N. Mahdavifar, M.Akbari, Z. Jalambadani — supervision, data analysis, critical review, scientific editing.

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# Отдалённые исходы COVID-19 при оценке функции почек: когортное исследование

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#### Аннотация

**Введение.** COVID-19 ассоциирован как с острыми, так и с хроническими внелёгочными осложнениями, включая почечную дисфункцию. Понимание долгосрочного влияния COVID-19 на функцию почек имеет важное значение для разработки алгоритма её восстановления у переболевших.

**Цель исследования.** Оценить влияние COVID-19 на функцию почек в отдалённом периоде с акцентом на изучение скорости клубочковой фильтрации (СКФ), уровня азота мочевины (АМК) и уровня креатинина в сыворотке крови у пациентов в Иране.

**Материалы и методы.** Проведено ретроспективное когортное исследование с использованием данных Мешхедского медицинского университета. В исследование включены пациенты с подтверждённым COVID-19 и минимальным периодом наблюдения 6 месяцев после выздоровления. Функцию почек оценивали путём измерения СКФ, АМК и уровня креатинина в сыворотке как на исходном этапе (при первоначальном диагнозе COVID-19), так и при последующем наблюдении. Проведён статистический анализ для изучения связи между почечными исходами и различными факторами, включая пол, тяжесть течения COVID-19 и уровень артериального давления.

**Результаты.** Среди пациентов 55,3% были мужчинами, 44,7% — женщинами. Средний возраст участников — 51,38 ± 13,41 года. Разница в среднем уровне креатинина между исходным этапом и последующим наблюдением была значимой (р < 0,001). Разница в средней СКФ между исходным этапом и последующим наблюдением также была значимой (р < 0,001). У мужчин разница среднего уровня АМК при первом визите и при последующем наблюдении не была статистически значимой (р = 0,241). У женщин среднее содержание АМК статистически значимо снизилось (р = 0,003). Другие параметры, включая креатинин и СКФ, не показали значительных различий ни в мужской, ни в женской группах во время госпитализации и последующего наблюдения.

**Заключение.** Результаты исследования показывают, что COVID-19 может влиять на функцию почек, особенно в сочетании с такими факторами, как гипертония и диабет, а также женский пол, которые могут быть факторами риска более тяжёлых почечных осложнений у пациентов с COVID-19. Снижение СКФ у пациентов с гипертонией и диабетом подчёркивает важность контроля этих заболеваний у пациентов с COVID-19. В целом, исследование показало, что COVID-19 может иметь долгосрочные последствия для функции почек у пациентов.

**Ключевые слова:** COVID-19; функция почек; долгосрочные исходы; скорость клубочковой фильтрации (СКФ); уровень азота мочевины в крови (АМК); креатинин; гендерные различия

Финансирование. Авторы заявляют об отсутствии внешних источников финансирования. Раскрытие интересов. Авторы заявляют об отсутствии конфликта интересов. Благодарности. Авторы выражают искреннюю благодарность Научно-исследовательскому центру не-инфекционных заболеваний, заместителю по исследованиям и технологиям Сабзеварского медицинского университета (Сабзевар, Иран), а также когорте Мешхедского медицинского университета за помощь в подготовке статьи. Этическое заявление. Исследование проведено в соответствии с положениями Хельсинкской декларации (пересмотрена в Форталезе, Бразилия, октябрь 2013 года) и одобрено Этическим комитетом Сабзеварского медицинского университета в Иране (IR.MEDSAB.REC.1402.022). Информированное согласие на участие в исследовании и обработку персональных данных.

**Вклад авторов:** С. Надери, К. Самади — концепция исследования, разработка дизайна исследования, анализ данных, составление рукописи; обзор литературы, составление рукописи, программное обеспечение; А.А. Зераати, Н. Махдавифар, А. Каффаш, З. Джаламбадани — сбор данных, анализ данных, статистическая обработка данных; Н. Махдавифар, М. Акбари, З. Джаламбадани — научное руководство, анализ данных, критическая рецензия, научный редактор.

