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Clinical And Biochemical Profile And Outcomes Of Covid-19 Patients With Chronic Kidney Disease

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Abstract

Background: Patients with a chronic kidney disease(CKD) might be at increased risk of developing severe COVID-19 disease. The data on clinical characteristics and biochemical profile of COVID-19-infected patients with CKD remains largely unknown.

Objective: To study the clinical and biochemical profile of patients with CKD and COVID-19 infection and to evaluate the outcomes in terms of severity of disease and mortality of patients with CKD and COVID-19.

Methods: This prospective study included 149 adult patients with CKD who presented with COVID-19 infection confirmed by real time RT-PCR, admitted to the hospital. Data of these patients was collected. Severity of COVID-19 illness was based on WHO criteria. Clinical outcome of patients was assessed based on length of hospital stay, co-morbidities, oxygen therapy and mortality. Relevant blood investigations were done.

Results: A Total of 149 patients with CKD were included(mean age= 53.8years, median 54.5) with 108 males(72.5%) and 41 females(27.5%). Patients were classified as mild(48), moderate(32) and severe(69). Most common co-morbidity was hypertension(81.8%), followed by diabetes(51%). At the time of admission, 32(21%) were asymptomatic and 117(79%) were symptomatic with breathlessness(n=73, 49%) as most common symptom. 101(67.8%) required oxygen support. Patients with severe illness had raised NLR (16.3), D-Dimer(2.1), LDH(512), CRP(140) Ferritin(1268). In-hospital stay was 9.96days and mortality rate was 32.9%(n=49)

Conclusion: The results of this study revealed significant correlation between the clinical severity of COVID-19 illness with CKD and higher mortality, raised NLR and inflammatory markers. Early detection of renal impairment with elevated inflammatory markers and effective intervention may reduce the mortality.

Keywords: NIL

Introduction

Coronavirus disease is a respiratory tract infection caused by a newly emergent coronavirus, that was first recognized in Wuhan, China, in December 2019. [1] Genetic analysis revealed it is a betacoronavirus which is closely linked to the SARS virus. Since then, the infection has been spreading to various parts of the world at an exponential rate. It was recognized as a pandemic by WHO on 30th January 2020 and the infection caused by the virus was named as COVID 19 disease on 11th February 2020. [2] The first reported case of COVID 19 in India was on 30th January 2020.

Majority of the patients infected with novel coronavirus have a mild disease without any complications. However, a small section of the patients can progress to severe illness. Patients who belong to higher age groups and those with co-morbidities are more prone to severe forms of the disease. The mortality in such groups is also higher.

Hence, such patients need specialized care and better monitoring to reduce the morbidity and mortality. One such vulnerable group is patients with chronic kidney disease. The risk of CKD patients developing both inpatient and outpatient pneumonia is 1.97 times more than general population.[3] Patients with chronic kidney disease developing pneumonia have a mortality rate that is 14-16 times higher than in the general population. [4]

Various biochemical investigations are currently being studied to identify early markers of severe illness in patients with chronic kidney disease for effective risk stratification. However, due to the exponential rise in the number of cases, it is essential to identify rapid, effective and inexpensive methods to identify the patients who may develop severe forms of the disease. This will enable reallocation of hospital resources optimally which can reduce the morbidity and mortality in patients with chronic kidney disease who contract covid-19 infection. This will also reduce the burden on the existing healthcare infrastructure.

Methodology:

The prospective study was carried out between January 2021 and April 2021 at a Bengaluru-based tertiary care centre. After obtaining approval and clearance from the institutional ethics committee, the patients fulfilling the inclusion criteria were enrolled for the study after obtaining informed consent. The study included patients aged ≥ 18 years of both the gender, diagnosed with COVID-19 infection by RT-PCR technique with past history of chronic kidney disease. The study excluded patients <18 years and those not willing to provide signed informed consent prior to the study. Case record forms with follow up chart were used to record the duration of disease, clinical features and complications.

