Covid 19 and renal failure: Likelihood of development of renal failure among Covid-19 patients and its clinical consequences

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ABSTRACT

Objective: To determine the frequency of renal failure among the Covid-19 infected patients and to explore clinical consequences among them by assessing the frequency of respiratory support, general symptoms, sequential organ failure assessment score, and mortality rate.

Study Design: A cross-sectional analytical study.

Place and Duration: From 1ST June 2020 to 1ST December 2020 at Covid ward of Nishtar Medical University and Hospital Multan.

Methodology: After confirmation of SARS-CoV-2 infection through Real-time RT-PCR, Patients were regularly evaluated for serum creatinine level, in compliance with the Kidney Disease Improving Global Outcomes guidelines. Based on creatinine level, patients were categorized into two groups: Group A comprised of patients who developed acute renal failure while group B consisted of patients whose renal system remained intact. The two groups were then observed during their covid-19 course for the development of associated symptoms, laboratory findings, and development of any complexity. Afterward, the sequential organ failure assessment score (SOFA) was calculated

Results: Out of the total studied population (n=158) , 18.1% of patients were positive for covid-19 and renal failure. There was no significant difference between underlying comorbidities and general covid-19 symptoms between the two study groups. However, renal failure patients recorded significantly high values of CRP (57mg/L±11 vs 45.9mg/L±8) and a significant number ($p<0.05$) required various means of respiratory support. 8.6% of renal failure patients in contrast to 20.6% suffered shock. A higher rate of mortality ($p=0.03$) was observed among covid-19 patients who developed renal failure.

Conclusion: A significantly high percentage of covid-19 infected patients develop renal failure and not only suffered from severe clinical outcomes but also had a high mortality rate.

Keywords: Renal failure, Renal injury, Covid-19, In-hospital consequences, Infection, Mortality.

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INTRODUCTION

Acute respiratory illness was found rapidly among the people of China in December, the year 2019. Later research found that the disease was caused by a virus known as severe acute respiratory syndrome coronavirus, also known as SARS-CoV-2[1]. The World Health Organization changed the name of this disease to Corona Virus Disease 2019 or COVID-19 in February 2020. The disease was not subtle as it was spread in multiple areas from Wuhan-China. According to the Chinese health authorities, it was declared that there were 79,389 cases of Covid-19 on February 29, 2020. Also, in overall provinces, 2838 deaths were reported. Whereas in Wuhan, the situation was uncontrollable as there were 48,557 cases reported, and in one day, 2169 people died of the disease. Afterward, the disease was spread to other countries as well, including Thailand, Japan, Korea, Germany, and Singapore[2]. Studies have shown that it spreads mainly from person to person mostly from those who are in close contact[3].

Renal failure is the abnormal presentation of morphological features or functionality of the kidney for more than 3 months[4]. Mostly underlying chronic kidney disease (CKD) acts as a risk

factor for acute renal failure (ARF). However, if the kidney injury becomes irreversible, ARF is transformed into chronic renal failure (CRF). The diagnostic criteria of CKD are the decline of glomerulus filtration rate (GFR) by less than 60ml/min/ /1.73m^2; secretion of at least 30mg of albumin in 24hrs, or persistence of other signs of kidney damage such as hematuria for more than 3 months[5]. According to US reports, more than 500,000 renal failure patients are currently under dialysis treatment[6]. It has been found that such patients not only have a depressed immune system but also have multiple underlying comorbidities which reduce the body's ability to fight against foreign pathogens. Similarly, being a regular visitor of crowded hospitals and hemodialysis centers multiplies the risk of covid-19 infection in renal failure patients[7].

Furthermore, renal epithelium expressing angiotensin-converting enzyme 2 (ACE2) acts as a receptor for SARS- CoV-2. Resultantly, renal epithelium suffers from severe injury and the normal metabolic function ACE2 is disturbed; thereby, aggravating the clinical presentation in patients with acute kidney disease[8]. We conducted this study with an objective to determine the frequency of renal failure among the Covid-19 infected patients and to explore clinical consequences among them by assessing the frequency of respiratory support, general symptoms, sequential organ failure assessment score, and mortality rate.

METHODOLOGY

This cross-sectional analytical study was performed at the Renal Department and Covid-19 Centers at Nishtar Medical University and Hospital, Multan, from 1st June 2020 to 1st December 2020. Patients aged more than 18 years from both genders were and who showed positivity for covid-19 infection were included in the study. All the participants were analyzed for their creatinine level at the time of participant enrollment in the study. Those who lie outside the standard creatinine range (<75 µmol/L for females and <105 µmol/L for males) were excluded from the study to avoid bias in the study results with the inclusion of pre-existing renal failure. Similarly, the covid-19 positive patients who declined to give consent were excluded from the study. Baseline characteristics including demographics and underlying comorbidities were recorded initially.