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#### **Introduction**

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has resulted in a global health crisis affecting millions worldwide [1, 2]. Initial attention has mostly been on the respiratory complications of the virus, but new evidence indicates that COVID-19 can also lead to significant extrapulmonary effects, such as acute and chronic kidney disease. Initial attention has mostly been on the respiratory complications of the virus, but new evidence indicates that COVID-19 can also lead to significant extrapulmonary effects, such as acute and chronic kidney disease [3]. The kidneys appear to be particularly vulnerable to SARS-CoV-2 due to the high expression of angiotensin-converting enzyme 2 (ACE2) receptors, which serve as the entry point for viral invasion into cells.

COVID-19 can impact the kidneys both directly and indirectly. Direct viral invasion can lead to tubular and endothelial cell damage, while indirect effects, such as cytokine-mediated inflammation and coagulation abnormalities, may further contribute to kidney injury. These mechanisms, together, increase the risk of both acute and long-term renal complications [4].

With the rising acknowledgment of renal complications in patients recovering from CO-VID-19, this study aims to evaluate the longterm kidney outcomes in individuals' postrecovery [5]. Specifically, the study seeks to determine changes in GFR and the prevalence of albuminuria, both of which are important indicators of renal health. By identifying the frequency and severity of these renal abnormalities, along with associated risk factors, this research aims to provide valuable insights for clinical practice and post-recovery management. Ultimately, this study seeks to contribute to the growing body of knowledge regarding the long-term effects of COVID-19 and to underscore the need for renal function monitoring in recovered patients.

Objective. This retrospective cohort study aimed to evaluate long-term renal complications in patients who recovered from COVID-19, specifically focusing on those with a follow-up period of six months or more post-recovery.

#### **Materials and methods**

The research utilized data from the cohort center at Mashhad University of Medical Sciences, which included all individuals registered since late 2019. The study assessed patients with a confirmed COVID-19 diagnosis, ensur-

ing they had at least six months of follow-up after their infection. The evaluation included changes in renal function, measured by blood urea nitrogen (BUN), serum creatinine, glomerular filtration rate (GFR), and other relevant renal parameters.

Ethical statement. This study was approved by the Research Ethics Committees of Sabzevar University of Medical Sciences in Iran (IR. MEDSAB.REC.1402.022).

Participants. The study population consisted of patients from the Mashhad University of Medical Sciences cohort who tested positive for COVID-19 using polymerase chain reaction (PCR) methods. The inclusion criteria required participants to have a confirmed COVID-19 infection and at least six months of follow-up after recovery. Patients with pre-existing kidney disease or severe underlying conditions, such as advanced cancer or severe heart failure, were excluded from the study to minimize confounding factors.

Data Collection. To assess the severity of COVID-19, we used the Quick COVID-19 Severity Index (qCSI). This index incorporates respiratory rate (RR), oxygen saturation (SpO2), and oxygen flow rate as key components. Data were collected retrospectively from the medical records maintained at the cohort center. Baseline demographic and clinical characteristics, including laboratory results from the initial COVID-19 diagnosis, were documented. Follow-up data were collected at least six months post-infection and included renal function tests such as BUN, serum creatinine, and GFR. Follow-up information was obtained either from patient medical records or by contacting participants via telephone to evaluate their health status and, where necessary, request further laboratory tests.

Outcome Measures. The primary outcome measures were changes in GFR. Secondary outcomes included BUN and serum creatinine levels. Renal function was assessed at two points: baseline (initial COVID-19 diagnosis) and follow-up (at least six months post-recovery). Additional analyses were conducted to explore renal function changes based on gender, COVID-19 symptom severity, and blood pressure status, consistent with the findings reported in the results section.

Statistical Analysis. We used descriptive statistics to summarize the baseline characteristics and the follow-up data. In this study used SPSS 26 version ("IBM Corporation", Armonk, NY, USA).