COVID-19 infection was diagnosed by RT-PCR technique. Patients were categorised based on their severity according to WHO criteria. Mild illness was defined as patients having symptoms without evidence of hypoxia. Moderate illness was defined as patients having clinical signs of pneumonia (fever, cough, dyspnoea, tachypnea) but no signs of severe pneumonia including oxygen saturation of ≥90% on room air. Severe illness was defined as patients fulfilling any one of the criteria: (1) Shortness of breath, Respiratory rate ≥30/min, (2)Oxygen saturation ≤93%, (3)PaO2/FiO2 ≤300mmHg.

Patients underwent biochemical investigations which included complete blood count, liver function test, renal function test, serum electrolytes, serology, quantitative CRP, Serum LDH, D-dimer and serum ferritin at the time of admission. Co-morbid conditions like metabolic disorders, endocrine disorders, renal disorders, cardiac disorders, respiratory disorders were confirmed with past medical history.

All patients were followed up until discharge or death. Patients were discharged when two consecutive throat/nasopharyngeal swabs taken 24 hours apart are negative for SARS-CoV-2 RNA by RT-PCR technique. Clinical profile and biochemical investigations were correlated with severity and prognosis of disease.

Statistical analyses were carried out using **SPSS (Statistical Package For Social Sciences)** version 20. [IBM SPASS statistics (IBM corp. Armonk, NY, USA released 2011)]. Continuous variables were expressed as means, and standard deviation and categorical variables were presented as counts and percentages. Patients were grouped according to WHO severity criteria and as survival and succumbed to death. Data was subjected to normalcy test (Shapiro-wilk test). Data showed non normal distribution. Hence non-parametric tests (Kruskal-wallis and Mann-whitney) were applied. Comparison of the clinical parameters based on WHO case type was done using krusakl-wallis test. Comparsion of the clinical parameters based on outcome was done using mann-whitney test. Comparison of the days of hospital stay was done using kruskal-wallis test. P value of <0.05 was considered as statistically significant.

Results:

A Total of 149 patients with CKD were included with mean age= 53.8years, median 55 years). The most common age group was 46-55 years (n=44, 29.5%) followed by 56-65 years. (n=36, 24.2%)

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Table 1: Distribution of the subjects based on age

	N	Minimum	Maximum	Median	IQR
Age	149	18	91	55	20

Table 2: Distribution of the subjects based on age and who case type

Age		WHO CASE TYPE			Total
		Mild	Moderate	Severe	
18 to 25 yrs	Count	1	2	2	5
	%	.7%	1.3%	1.3%	3.4%
26 to 35 yrs	Count	5	2	6	13
	%	3.4%	1.3%	4.0%	8.7%
36 to 45 yrs	Count	8	7	6	21
	%	5.4%	4.7%	4.0%	14.1%
46 to 55 yrs	Count	16	7	21	44
	%	10.7%	4.7%	14.1%	29.5%
56 to 65 yrs	Count	8	6	22	36
	%	5.4%	4.0%	14.8%	24.2%
66 to 75 yrs	Count	10	4	10	24
	%	6.7%	2.7%	6.7%	16.1%
Above 75 yrs	Count	0	4	2	6
	%	0.0%	2.7%	1.3%	4.0%
Total	Count	48	32	69	149
	%	32.2%	21.5%	46.3%	100.0%
Chi-square value- 17.47					
p value- 0.13					

According to the WHO severity criteria, patients were classified as mild(n=48, 32.2%), moderate(n=32, 21.5%) and severe(n=69,46.3%). The median age for mild, moderate and severe groups were 52, 52 and 55 years respectively with an interquartile range of 22, 28 and 16 years.

Table 3: Age distribution of the subjects based on who case type

	N	Minimum	Maximum	Median	IQR
Mild	48	21	75	52	22
Moderate	32	21	91	52	28
Severe	69	18	84	55	16

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There was a male preponderance with 108 males(72.5%) and 41 females(27.5%). Out of 69 severe cases, 49 were male (71%) and only 20 were female(29%)

Table 4: Gender wise distribution of the subjects based on who case type

Gender		WHO CASE TYPE			Total
		MILD	MODERATE	SEVERE	
FEMALE	Count	15	6	20	41
	%	10.1%	4.0%	13.4%	27.5%
MALE	Count	33	26	49	108
	%	22.1%	17.4%	32.9%	72.5%
Total	Count	48	32	69	149
	%	32.2%	21.5%	46.3%	100.0%
Chi-square value- 1.64					
p value- 0.44					

181.9 % (n=122) of the patients were symptomatic at the time of discharge. 18.1% (n=27) of the patients were asymptomatic at the time of diagnosis. 26% of asymptomatic patients progressed to have severe disease over the course of the disease.

