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Study of Three Years Follow Up Effect of Covid-19 Infection on Patients on Chronic Kidney Disease

Lamis Essam Khedr*, Saeed Abdel Wahab Saeed, Rehab Ahmed Fathallah Kheir, Khaled Gouda
Department of Internal Medicine & Nephrology, Faculty of Medicine, Ain Shams University, Egypt
***Corresponding author:** Lamis Essam Khedr**, Mobile: (+20)** 01276209993**, E-mail:** Lamis.khedr@med.asu.edu.eg

ABSTRACT

Background: Patients suffering from chronic kidney disease (CKD) are five times more likely to get a severe COVID-19 infection.

Objective: We aimed to determine the renal outcomes in patients with CKD who had been infected with Covid-19 and follow up its effect through 3 years.

Methods: This retrospective observational study was conducted on data of total 60 adults CKD patients with diagnosis of Covid-19 infection, at Nephrology Outpatient Clinic of Ain Shams University Hospital. Participants were categorized into 3 groups according to CKD stage; group 1: CKD 1 (n=3), group 2: CKD 2 (n=27) and group 3: CKD 3 (n=30).

Results: The quick COVID-19 severity index (qCSI) was significantly higher in in CKD 3 group compared to CKD 1 and CKD 2 groups (P= 0.001 & 0.001). Intensive care unit (ICU) admission, mechanical ventilation (MV), incidence of AKI and mortality were significantly different among the studied groups ($P < 0.05$), being higher in CKD 3 and not observed in CKD 1 suggesting the increased risk with advanced CKD stage.

Conclusions: The severity and risk of COVID-19 tend to increase with advanced stage (stage 3) compared to stage-1 and 2. Additionally, creatinine level had been increased while glomerular filtration rate (GFR) had decreased significantly during the follow-up period. Stage-3 exhibited worse outcome such as ICU admission, increased demand for mechanical ventilation (MV) and higher incidence of AKI and mortality.

Keywords: Follow Up, Covid-19, CKD, Stage, Severity.

INTRODUCTION

Globally, the coronavirus disease (COVID-19) is thought to have killed 6 million people [1]. The more severe SARS-CoV-2 infection types have been linked to a number of risk variables, the most significant of which are male gender and advanced age for an increased risk of fatality. Numerous underlying comorbidities, including obesity, hypertension, diabetes mellitus, chronic disease, and cancer, have been reported to be related with the mortality of SARS-CoV-2 in addition to age and male gender [2]. Due to their immunosuppressive condition and continuous systemic inflammation, patients with CKD are five times more likely than the general population to experience a severe COVID-19 infection [3].

It is important to comprehend the effects of AKI in COVID-19 patients, with a particular emphasis on the post-acute phase, in order to effectively manage renal disease going forward. Prior research mostly focused on the impact of COVID-19-related AKI on hospitalized renal status; however, there is a paucity of information on the pandemic's effects on the health and treatment of CKD patients and their caregivers [4, 5]. Therefore, we performed this study to determine the renal outcomes in patients with CKD who had been infected with Covid-19 and follow up its effect through three years.

PATIENTS AND METHODS

This retrospective observational study was conducted on data of total 60 adults CKD patients aged above 18 years and below 65 years, from stage 1 to stage 3 with diagnosis of the Covid- 19 infection, which was confirmed by a positive real-time reverse-transcriptase polymerase chain reaction (RT-PCR) result from nasopharyngeal swabs were enrolled in the study. It was conducted at Nephrology Outpatient Clinic, Ain Shams University Hospital through the period from 2020 to 2023. Three to six months after date of infection of covid-19 and three years follow up. Case criteria for confirmed SARS-Cov-2 infections in humans follow the WHO's interim guidelines [6]. In this study, only patients with an infection verified by a laboratory were included.