Continuous variables were presented as means and standard deviations (SD). Categorical variables were reported as frequencies and percentages. Data were analyzed using paired statistical tests to evaluate the differences in biochemical parameters between two time points: the first visit (baseline) and the follow-up period. Continuous variables were expressed as mean ± standard deviation (SD). For each parameter, a paired t-test was used to assess the significance of changes between the baseline and followup values. This test was appropriate given that the data consisted of paired measurements taken from the same subjects at two different times, and it was assumed that the differences followed a normal distribution. Subgroup analyses were conducted based on gender, disease severity (mild, moderate, severe), and blood pressure status (normal, high blood pressure) to further explore potential differences in treatment response. For each subgroup, paired t-tests were similarly applied to compare baseline and follow-up values for the following parameters: BUN, creatinine, and GFR. A P-value of < 0.05 was considered statistically significant for all tests. The sample size was calculated using the events per predictor variable (EPV) method, as outlined by Vittinghoff and McCulloch. It was estimated that 18 parameters would be assessed and using the EPV method (with 10 events per parameter), a minimum of 180 individuals with renal complications would be required. Considering previous reports indicating a 35% incidence of renal complications among COVID-19 patients the total sample size was set at a minimum of 515 participants to ensure the desired number of events. Simple random sampling was applied to select participants from the cohort population. Of the 515 selected samples, 318 participants entered the follow-up phase.

#### **Results**

Baseline Laboratory and Clinical Characteristics. The study included 318 patients, with a mean age at enrollment of  $51.38 \pm 13.00$ 

**Table 1.** Demographic and baseline characteristics of patients

Variable	Mean ± SD				
Age at enrollment (years)	51.38 ±13.41				
Age at follow-up (years)	54.36 ±13.46				
Length of hospital stay (days)	6.35 ±5.81				
Length of ICU stay (days)	1.33 ±4.31				
Gender	n (%)				
Male	176 (55.3)				
Female	142 (44.7)				
Comorbidities	n (%)				
Diabetes	55 (17.6)				
Hypertension	66 (21.0)				
Heart disease	32 (10.2)				
Chronic kidney disease	0 (0.0)				
Hyperlipidemia	19 (6.0)				
Thyroid disease	8 (2.5)				

years, which increased to  $54.36 \pm 13.46$  years by the follow-up period. The Demographic and Baseline Characteristics of Patients were summarized in Table 1.

The average length of hospital stay was  $6.35 \pm 5.81$  days, while the mean ICU stay was  $1.33 \pm 4.31$  days. Of the total participants, 55.3% (n = 176) were male, and 44.7% (n = 142) were female, reflecting a slightly higher representation of males. Comorbid conditions were common among the participants. Hypertension was the most prevalent, affecting 21% (n = 66) of patients. Diabetes was present in 17.6% (n = 55), while 10.2% (n = 32) had a history of heart disease. None of the patients had chronic kidney disease (CKD). Hyperlipidemia was observed in 6% (n = 19), thyroid disease in 2.5% (n = 8).

Analytical Findings. Renal function was evaluated at two time points: the initial visit and the follow-up. Measurements of renal function over time are illustrated in Table 2.

The mean BUN level decreased significantly from 38.74 mg/dL at the initial visit to 31.24 mg/dL at follow-up, with a mean difference of 7.50 mg/dL (p = 0.004). The normal BUN level is approximately 7 to 20 mg/dL. Creatinine levels showed a non-significant reduction from 1.31 mg/dL to 1.19 mg/dL (p = 0.372). The normal range for serum creatinine levels in

 Table 2. Renal function parameters over time (paired samples)

Parameter	Mean (First Visit)	Mean (Follow-Up)	Paired Difference	Standard Deviation	t-value	p-value
Blood urea nitrogen (mg/dL)	38.74	31.24	7.50	46.60	2.866	0.004*
Creatinine (mg/dL)	1.31	1.19	0.11	2.24	0.894	0.372
Glomerular filtration rate (ml/min/1.73m²)	86.00	86.53	-0.53	35.81	-0.262	0.794

men: approximately 0.7 to 1.3 mg/dL, women, approximately 0.6 to 1.1 mg/dL. The GFR increased slightly from 86.00 ml/min/1.73 m² to 86.53 ml/min/1.73 m², but this difference was not statistically significant (p = 0.794). Normal GFR: about 90 to 120 mL/min/1.73 m². The difference in mean creatinine level between baseline and follow-up was significant (p < 0.001). The difference in mean GFR between baseline and follow-up was significant (p <0.001). The above results indicate that kidney function in COVID-19 patients has decreased over time.