Table 5: Distribution of the subjects based on presence or absence of symptoms at the time of diagnosis

		WHO CASE TYPE			Total
		MILD	MODERATE	SEVERE	
ASYMPTOMATIC	Count	19	1	7	27
	%	12.8%	0.7%	4.7%	18.1%
SYMPTOMATIC	Count	29	31	62	122
	%	19.5%	20.8%	41.6%	81.9%
Total	Count	48	32	69	149
	%	32.2%	21.5%	46.3%	100.0%
Chi-square value- 22.71					
p value- 0.00*					

*significant

At the time of diagnosis, the most common symptom was cough (57%), followed by breathlessness (56.4%), fever(35.6%) and myalgia (23.5%). Cough, breathlessness were statistically significant symptoms. 71% of patients with severe disease had cough and breathlessness whereas 50% of patients with severe disease had fever.

Table 6: Distribution of the subjects based on symptoms

	WHO CASE TYPE	Total	Chi-square	p value

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		Mild	Moderate	Severe		value	
FEVER	NO	38	24	34	96	13.02	0.001*
	YES	10	8	35	53		
BREATHLESSNESS	NO	33	6	26	65	21.36	0.00*
	YES	15	26	43	84		
COUGH	NO	31	13	20	64	14.73	0.001*
	YES	17	19	49	85		
MYALGIA	NO	37	23	54	114	0.5	0.77
	YES	11	9	15	35		

*significant

The most common comorbidity was hypertension (81.8%) followed by diabetes (51%) and Ischaemic heart disease (10.1%). Among patients with severe disease, 80% had hypertension, whereas 60% had diabetes and 13% had ischemic heart disease.

Table 7: Distribution of the subjects based on co-morbidities other than CKD

		WHO CASE TYPE			Total	Chi-square value	p value
		Mild	Moderate	Severe			
Diabetes	NO	27	18	28	73	3.64	0.16
	YES	21	14	41	76		
Hypertension	NO	6	7	14	27	1.54	0.46
	YES	42	25	55	122		
Ischemic heart disease	NO	46	27	61	134	3.11	0.21
	YES	2	5	8	15		

*significant

99 (66.4%) of the patients required oxygen support out of which 69 belonged to severe disease and 30 belonged to moderate disease.

Table 8: Distribution of the subjects based on requirement of oxygen

OXYGEN REQUIREMENT	WHO CASE TYPE			Total
	MILD	MODERATE	SEVERE	
No	48	2	0	50
Yes	0	30	69	99
Total	48	32	69	149

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Remdesivir was given to only those patients who gave consent for its administration. 22 patients (14.8) received remdesivir out of which 13 belonged to severe disease.

Table 9: Distribution of the subjects based on treatment with Remdesivir

Remdesivir		WHO CASE TYPE			Total
		MILD	MODERATE	SEVERE	
No	Count	46	25	56	127
	%	30.9%	16.8%	37.6%	85.2%
Yes	Count	2	7	13	22
	%	1.3%	4.7%	8.7%	14.8%
Total	Count	48	32	69	149
	%	32.2%	21.5%	46.3%	100.0%
Chi-square value- 6.48					
p value- 0.039*					

The median hospital stay for mild, moderate and severe disease was 52, 52 and 55 days respectively

Table 10: Comparison of the days of hospital stay using Kruskal-Wallis test

	N	Minimum	Maximum	Median	Mean
Mild	48	4	18	10	10.85
Moderate	32	7	19	10.5	10.46
Severe	69	3	23	11	11.7

Out of 149 covid 19 patients with CKD, 100 survived (67.1%) and 49 (32.9%) died.