Exclusion criteria: Patients who declined the informed consent, CKD pregnant women, ESKD patients on regular haemodialysis (stage 5), patients who were vaccinated with Covid-19 vaccines before enrolment, had a confirmed diagnosis of malignancy or expected survival rate of less than 6 months, and previous history of kidney transplant.

Grouping: Participants were categorized into 3 groups according to CKD stage: Group 1: CKD 1 (n=3), group 2: CKD 2 (n=27) and group 3: CKD 3 (n=30).

Clinical, laboratory, and radiological data were taken from the patients' medical records, where all patients underwent history taking including personal (age, gender, smoking history, work state and comorbidities), medical, surgical and drug history, CKD specification (stage, etiology and duration), Covid-19 specification (severity, place of treatment if ward or ICU, treatment was given and vaccines had been given later), clinical examination, and laboratory investigations including (serum creatinine level recorded, GFR, CBC, Iron profile, Na, K, Protein / Creatinine ratio and ABG recorded).

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Serum creatinine level was recorded at the last visit preadmission with infection of Covid-19 (baseline serum creatinine), at time of admission after getting infected (Day 0) with serially follow up during admission and at the third and sixth month after infection then for every single year till the baseline serum creatinine now. GF was calculated using the Modified Diet in Renal Disease (MDRD) Equation. The MDRD equation estimates GFR from serum creatinine and is more accurate for GFR < 60 ml/min/1.73 m^2. The estimated GFR (eGFR) was determined for each patient using the baseline serum creatinine value [7] . CBC, iron profile, Na, K, protein/creatinine ratio and ABG recorded before getting infected, during admission at hospital within infection and the last recorded result now. The day of the first positive swab for Covid-19 was designated as day 0 of sickness for the study.

Ethical approval: Ain Shams University's Faculty of Medicine Ethics Committee authorized the study [reference number: FAMSU MS700/2023]. Written informed consents were acquired from the patients or their family members. The Helsinki Declaration was followed at every level of the study.

Statistical analysis

SPSS Version 28.0 was utilized for doing statistical analysis. The data distribution's normality was assessed using the Shapiro-Wilks test and histograms. Tukey's Post-Hoc analysis was performed using the ANOVA (F) test on quantitative parametric data, which were shown as Mean ± SD. When comparing each group, the Kruskall-Wallis test and the Mann-Whitney test were used to analyze the quantitative non-parametric data, which were reported as the median and IQR. Utilizing the X^2-test, qualitative variables were analyzed and reported as frequency and percentage (%). For statistical significance, a two-tailed P value of ≤ 0.05 was used.

RESULTS

On admission, there was an insignificant difference among the studied groups regarding Hb, K^+, iron, ferritin, P/C ratio, $PaCO_2$ and creatinine (Table 1).

Table (1): Baseline characteristics and data on admission of the studied groups of different CKD stages