Renal Function Based on Gender. Measurements of renal function distributed by gender are illustrated in Table 3.

In men, the mean blood urea nitrogen at the first visit was 37.59 mg/dL and at the follow-up was 33.30 mg/dL. Although a decrease was observed, this difference was not statistically significant (p = 0.241). In women, the mean blood urea nitrogen at the first visit was 40.17 mg/dL and at the follow-up was 28.71 mg/dL, which was a statistically significant decrease (p = 0.003).

Other parameters, including creatinine and GFR, did not differ significantly in both male and female groups at the time of admission and follow-up.

The mean difference in GFR and CR at baseline and follow-up was statistically significant for both sexes. However, the mean difference between baseline and follow-up was different for both sexes and was statistically significant. This finding indicates that changes in kidney function over time differed between men and women, and that women experienced a more severe decline in kidney function.

Renal Function Based on COVID-19 Symptom Severity. Renal function was also analyzed according to the severity of COVID-19 symptoms and provided in Table 4.

In patients with mild or moderate symptoms, no significant changes in BUN, creatinine, or GFR were observed. However, among patients with severe symptoms, a significant reduction in BUN was observed, decreasing from 42.98 mg/dL to 30.10 mg/dL (p = 0.017). No significant changes were noted in creatinine or GFR across severity groups, suggesting that BUN reduction may be more pronounced in patients with severe COVID-19 symptoms.

Renal Function Based on Blood Pressure Status. These results indicate that patients with normotensive blood pressure had greater improvement in blood urea nitrogen, but hypertension had no significant effect on renal parameters (Table 5).

In patients with normotensive blood pressure, mean blood urea nitrogen decreased significantly (p = 0.011), but no significant changes were observed in creatinine and GFR.

**Table 3.** Renal function parameters by gender (paired samples)

Gender	Parameter	Mean (First Visit)	Mean (Follow-Up)	Paired Difference	Standard Deviation	t-value	p-value
Male	Blood urea nitrogen (mg/dL)	37.59	33.30	4.29	48.19	1.178	0.241
	Creatinine (mg/dL)	1.18	1.16	0.02	1.78	0.141	0.888
	Glomerular filtration rate (ml/min/1.73m²)	94.36	92.02	2.34	34.24	0.901	0.369
Female	Blood urea nitrogen (mg/dL)	40.17	28.71	11.46	44.42	3.074	0.003*
	Creatinine (mg/dL)	1.47	1.24	0.23	2.71	1.004	0.317
	Glomerular filtration rate (ml/min/1.73m²)	75.60	79.69	-4.09	37.50	-1.292	0.199

 Table 4. Renal function parameters by COVID-19 symptom severity (paired samples)

Severity	Parameter	Mean (First Visit)	Mean (Follow-Up)	Paired Difference	Standard Deviation	t-value	p-value
Mild	Blood urea nitrogen (mg/dL)	38.33	33.46	4.87	38.36	1.264	0.209
	Creatinine (mg/dL)	1.19	1.21	-0.02	1.75	-0.110	0.912
	Glomerular filtration rate (ml/min/1.73m²)	85.46	88.43	-2.97	38.97	-0.754	0.453
Moderate	Blood urea nitrogen (mg/dL)	33.50	30.42	3.08	33.06	0.893	0.374
	e Creatinine (mg/dL)	1.25	1.24	0.01	1.78	0.030	0.976
	Glomerular filtration rate (ml/min/1.73m <sup>2</sup> )	85.01	83.21	1.80	30.56	0.563	0.575
Severe	Blood urea nitrogen (mg/dL)	42.98	30.10	12.87	59.33	2.426	0.017*
	Creatinine (mg/dL)	1.45	1.15	0.30	2.83	1.170	0.244
	Glomerular filtration rate (ml/min/1.73m <sup>2</sup> )	86.98	87.28	-0.30	37.06	-0.090	0.929