Table 11: Distribution of the subjects based on outcome

Outcome	WHO CASE TYPE			Total
	MILD	MODERATE	SEVERE	
DEATH	0	0	49	49
	0.0%	0.0%	32.9%	32.9%
DISCHARGED	48	32	20	100
	32.2%	21.5%	13.4%	67.1%
Total	48	32	69	149
	32.2%	21.5%	46.3%	100.0%

*significant

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Table 12: Comparsion of the biochemical parameters based on WHO case type using Krusakl-Wallis test

Clinical parameters	WHO case type	N	Mean	Median	IQR	p value
Hb	Mild	48	9.45	8.45	1.9	0.00*
	Moderate	32	9.65	8.5	2.1	
	Severe	69	9.88	9.8	2.8	
TC	Mild	48	7098	8400	3975	0.518
	Moderate	32	7041	8300	8825	
	Severe	69	10210	10300	7650	
NLR	Mild	48	6.2	6	9.83	0.01*
	Moderate	32	12.9	12..5	13.9	
	Severe	69	16.3	16.25	13.79	
PLT	Mild	48	2.24	2	1.23	0.58
	Moderate	32	2.33	2.04	1.47	
	Severe	69	2.25	1.97	1.09	
D Dimer	Mild	48	0.69	0.8	1.09	0.05*
	Moderate	32	1.18	1.3	1.7	
	Severe	69	2	0.9	1.16	
LDH	Mild	48	303	306.5	186	0.30
	Moderate	32	366	330.5	168	
	Severe	69	512	533	315	
CRP	Mild	48	42	43.28	81.3	0.04*
	Moderate	32	79	70	87	
	Severe	69	140	138	111.9	

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Ferritin	Mild	48	995	1221.5	1631.5	0.89
	Moderate	32	922	816	1554	
	Severe	69	1268	1054	1498.25	
Urea	Mild	48	86	85	89	0.23
	Moderate	32	79	86	72	
	Severe	69	109	108	72	
Creatinine	Mild	48	5.27	5.55	5.8	0.016*
	Moderate	32	5.52	6.15	4.3	
	Severe	69	6.19	7.1	4.4	
Sodium	Mild	48	131	136	10	0.65
	Moderate	32	134	135	6	
	Severe	69	135	135	8	
Potassium	Mild	48	4.89	5.1	1.47	0.063
	Moderate	32	4.86	5.3	1.15	
	Severe	69	4.9	4.8	1.25	

*significant

Neutrophil-Lymphocyte ratio, D-dimer, C-reactive protein, Serum Creatinine were higher in patients with severe disease and was found to be statistically significant. S.LDH, Ferritin, S.urea were higher in patients with severe disease but were not found to statistically significant.

Table 13: Comparison of the clinical parameters based on outcome using Mann-Whitney test

Clinical parameters	Outcome	N	Minimum	Maximum	Median	IQR	p value
Hb	Death	49	4	15	9	2	0.81
	Discharged	100	4	13	9	2	
TC	Death	49	2700	42500	13600	9450	0.00*
	Discharged	100	6	19100	7950	4960	
N	Death	49	55	97	88	11	0.00*
	Discharged	100	21	99	79	19	

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L	Death	49	2	35	6	7	0.00*
	Discharged	100	1	65	13.5	15	
NLR	Death	49	1.57	48.5	14.5	15.09	0.00*
	Discharged	100	0.32	99	5.77	9.83	
PLT	Death	49	1	4	2	1	0.005*
	Discharged	100	1	6	2	1	
D Dimer	Death	49	0	10	2	1	0.00*
	Discharged	100	0	5	1	1	
LDH	Death	49	103	1373	476	340	0.00*
	Discharged	100	3	765	316	158	
CRP	Death	49	1	663	108	194	0.00*
	Discharged	100	1	2341	30.5	60.3	
Ferritin	Death	49	113	2000	1409	1597	0.17
	Discharged	100	12.56	2000	1041.5	1247.75	
Urea	Death	49	40	341	129	70	0.00*
	Discharged	100	20	348	93.5	64	
Creatinine	Death	49	2	17	6	3	0.82
	Discharged	100	2	72	6	6	
Sodium	Death	49	113	154	136	9	0.07
	Discharged	100	4	152	135	7	
Potassium	Death	49	3	7	5	2	0.09
	Discharged	100	3	135	5	1.88	

*significant

Total counts, NLR, platelets, D-dimer, LDH, CRP, Urea are significantly raised in mortality group.

