The Clinical Course and Prognostic Factors of COVID-19 in Patients with Chronic Kidney Disease, A Study in Six Centers

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Introduction. Coronavirus disease 19 (COVID-19), has recently emerged as a great health challenge. The novel corona virus may affect the kidneys mainly as acute kidney injury (AKI). Also, the outcome of COVID-19 may be different in patients with underlying kidney disease. The aim of this study was to compare the outcome of COVID-19 in patients with and without underlying kidney disease.
Methods. This was a retrospective study on 659 hospitalized COVID-19 patients in six centers of Iran. Patients were classified into kidney (chronic kidney disease (CKD), end-stage kidney disease (ESKD) or kidney transplantation) and non-kidney groups. The clinical conditions and laboratory data were extracted from the charts. Outcome was defined as death during hospitalization or within 30 days of discharge.
Results. Among 659 COVID-19 patients (mean age: 60.7 ± 16.4, 56% male), 208 were in the kidney group (86 ESKD, 35 kidney transplants, and 87 CKD patients). AKI occurred in 41.8%. Incidence of AKI was 34.7% in non-kidney, 74.7% in CKD, and 51.4% in kidney transplant patients ($P < .001$). Totally 178 patients (27%) died and mortality rate was significantly higher in CKD patients (50.6 vs. 23.4%, $P < .001$). AKI was associated with increased mortality rate (OR = 2.588, CI: 1.707 to 3.925). Initial glomerular filtration rate (GFR) < 44.2 mL/min and elevated lactate dehydrogenase (LDH) and C-reactive protein (CRP) had significant association with mortality.
Conclusion. We showed a higher mortality rate in COVID-19 patients with AKI and CKD. Low initial GFR and elevated LDH and CRP were associated with high mortality in COVID-19 patients.

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INTRODUCTION

Since the first official report of severe acute respiratory syndrome (SARS)-CoV-2 or coronavirus disease 19 (COVID-19) on December 2019 in Wuhan, the disease has become a great health challenge around the world.[1] On March 2020 COVID-19 was announced as pandemic by the World Health Organizations (WHO) and at the

time of this writing, coronavirus positive cases are over 47 million patients throughout the world and the mortality has been over 1,200,000 cases.[2] In addition to the lungs, serious involvement of other major organs such as heart and kidney may occur in COVID-19; although the frequency of acute kidney injury (AKI) has been variable in different reports, i.e. between 0.5% to 36.4% in critical cases.[1,3] Various mechanisms have been suggested for kidney damage with SARS-CoV-2. Detection of virus RNA in urine and kidney tissue may indicate direct damage to the kidney by the virus.[4] Also invasion of virus to proximal tubular cells and podocytes, has been reported. Cytokine storm and clot formation in the small vessels are the other mechanisms of kidney damage in these patients.[5-7]

Wang, *et al.* have shown that kidney is not a common victim of this virus and it has not caused exacerbation of the existing chronic kidney failure.[8] However, in some reports AKI has been reported in up to 36% of patients and usually accompanied by proteinuria and hematuria.[9] The manifestations and outcomes of COVID-19 may be different in patients with underlying kidney disease including chronic kidney disease (CKD), end stage kidney disease (ESKD) and kidney transplant recipients, due to their overall immunocompromised status, medications and primary diseases. However, considering the new emergence of the virus, there is still a paucity of data regarding the behavior of SARS-CoV-2 in patients with different types of kidney involvement.

The aim of this study was to compare the outcome of COVID-19 in patients with underlying kidney disease, including CKD, ESKD, and kidney transplant recipients, with those without any previous kidney disease and to find the risk factors for mortality.

MATERIALS AND METHODS

This was a retrospective, observational study carried on in six centers. All patients who had been admitted with diagnosis of COVID-19 in six different hospitals of Iran from February 21th to august 2nd, 2020, were enrolled in the study. Inclusion criteria consisted of patients with an age more than 16 years admitted with a diagnosis of COVID-19 in any of the mentioned centers.

The demographic characteristics, clinical findings, laboratory data and medications were extracted from the hospital information systems.