	<u> </u>						
Blood Pressure	Parameter	Mean (First Visit)	Mean (Follow-Up)	Paired Difference	Standard Deviation	t-value	p-value
Normal	Blood urea nitrogen (mg/dL)	37.12	30.00	7.12	43.86	2.563	0.011*
	Creatinine (mg/dL)	1.27	1.18	0.09	2.14	0.700	0.484
	Glomerular filtration rate (ml/min/1.73m²)	88.35	90.16	-1.81	36.08	-0.788	0.431
High	Blood urea nitrogen (mg/dL)	45.03	35.97	9.06	56.70	1.298	0.199
	Creatinine (mg/dL)	1.46	1.28	0.18	2.65	0.552	0.583
	Glomerular filtration rate (ml/min/1 73m <sup>2</sup> )	76 62	72 32	4 30	35 21	0 993	0 325

Table 5. Renal function parameters by blood pressure status (paired samples)

In patients with hypertension, no significant differences were observed in renal parameters.

Creatinine Levels in Diabetic and Non-Diabetic Patients. The results of the comparison of creatinine levels based on diabetes status are presented. In non-diabetic patients, the difference between baseline creatinine and creatinine at follow-up was significant (p < 0.001). Additionally, in diabetic patients, a significant difference was observed between baseline creatinine and follow-up creatinine (p < 0.02). However, the difference in creatinine levels at follow-up between these two groups was not significant. The normal range for non-diabetic patients usually (around 0.8 - 1.1 mg/dL). The normal range for diabetic patients often ranging from about 1.0 to 1.5 mg/dL or higher, depending on disease severity.

Creatinine Levels in Hypertensive and Non-Hypertensive Patients. In hypertensive patients, mean baseline creatinine and follow-up creatinine levels differed significantly (p < 0.05). Non-hypertensive patients also demonstrated a significant change between baseline and follow-up creatinine levels (p < 0.001). However, no significant difference in follow-up creatinine levels was noted between hypertensive and non-hypertensive groups.

Creatinine Levels Based on Symptom Severity. Patients with severe symptoms exhibited significantly different mean baseline and follow-up creatinine levels compared to those with mild or moderate symptoms (p < 0.05). Despite this, no significant differences were found in follow-up creatinine levels among patients with different symptom severities.

GFR in Diabetic and Non-Diabetic Patients. Diabetic patients experienced a significantly greater decline in GFR compared to non-diabetic patients (p < 0.001). The difference between baseline GFR and follow-up GFR was statistically significant in both diabetic and non-diabetic groups.

GFR in Hypertensive and Non-Hyperten-

sive Patients. Hypertensive patients showed a more pronounced decline in GFR compared to non-hypertensive patients, with significant reductions noted in baseline and follow-up GFR as well as during the initial visit (p < 0.05).

GFR Based on Symptom Severity. A greater decline in GFR was observed in patients with severe symptoms compared to those with mild or moderate symptoms (p < 0.05). However, no significant differences were noted between the GFR measured during the first visit and the follow-up GFR in these patients.

#### **Discussion**

This retrospective cohort study evaluated the long-term renal outcomes in COVID-19 survivors, with a particular focus on serum creatinine levels and GFR. Findings of the present study demonstrate that, COVID-19 can affect kidney function, especially in association with underlying factors such as hypertension and diabetes, and female gender, which may be risk factors for more severe renal complications in patients with COVID-19. Contrary to some reports, such as B. Bowe et al. (2021), who identified a decline in GFR among CO-VID-19 survivors, our study did not find statistically significant changes in GFR [6]. The differences may be due to varying follow-up durations, patient populations, or methods of renal function assessment.