		CKD 1 (n=3)	CKD 2 (n=27)	CKD 3 (n=30)	P value
Age (years)		51.33 ± 1.53	52.44 ± 13.78	61.03 ± 15.56	0.075
Gender	**Male**	2 (66.67%)	18 (66.67%)	16 (53.33%)	0.574
	Female	1 (33.33%)	9 (33.33%)	14 (46.67%)	
BMI (Kg/m^2)		35.33 ± 0.58	26.47 ± 5.47	23.55 ± 5.13	**0.001***
		P1= 0.019*, P2= 0.001*, P3= 0.096			
Duration (years)		1.0 ± 0	6.81 ± 3.49	10.17 ± 5.77	**0.002***
		P1= 0.118, **P2= 0.006*, P3= 0.027***			
Comorbidities					
Smoking		0 (0.00%)	15 (55.56%)	12 (40.00%)	0.137
DM		3 (100%)	15 (55.56%)	18 (60.00%)	0.329
HTN		3 (100%)	12 (44.44%)	21 (70.00%)	0.051
COPD		0 (0.00%)	12 (44.44%)	9 (30.00%)	0.223
CVD		3 (100%)	15 (55.56%)	12 (40.00%)	0.104
Vital signs at day 0					
Temperature (° c)		38.0 ± 0.01	38.05 ± 0.49	37.86 ± 0.42	0.256
HR (bpm)		100.0 ± 0.01	88.78 ± 11.64	88.2 ± 10.27	0.199
SBP (mmHg)		140.0 ± 0.01	140.0 ± 23.53	150.0 ± 29.57	0.348
DBP (mmHg)		80.0 ± 0.01	88.33 ± 11.27	90.0 ± 17.17	0.512
O_2 saturation (%)		95.0 ± 0.01	91.89 ± 1.95	87.7 ± 4.92	**< 0.001****
		P1= 0.376, **P2= 0.006*, P3< 0.001****			
Baseline laboratory data					
Hb (g/dL)		10.0 ± 0.01	10.56 ± 0.89	9.46 ± 1.25	**0.001***
		P1=0.674, P2=0.686, **P3= 0.001***			
PLT (10^3/µL)		200.0 ± 0.01	276.33 ± 18.21	221.9 ± 53.32	**0.035***
		P1=0.290, P2=0.900, **P3=0.042***			
TLC (10^3/µL)		11.0 ± 0.01	7.01 ± 1.64	6.44 ± 1.3	**< 0.001****
		P1< 0.001, P2< 0.001**,** P3=0.305			
Na (mEq/L)		142.0 ± 0.01	139 ± 4.05	138.4 ± 3.02	0.231
K (mEq/L)		5.0 ± 0.01	4.75 ± 0.4	4.89 ± 0.42	0.304
Iron (mcg/dL)		45.0 ± 0.01	63.89 ± 15.54	59.3 ± 13.98	0.282
Ferritin (ng/dL)		200.0 ± 0.01	248.78 ± 61.87	247.5 ± 60.64	0.801

	CKD 1 (n=3)	CKD 2 (n=27)	CKD 3 (n=30)	P value
P/C ratio	600.0 ± 0.01	400.89 ± 98.86	459 ± 112.91	0.803
pH	7.4 ± 0.01	7.38 ± 0.03	7.38 ± 0.04	0.740
$PaCO_2$ (mmHg)	38.0 ± 0.01	42.89 ± 7.07	45.6 ± 6.11	0.082
HCO_3 (mmol/L)	23.5 ± 0.01	21.72 ± 1.25	21.33 ± 1.53	**0.036***
	P1= 0.095, **P2= 0.032*,** P3= 0.535			
Creatinine (mg/dL)	2.0 ± 0.01	2.78 ± 0.68	3.48 ± 0.56	**< 0.001****
	P1= 0.160, **P2=0.002*, P3= 0.001***			
GFR (mL/min/1.73 m^2)	70.0 ± 0.01	74.22 ± 5.88	54.9 ± 3.17	**< 0.001****
	P1= 0.290, **P2< 0.001**, P3< 0.001****			
Laboratory data on admission				
Hb (g/dL)	10.0 ± 0.01	9.65 ± 1.25	9.42 ± 0.8	0.512
PLT (10^3/µL)	255.0 ± 0.01	285.44 ± 70.62	226.1 ± 55.42	**0.030***
	P1= 0.814, P2= 0.829, **P3= 0.022***			
TLC (10^3/µL)	14.0 ± 0.01	13.71 ± 2.69	16 ± 3.01	**0.011***
	P1= 0.984, P2= 0.473, **P3= 0.009***			
Na (mEq/L)	144.0 ± 0.01	143 ± 3.78	139 ± 5.61	**0.006***
	P1= 0.936, P2= 0.199, **P3= 0.007***			
K (mEq/L)	5.6 ± 0.01	5.7 ± 0.67	5.83 ± 0.7	0.704
Iron (mcg/dL)	45.0 ± 0.01	61.78 ± 15.01	58.9 ± 13.38	0.298
Ferritin (ng/dL)	400.0 ± 0.01	593.56 ± 146.91	637.7 ± 157.81	0.193
P/C ratio	600.0 ± 0.01	461.89 ± 112.89	526.8 ± 130.78	0.692
pH	7.35 ± 0.01	7.32 ± 0.07	7.27 ± 0.06	**0.005***
	P1= 0.710, P2=0.094, **P3= 0.010***			
$PaCO_2$ (mmHg)	40.0 ± 0.01	50.44 ± 6.32	48.8 ± 8.59	0.077
HCO_3 (mmol/L)	24.0 ± 0.01	19.37 ± 1.75	18.7 ± 2.27	**< 0.001****
	P1= 0.001*, P2< 0.001,** P3= 0.426			
Creatinine (mg/dL)	4.0 ± 0.01	5.17 ± 1.22	5.3 ± 1.31	0.354
GFR (mL/min/1.73 m^2)	60.0 ± 0.01	63.56 ± 7.27	50.5 ± 4.8	**< 0.001****
	P1= 0.595, **P2= 0.030*, P3< 0.001****			