Real-time RT-PCR was used to analyze the Oropharyngeal swab samples of the SARS-CoV-2 RNA. The renal condition of the patient was assessed through serum level analysis of serum urea and creatinine, along with volume status and urine output. This was done to exclude any patient pre-existing tendency of renal failure. The prime outcome of acute kidney injury (AKI) was characterized as a rise in serum creatinine by ≥26.5 µmol/L within 48 h or an alteration in serum Cr by ≥ 1.5 times of baseline within 1 week, based on Kidney Disease Improving Global Outcomes Guidelines[9]. Participants were then categorized into two study groups based on their renal failure status. Based on the above-defined criteria of AKI, Group A comprised of those who developed renal failure while group B included Covid positive patients with the intact and fully functional renal system. The two groups were then observed during their covid-19 course for the development of associated symptoms, derangement in laboratory findings, and development of any complexity especially in terms of the need for respiratory support. Afterward, the sequential organ failure assessment score (SOFA) was calculated[10].

Data Analysis: The data recorded of the COVID-19 patients who developed either chronic renal failure or acute renal failure and the ones who do not have renal failure were compared. The student's *t*-test was used for the analysis of continuous variables. In contrast, the χ^2 test was used for the analysis of categorical variables. Median and mean standard deviation of the variables were calculated. The study to determine the clinical outcomes of renal failure was also done with a 95% confidence interval. The analysis was done by SPSS 23 version and the P-value less than 0.05 was considered significant.

RESULTS

One hundred fifty-eight patients were enrolled in the study out of which 100 were males, and 58 were females. Forty-two patients were excluded due to testing negative for Covid-19. Among the final study population (N=116), renal failure was diagnosed in 21 (18.1%) patients. The data collected from the rest of the patients are explained below. Cardiovascular diseases were the most prevalent underlying comorbidity in both groups (32.7% in non-renal failure patients and 8.6% in renal failure patients). Further, the time of appearance of symptoms was almost similar in both the groups, and an insignificant difference was found in the immune status of both the groups (Table-I).

Table-I: Prehospital characteristics of patients suffering from COVID-19 (n=116)

	Group A (n=21)	Group B (n=95)	*P*-value
Sex(male)	12 (10.3%)	54 (46.5%)	0.12
AGE(years)	61.05±12	58.5±14	0.47
BMI (mean± SD)	23.9±6	23.1±2	0.44
Comorbidity (n, %)			
Diabetes mellitus	2 (1.7%)	26 (22.4%)	0.2
Hypertension	9 (7.7%)	29 (25%)	0.4
Cardiovascular diseases	10 (8.6%)	38 (32.7%)	0.6
Respiratory diseases	4 (3.4%)	10 (8.6%)	0.4
Time from symptom onset to hospital days (mean± SD)	10.8 ± 12.3	10.4 ± 7.8	0.8
Antiviral use before hospital admission	8 (6.8)	45 (38.7)	0.5
immunosuppressed	2 (1.7)	5 (4.3)	0.8

On observing in hospital condition of participants from both the groups, it was found that general covid-19 symptoms such as fever, cough, myalgia, and diarrhea were common between both the groups and no significant difference was found in terms of their occurrence rate; however, then renal failure patients had a significantly high level of C- reactive protein (CRP) with a mean value of 57 mg/L as compared to mean value of 45.9 mg/L. Similarly, a significant number of patients (P=0.05) in the renal failure group developed serious respiratory complications who

required respiratory support as compared to another studied group. 10 renal failure patients (8.6%) in contrast to 24 (20.6%) suffered shock reflecting a significantly higher number of affected renal failure patients (p=0.04) (Table-II).

Table II: In-hospital situation of coronavirus patients (n=116)

		Group A (n=21)	Group B (n=95)	P-value
In a hospital situation (n, %)	Fever	21 (18.1%)	78 (67.2%)	0.06
	Cough	17 (14.6%)	62 (53.4%)	0.16
	Myalgia	5 (4.3%)	24 (20.6%)	0.8
	Diarrhea	4 (3.4%)	26 (22.4%)	0.4
Laboratory findings (mean ± SD)	WBC × 109/L	6.8± 1.2	5.43± 2.5	0.44
	LYM, ×109/L	0.7± 0.65	0.83± 0.63	0.22
	NT-ProBNP, pg/ml	471± 71	253± 75	0.68
	D-Dimer, mg/L	0.5± 1.2	0.53± 0.9	0.91
	Hs-CRP,mg/L	57± 11	45.9± 8	0.5
	ESR, mm/h	37± 12	39± 15	0.97
	Ferritin, µg/L	515± 100	618± 187	0.669
	IL-6, pg/mL	46± 13	22± 15	0.938
Disease severity status (n, %)	General	4 (3.4%)	37 (31.8%)	0.08
	Severe	6 (5.1%)	31 (26.7%)	0.71
	Critical	11 (9.4%)	26 (22.4%)	0.02+
	SOFA score	4.5±2.1	2.8±1.4	0.002+
Respiratory support (n, %)	Ambient air	1 (0.86%)	22 (18.9%)	0.1
	Nasal cannula	6 (5.1%)	47 (40.5%)	0.13
	HFNC	3 (2.5%)	6 (5.1%)	0.43
	NIPPV	2 (1.7%)	8 (6.8%)	1
	IPPV	6 (5.1%)	7 (6.0%)	0.01
	ECMO	3 (2.5%)	4 (3.4%)	0.05
	Shock	10 (8.6%)	24 (20.6%)	0.04