Notably, in subgroup analyses, hypertension and diabetes emerged as significant factors associated with renal function decline. Hypertensive patients exhibited a statistically significant decrease in GFR compared to nonhypertensive individuals, indicating that pre-existing hypertension may predispose patients to a greater risk of long-term kidney impairment post-COVID-19. Hypertension has been identified as a significant risk factor for adverse renal outcomes in COVID-19 patients. A study found that pre-existing hypertension was associated with an increased risk of developing AKI during

COVID-19 hospitalization, which subsequently led to poorer long-term renal recovery. The study highlighted that hypertensive patients had a higher incidence of major adverse kidney events (MAKE), including progression to endstage kidney disease (ESKD) and increased mortality rates [7]. Furthermore, a retrospective cohort study assessed long-term kidney outcomes in patients with COVID-19-associated AKI. The study reported that individuals with a history of hypertension had a higher likelihood of persistent renal dysfunction and a steeper decline in estimated glomerular filtration rate (eGFR) over time compared to normotensive counterparts. These findings suggest that hypertension exacerbates the vulnerability of renal function in the context of COVID-19, necessitating vigilant monitoring and management of blood pressure to mitigate long-term renal complications [8]. Additional evidence supports the role of specific antihypertensive medications in modulating renal outcomes during COVID-19. A study examining the effects of COVID-19 on patients with stage 1–2 hypertension and CKD found that the use of angiotensin-converting enzyme inhibitors (ACEi) was associated with a more pronounced decline in renal function. This was evidenced by increased serum creatinine levels and decreased estimated glomerular filtration rate (eGFR). The findings suggest that ACEi may exacerbate renal dysfunction during COVID-19 due to their role in modulating the renin-angiotensin system (RAS) [9]. By contrast, hypertensive patients without COVID-19 did not exhibit such significant changes in creatinine levels, underscoring the direct impact of CO-VID-19 on renal parameters. Moreover, serum creatinine has been identified as a potential predictor of COVID-19 severity in hypertensive patients. An observational study analyzing hospitalized COVID-19 patients with hypertension demonstrated a significant positive correlation between elevated serum creatinine levels and worse clinical outcomes. Each unit increase in creatinine was associated with a 72% higher risk of severe disease, suggesting that creatinine can serve as a reliable biomarker for renal impairment and an indicator of poor prognosis in this patient population [10]. Another retrospective study evaluated the interplay between comorbidity burden and renal outcomes in hypertensive COVID-19 patients. It revealed that individuals with additional comorbidities, such as diabetes, coronary artery disease, and chronic obstructive pulmonary disease (COPD),

had significantly higher creatinine levels compared to those with hypertension alone. The study further identified elevated creatinine as a risk factor for mortality, highlighting the compounded vulnerability of patients with multiple comorbidities [11].

Similarly, diabetic patients experienced a significantly greater GFR decline compared to non-diabetic patients. These findings underscore the importance of closely monitoring kidney function in high-risk groups following COVID-19 recovery. A systematic review and meta-analysis demonstrated that COVID-19 is associated with a two-fold increase in nephropathy and AKI in patients with type 2 diabetes compared to non-diabetic individuals. The study underscored that diabetic patients not only had a higher incidence of AKI during acute COVID-19 illness but also faced greater challenges in renal recovery, with increased rates of progression to CKD [12]. Additionally, research evaluated the long-term renal outcomes of critically ill COVID-19 patients with AKI requiring continuous renal replacement therapy (CRRT). The study found that diabetic patients exhibited lower rates of renal recovery and higher dependency on dialysis at 6- and 12-months post-infection compared to nondiabetic patients. A study demonstrated that in hospitalized patients with COVID-19 and type 2 diabetes, serum creatinine levels were notably higher in those who succumbed to the disease compared to survivors. By the second week of hospitalization, creatinine levels in deceased patients had risen significantly, indicating its role as a prognostic marker in diabetic patients with COVID-19. Furthermore, the combination of elevated body mass index (BMI) and high creatinine levels was associated with an increased risk of mortality, underscoring the compounded impact of obesity and renal dysfunction in this population [13].