Table 14: Outcomes based on age

AGE GROUP	RECOVERED	MORTALITY	TOTAL
18-30	6	4 (40%)	10
30-40	17	4 (19%)	21
40-50	19	6 (24%)	25
50-60	25	17 (41%)	42
60-70	22	12 (35%)	34
70-80	9	5 (36%)	14

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>80	2	1 (33%)	3
TOTAL	**100**	**49 (33%)**	**149**

Discussion:

Patients with chronic kidney disease may be more susceptible to Covid 19 infection than the general population due to multiple factors like anemia of chronic disease, hypoalbuminemia, multiple admissions for dialysis, etc. Due to lowered immunity, they are more likely to have a severe Covid-19 disease. [5]

In our study, the age group with highest mortality was 50-60 years followed by 70-80 years with a mortality of 41% and 36% respectively. In a similar study done by Mahmut Gok et al, the average age of CKD patients with Covid-19 who died was 70.8 years. Multiple studies have shown that patients with multiple comorbidities have increased risk of developing severe disease and increased mortality risk in covid 19.[6,7]

Previous studies have shown that diabetes, hypertension, cardiac illness, chronic lung diseases, chronic kidney disease and malignancy are associated with pooper outcomes in patients infected with MERS-Cov and influenza. [8,9,10] In our study, the most common comorbidity was hypertension followed by diabetes and Ischemic heart disease. Similarly, study done by Gok M et al showed hypertension, diabetes and chronic kidney disease are associated with poor outcomes in patients with Covid 19 disease. [11] Studies have shown that dialysis patients and kidney transplant patients are at an increased risk of mortality. [12] Frequent visits to the hospitals for dialysis itself is a risk factor for Covid 19 infection. [13]

In our study, CKD patients with severe COVID-19 illness had higher incidence of symptoms like fever, cough and breathlessness at the time of admission. Patients who expired had higher NLR (16.7), D-dimer(2.1), LDH (562), CRP(172.1) and ferritin (1213) as compared to patients who had recovered (NLR-10, D-dimer-1.1, LDH-341, CRP-77, ferritin-1053). In a study done by Gok M et al, inflammatory markers were significantly raised. LDH, CRP Ferritin and D-dimer were 1589 U/L, 204mg/dL, 4805ng/mL,7319ng/mL respectively in mortality group as compared to patients who had recovered. (LDH-570, CRP-77,Ferritin-543,D-dimer-1431). [11]

The most common immediate cause of death in our patients was Acute respiratory distress syndrome seen in 55% of the patients followed by sepsis and uremic encephalopathy (18.3% each). Acute coronary syndrome(6%) and Aspiration (4%) were the other causes of death in our patients. In a similar study done by Jianlei Cao, 88% of patients in mortality group had developed ARDS and 88% developed AKI. [7]. Covid 19 also leads to glomerular injury which causes acute kindey injury.[14] AKI superimposed on CKD can further increase the mortality risk.[15,16] Nephrons express ACE2 receptors which is essential for viral entry. [17] Hence direct renal cell infection by Covid-19 virus can occur which was demonstrated in a study done by Farkash et al.[18] Also, recent studies have shown that cytokine storm occurs in patients with severe covid 19 disease.[19,20] This can cause tissue injury and lead to AKI and glomerulopathy.[21,22] Hence they can be used to assess the progression of the disease and as predictors of mortality.

Conclusion:

The results of this study shows CKD to be associated with increased risk of severe COVID-19 infection and mortality. Patients with CKD should hence be advised to take extra precaution to minimize risk exposure to the virus. Symptoms like fever, breathlessness, cough are associated with severe disease. Total counts, NLR, platelets, D-dimer, LDH, CRP, Urea are significantly raised in mortality group. Hence, Physicians should closely monitor CKD patients with suspected COVID-19, for timely detection of signs of disease progression.

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