BMI: body mass index, CVD: cardiovascular disease, Hb: hemoglobin, PLT: platelets. TLC: total leucocytic count, P/C: protein to creatinine ratio, GFR: glomerular filtration rate, *: statistically significant as p value <0.05, P1: p value between CKD1&2, P2: p value between CKD1&3, P3: p value between CKD2&3.

*: Significant, P1: p value between CKD1&2, P2: p value between CKD1&3, P3: p value between CKD2&3.

The quick COVID-19 severity index (qCSI) was significantly higher in CKD 3 group compared to CKD 1 and CKD 2 groups (P= 0.001, 0.001), with no significant difference between CKD 1 and CKD 2 groups. The place of treatment either ward or ICU was insignificantly different among the studied groups. Regarding the outcome, ICU admission, mechanical ventilation (MV), incidence of AKI and mortality were significantly different among the studied groups (P<0.05), being higher in CKD 3 and not observed in CKD 1 suggesting the increased risk with advanced CKD stage (Table 2 & Figure 1).

Table (2): COVID severity and outcome of the studied groups of different CKD stages

		CKD 1 (n=3)	CKD 2 (n=27)	CKD 3 (n=30)	P value
Quick COVID-19 severity index (qCSI)		1.0 ± 0.0	2.67 ± 0.96	4.0 ± 1.51	**< 0.001****
		P1=0.083, **P2= 0.001*, P3= 0.001***			
Place of treatment	**Ward**	3 (100%)	21 (77.8%)	18 (60.0%)	0.174
	ICU	0 (0%)	6 (22.2%)	12 (40.0%)	0.174
ICU admission		0 (0%)	12 (44.4%)	27 (90.0%)	**< 0.001****
MV		0 (0%)	0 (0%)	12 (40.0%)	**0.001***
AKI		0 (0%)	15 (55.6%)	27 (90.0%)	**< 0.001****
Mortality		0 (0%)	0 (0%)	9 (30.0%)	**0.005***

Significant, P1: p value between CKD1&2, P2: p value between CKD1&3, P3: p value between CKD2 & 3