[HFNC: High flow nasal cannula; NIPPV: non-invasive positive pressure ventilation; IPPV: Invasive positive pressure ventilation; ECMO: extracorporeal membrane oxygenation]

Further, it has been shown that mortality rates and SOFA were significantly higher in renal failure patients (Table-III). Table IV refers to disturbances in body functionality in renal failure.

Table-III: Outcomes related to Renal Failure (N=158)

Outcomes	P=Value
Mortality	0.03
SOFA Score	0.02

Table-IV: Fluid Balance in patients with and without Renal Failure (N=158)

	Group A	Group B	P-value
Urine Output (mean± SD)	0.5±0.7	1.2±0.4	0.07
Fluid Balance	457.2±123.6	182.1±78.9	0.03

DISCUSSION

Covid-19 has taken the world by storm since its first diagnosis. Even healthy people from around the world, with an intact immune system, have become victims of this novel pathogen. In this study, it was found that around 21% of the studied population developed renal failure, with the course of the disease. These incidences lie within the reported range of the previous studies from 0.5 to 36.6%[11,12]. Among some studies, an incidence rate as low as 8.1% has been found. This difference is more likely due to variation in definitions of acute kidney failure being considered[13]. The higher incidence rate in our study may be due to the inclusion of older patients, aged 61 years on average, with more comorbidities than the previous studies since the cohort study that reported an incidence of 8.1% included younger patients with a median age of 46 years. Our study results can further be validated with the results of the recent study in New York that examined kidney injury in Covid positive patients, aged 64 years on average[14]. In the US research, the incidence of kidney failure was found to be 36.6%, which is close to our study results.

It is also necessary to understand that our study was conducted during the second wave of the outbreak in Pakistan. Therefore, relatively critical infectious cases were admitted. Moreover, patients who developed renal disease posed a significant health burden with the requirement of ICU, extended hospitalization, and greater death risk. Thus, it was necessary to explore underlying factors that predisposed to the development of kidney failure in Covid-19 patients.

We have observed that although the renal failure patients presented with underlying comorbidities, yet their frequency was less than those in non-renal failure patients. This difference doesn't however affect the clinical presentation of covid-19 in renal failure patients as they still experienced severe complications. Between the two study groups, CRP was raised significantly among renal failure patients while other parameters were characteristic. Raised CRP is already being established as a common finding of covid-19 infection and an important predictor between mild and severe covid-19 infection[15]. C-reactive protein is usually synthesized by the liver. It has been found that liver function is disturbed by SARS-CoV-2 infection as other parameters like Alkaline Transaminase (ALT) and Aspartate Transaminase (AST) are also found to be disturbed in infected patients[15]. Therefore, it is safe to predict that difference in CRP values between the two study groups shows that in renal failure patient's liver was more severely affected than non-renal failure patients. Moreover, it is also found that liver damage in mild covid-19 cases is reversible while severe condition requires long-term treatment[16].

In our study significant (p=0.02) several renal failure patients went critical during their disease course; thereby requiring respiratory support to maintain their oxygen saturation. Similarly, 47.6% of renal failure patients suffered shock as their condition worsened. In another study Gupta et Al., recorded the causes behind critically ill patients. They found that hypoxemia, renal dysfunction, and liver malfunctions were the basic reason behind the increased mortality rate among covid-infected patients[17]. In our study, aggravation of renal failure was noted in acute renal failure patients after apparent worsening of symptoms which then lead to chronic renal failure.

Moreover, the coronavirus patients with acute renal failure had low urine output and fluid accumulation, leading to edema in them as compared to regular acute renal failure patients. At the

same time, the patients of early diagnosed renal failure have less fluid accumulation than patients with late renal failure diagnosis. This proves that prolonged hospital stay, high mortality rate, and dysfunction of the organ may be caused by fluid accumulation. The treatment or solution for this condition is to determine the optimum hydration level for coronavirus patients who are still unknown.

CONCLUSION

A significantly high percentage of covid-19 infected patients develop renal failure and not only suffered from severe clinical outcomes but also had a high mortality rate.

AUTHOR'S CONTRIBUTION

Khalid P: Conceived idea, Design research methodology, Data analysis, Manuscript writing
Wazir Z: Data collection, Data analysis, Literature review
Khan FY: Manuscript writing, Data analysis, Data collection, Literature review
Abbas G: Design research study, Data analysis, Manuscript writing
Khan L: Manuscript writing, Data analysis
Rehman FU: Manuscript drafting, Data analysis, Data collection, Literature review

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