Another investigation revealed that during the pandemic isolation period, glycemic control worsened in patients with type 2 diabetes, leading to increased fasting glucose and creatinine levels. This deterioration in blood glucose regulation was attributed to disrupted routine medical care, which likely contributed to heightened renal stress and elevated creatinine concentrations [14].

Additionally, research indicated that diabetic patients with COVID-19 commonly presented with persistent hyperglycemia, elevated serum creatinine, and higher markers of

inflammation and coagulation. These factors were associated with a more severe clinical course, highlighting the significant interplay between diabetes and COVID-19 in exacerbating renal dysfunction [15].

The severity of COVID-19 has a profound impact on renal function, as evidenced by elevated serum creatinine levels and changes in biochemical markers. Severe cases of COVID-19 are consistently associated with higher levels of creatinine, which serve as indicators of kidney stress and damage. Research on kidney transplant recipients (KTRs) highlighted that individuals who experienced severe COVID-19 showed a significant decline in eGFR one year after recovery. This effect was particularly pronounced among male patients, indicating the lasting impact of severe infection on renal function [16].

Another study focusing on biochemical changes during COVID-19 demonstrated that patients with moderate and severe disease had significantly higher creatinine levels compared to those with mild cases. Elevated inflammatory markers, such as C-reactive protein (CRP) and ferritin, were also associated with worsening kidney function in severe cases. These markers were linked to an increased risk of acute kidney injury (AKI) and long-term renal dysfunction, underscoring the critical role of systemic inflammation in renal outcomes [17]. Furthermore, early changes in creatinine levels and eGFR during COVID-19 have been identified as prognostic indicators of mortality. A study found that a creatinine level above 1.05 mg/dL on the first day of hospitalization and a decline in eGFR were strong predictors of poor outcomes in patients. These findings underscore the importance of monitoring renal parameters in severe cases to inform early intervention and enhance patient outcomes [18].

This study has several limitations that should be considered. The sampling in this study was both retrospective and prospective. Given that part of the sampling was retrospective, this may have introduced bias in data collection. Also, the study examined short-term and medium-term kidney function after recovery from COVID-19, and long-term outcomes are not yet well known.

#### **Conclusion**

Overall, the results of this study suggest that COVID-19 can affect kidney function, especially in association with underlying factors such as hypertension and diabetes, and female gender, which may be risk factors for more severe renal complications in patients with COVID-19. The decrease in GFR in patients with hypertension and diabetes highlights the importance of controlling these diseases in patients with COVID-19. Although no significant changes in creatinine and GFR levels were observed based on the severity of the disease, continuous monitoring of kidney function in these patients, especially in the presence of risk factors, seems necessary. Based on the findings of this study, future research should focus on the long-term kidney function in patients who have recovered from COVID-19. It is essential to examine how various factors, such as the type of treatment received, the specific medications used during hospitalization, and any underlying diseases, affect kidney outcomes. This can help us gain a better understanding of the long-term effects of COVID-19 on kidney health. Additionally, future studies should consider investigating gender differences and the impact of blood pressure on kidney outcomes in patients with COVID-19. Drawing from the findings of this study, it is essential that future research thoroughly investigates long-term kidney function in patients who have recovered from COVID-19. Specifically, studies should focus on the incidence of chronic kidney disease and other renal complications that may arise post-infection.

Researchers must examine a variety of factors that could influence kidney outcomes, including the nature of the treatment regimen — such as the use of antiviral drugs, corticosteroids, or other therapeutic interventions — alongside the specific medications administered during hospitalization. The presence of underlying health conditions, like hypertension, diabetes, or pre-existing kidney disease, should also be carefully considered as they may exacerbate kidney dysfunction after recovery from COVID-19.

Moreover, it is critical for future studies to address the issue of gender differences in kidney outcomes, as biological and hormonal variations may lead to disparate effects in male and female patients. Additionally, the role of blood pressure management in the post-recovery phase ought to be examined, as fluctuations in blood pressure can significantly impact renal health. Understanding these dynamics will provide crucial insights into the long-term effects of COVID-19 on kidney function and guide clinical practices for better patient management.

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