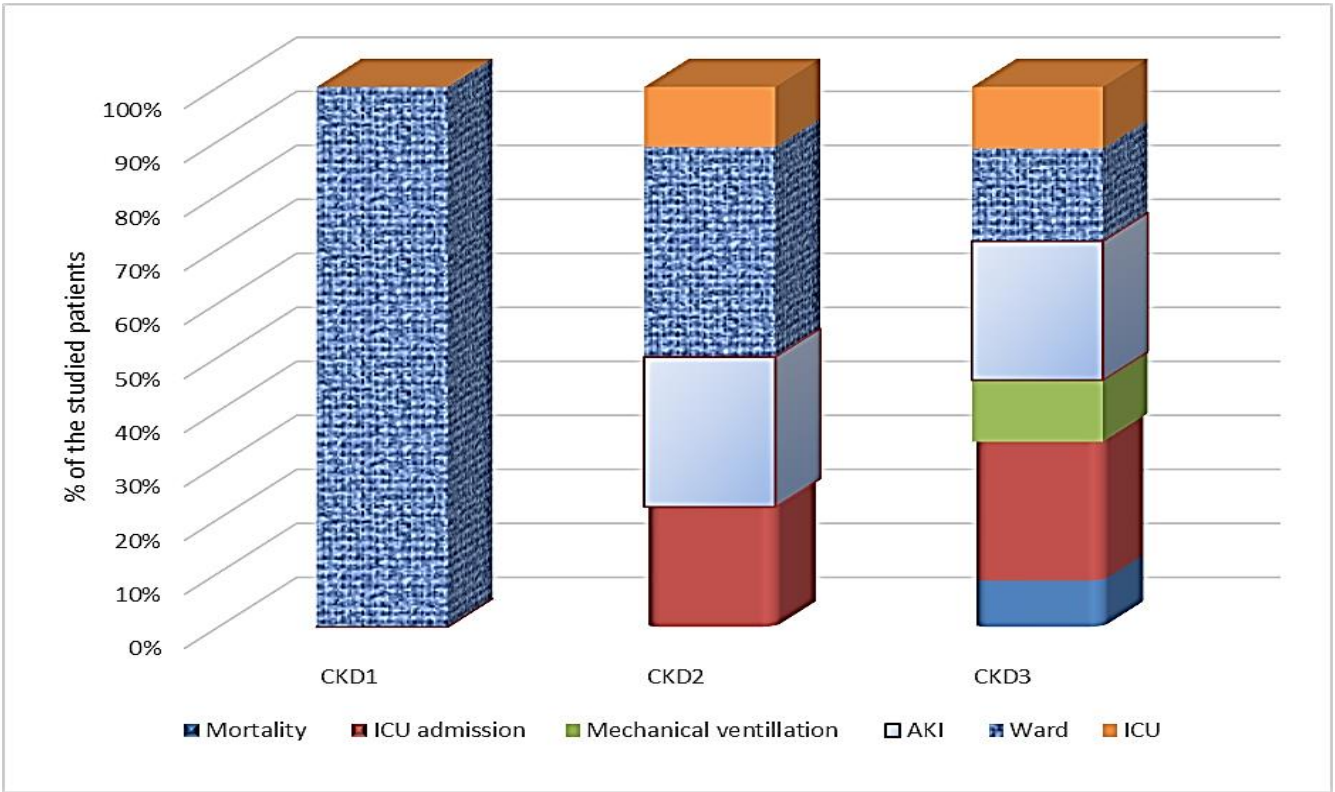

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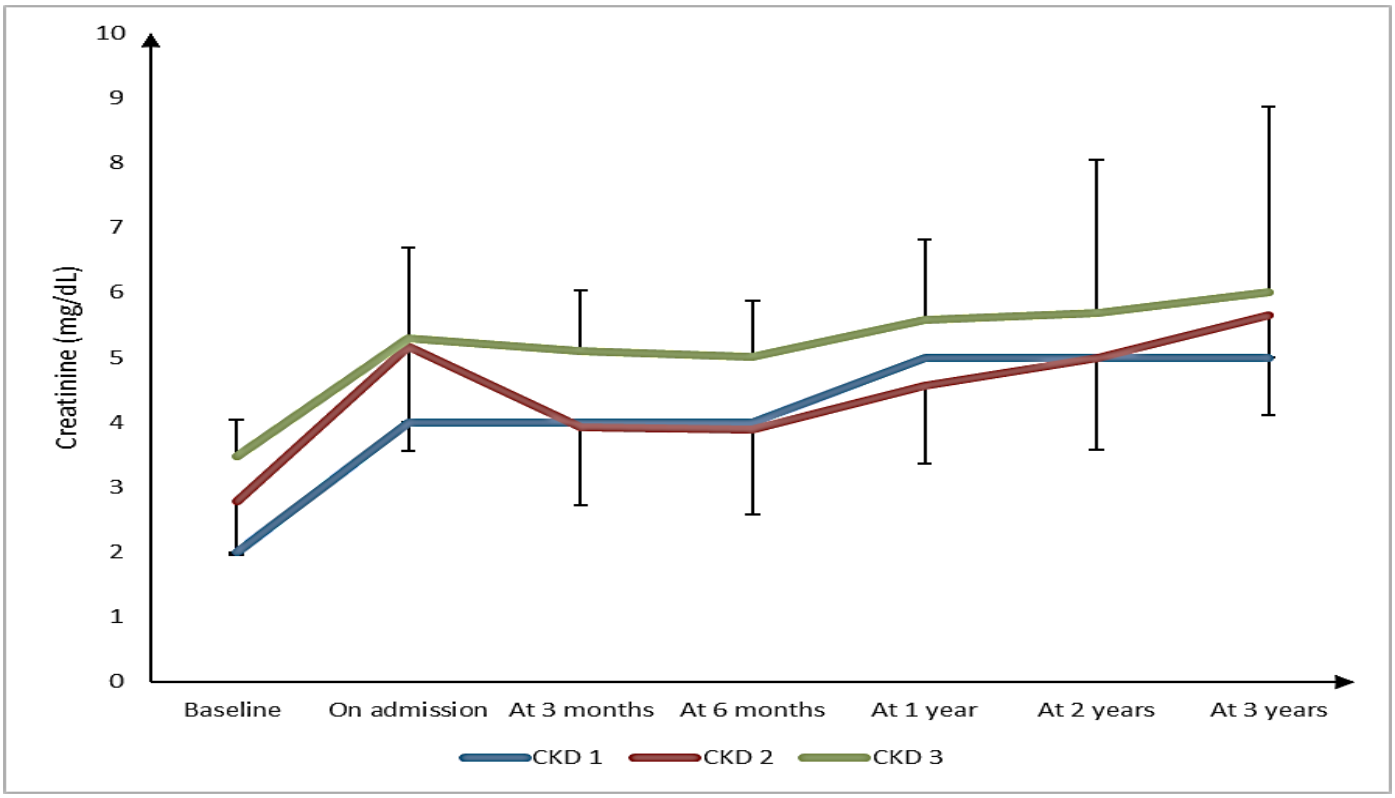
Figure (1): Outcome of the studied groups of different CKD stages.

Table (3) showed in all stages of CKD (1, 2, 3) that creatinine level had significantly increased on admission, at 3 and 6 months, at 1, 2 and 3 years compared to baseline (P<0.05), while GFR level had significantly decreased on admission, at 3 and 6 months, at 1, 2 and 3 years compared to baseline (P < 0.05) (Figure 2 & Figure 3).

Table (3): Creatinine and GFR of the studied groups of different CKD stages

	Creatinine (mg/dL)						
	Baseline	**Admission**	**3 months**	**6 months**	**1 year**	**2 years**	**3 years**
CKD 1 (n=3)	2.0 ± 0.01	4.0 ± 0.01	4.0 ± 0.01	4.0 ± 0.01	5.0 ± 0.01	5.0± 0.01	5.0± 0.01
CKD 2 (n=27)	2.78± 0.8	5.17 ± 1.62	3.91±1.18	3.89±0.31	4.56±1.19	5 ± 1.42	5.64±1.53
P value within group		**< 0.001****	**< 0.001****	**< 0.001****	**< 0.001****	**< 0.001****	**< 0.001****
CKD 3 (n=30)	3.48± 0.6	5.3 ± 1.39	5.1 ± 0.93	5.01±0.87	5.59±1.24	5.69±1.4	6 ± 1.87
P value within group		**< 0.001****	**< 0.001****	**< 0.001****	**< 0.001****	**< 0.001****	**< 0.001****
	GFR (mL/min/1.73 m^2)						
	Baseline	**Admission**	**3 months**	**6 months**	**1 year**	**2 years**	**3 years**
CKD 1 (n=3)	70.0 ±0.0	60.0±0.01	60.0±0.01	60.0±0.01	55.0±0.01	55.0±0.01	55.0±0.01
CKD 2 (n=27)	74.2±5.9	63.6±7.3	66.1±8.2	66.1±8.4	62.8±6.4	60±7.9	48.9±8.3
P value within group		**< 0.001****	**< 0.001****	**< 0.001****	**< 0.001****	**< 0.001****	**< 0.001****
CKD 3 (n=30)	54.9±3.2	50.5±4.8	50±4.55	49.8±4.26	47.3±7.65	48.1±9.8	45.9±2.5
P value within group		**< 0.001****	**< 0.001****	**< 0.001****	**< 0.001****	**< 0.001****	**< 0.001****



*: Significant

Figure (2): Creatinine of the studied groups of different CKD stages.

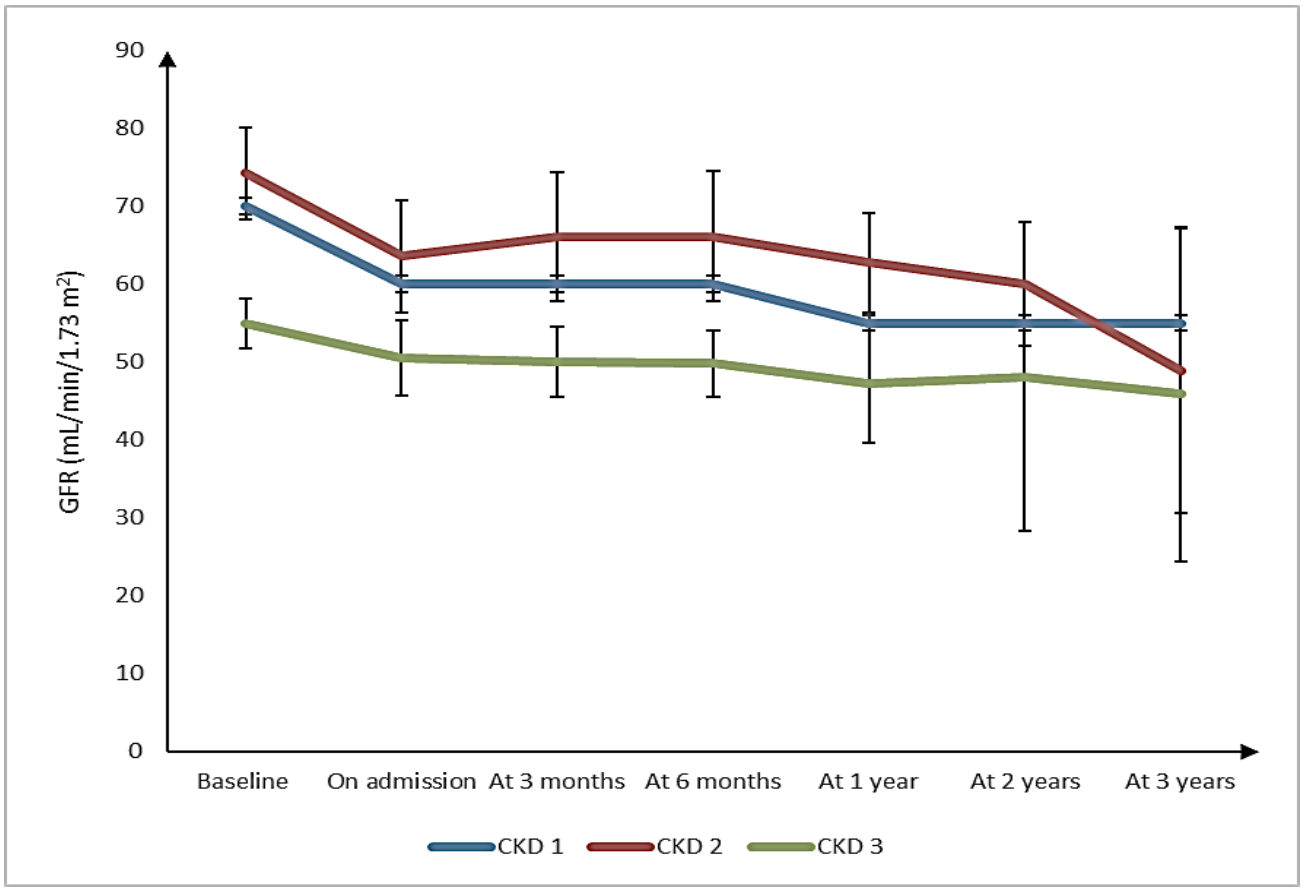


Figure (3): GFR of the studied groups of different CKD stages.

DISCUSSION

Kidney damage is common among hospitalized COVID-19 patients and is linked to an increased risk of death within the hospital. Oxidative stress, immunological dysregulation, and lymphopenia are linked to CKD and may contribute to the increased severity of COVID-19 in these individuals [8].

In the current investigation, it was discovered that around 5% of patients had stage 1, 45% had stage 2, and 50% had stage 3. In the present study, regarding history of ICU admission, MV, incidence of AKI and mortality were significantly different among the studied groups ($P < 0.05$), being higher in CKD 3 and not observed in CKD 1 suggesting the increased risk with advanced CKD stage. **Karadag *et al.*** [9] study, in which 173 patients were included, showed that about 65% of patients had ICU admission, 20% had MV, and 2.9% suffered mortality. AKI development occurred in 54.8% of hospitalized patients, whereas 7.9% of patients needed dialysis.

In our work we stated that in all stages of CKD (1, 2, 3) creatinine level had significantly increased on admission, at 3 months, at 6 months, at 1 year, at 2 years and at 3 years compared to baseline ($P < 0.05$), while GFR level had significantly decreased on admission, at 3 months, at 6 months, at 1 year, at 2 years and at 3 years compared to baseline ($P<0.05$). This is in agreement with **Nugent *et al.*** [10] study, which was conducted at five hospitals to evaluate the rate of change in eGFR following hospital discharge in 1,430 patients with AKI unrelated to COVID-19 and 182 patients with AKI associated with COVID-19. Once baseline comorbidities were taken into account, patients with COVID-19-associated AKI experienced a higher decline in eGFR (-12.4 ml/min/1.73 m^2/year). **Stockmann *et al.*** [11] reported that 74 patients with AKI with serious COVID-19 disease who needed renal replacement therapy (RRT) had their long-term results retrospectively examined. 76.5 ml/min/1.73 m^2 was the median baseline eGFR rate. 36 patients had passed away while receiving RRT, 1 patient remained in the hospital, and 37 patients had been released after a median follow-up of 151 days following the start of RRT. At the conclusion of the follow-up, 34 patients had recovered their kidneys to varying degrees, and 3 patients had not recovered their kidney function. **Moeinzadeh *et al.*** [12] found a highly significant decrease in follow-up GFR measurements and a highly significant increase in follow-up creatinine measurements in CKD patients. The research conducted by **Li *et al.*** [13] found that both critically ill and non-critically infected COVID-19 patients had a continuous reduction in kidney function one year after being discharged.

Limitations: This study had certain limitations as it was retrospective study that may increase bias probability, small sample size and being was single centre study. Therefore, we recommended provide larger sample size with multicentre cooperation to validate and generalize our results.

CONCLUSION

Patients with CKD are at high risk for COVID-19, but the severity and risk tend to increase with advanced stage (stage 3) compared to stage-1 and 2. Additionally, creatinine level had been increased while GFR had decreased significantly during the follow-up period. Stage-3 exhibited worse outcome such as ICU admission, increased demand for MV, higher incidence of AKI and mortality.

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