Clinical signs and symptoms included fever ≥ 37.2, dyspnea, cough, sore throat, chills, nausea, vomiting, diarrhea, body pain, and anosmia. Laboratory data consisted of complete blood count (CBC), alanine aminotransferases (ALT), aspartate aminotransferases (AST), alkaline phosphatase, serum creatinine (Cr), serum sodium, potassium, magnesium, phosphate, D-dimer, prothrombin time (PT), international normalized ratio (INR), partial thromboplastin time (PTT), serum high-sensitivity C-reactive protein (hsCRP), lactate dehydrogenase (LDH) and vitamin D and hematuria and proteinuria in urinalysis. Clinical outcome was monitored up to August 2020, until one month after discharge.

In the six centers real-time polymerase chain reactions test (RT-PCR) was done with 5 kits in including: 1) The COVID-19 One-Step RT-PCR Kit, Pishtaz Teb Diagnostics, Iran, 2) Viral DNA/RNA Extraction kit, Payesh gene, Iran, 3) RNJia Viruse kit, Rojetechnologies, Iran, 4) Nucleic Acid reagent test kit for novel coronavirus 2019-nCoV (fluorometric PCR), Sansure Biotech Inc, China, and 5) Nucleic Acid reagent test kit for novel coronavirus 2019-nCoV (fluorometric PCR), Da An Gene Co, China.

All chest computerized tomographic (CT) scans were performed with a section thickness of 5 mm and without contrast agent. The chest CT scans were reported according to Coronavirus disease 2019 (COVID-19) Reporting and Data System (CO-RADS), and we further classified the CT scans with CO-RADS grade 5 as typical and those with CO-RADS 3 and 4 as atypical chest CT scans.[10]

Diagnosis of COVID-19 was based on any or a combination of the bellow findings: 1) Positive result of RT-PCR assay for COVID-19, 2) Typical abnormalities in the chest computerized tomography (CT) scan consistent with lung involvement in COVID-19, 3) Clinical findings consistent with COVID-19, including the mentioned clinical signs and symptoms and/or history of recent close contact with definite case of COVID-19, associated with atypical chest CT scan (CO-RADS 3, 4).

Patients were classified into two groups: 1) Kidney group; those with a positive history of CKD, ESKD or kidney transplantation, 2) Non-kidney group; patients without any previous history or evidence of underlying kidney disease.

Outcome was defined as death due to respiratory failure or other complications of COVID-19 in hospital or within 1 month after discharge.

Severe cases were defined as those with either or any combination of dyspnea, respiratory rate > 30 breaths/min or oxygen saturation ≤ 93% or PaO_2/FiO_2 ≤ 300 mmHg or infiltration in more than 50% of the lung.[11]

AKI was defined according to the kidney disease improving global outcome (KDIGO) criteria, i.e. an increase in serum creatinine by 0.3 mg/dL within 48 hours or 50% increase in serum creatinine from baseline within 7 days.[12]

Chronic kidney disease was defined as decreased kidney function (glomerular filtration rate [GFR]) to less than 60 mL/min according to modification of diet in kidney disease (MDRD) formula, for at least three months before admission.[13]

End stage kidney disease (ESKD) was defined as GFR less than 15 ml/min that patients need to hemodialysis or peritoneal dialysis.

Statistical Analysis

Data analysis was performed by using SPSS software package version 25 (IBM Corp., 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). Continuous variables were expressed as mean ± standard deviation (SD) if distribution was normal, or median with range, if distribution was not normal. The comparison of discrete variables between groups was performed by using the Pearson $\chi 2$ test. Association of clinical and laboratory characteristics with mortality were evaluated by univariate and multivariate logistic regression. All differences were considered significant at *P* values of less than .05. Receiver operating characteristic (ROC) curve was plotted to obtain a numerical cut-off for the effect of GFR on prognosis of the patients.

RESULTS

Among 659 patients hospitalized with COVID-19, 369 (56%) were male and 290 (44%) female, with a median age of 62 (17 to 95) years old. From these, 451 (68.4%) were in the non-kidney, and 208 (31.6%) were in the kidney groups, including 86 patients with ESKD, 35 with kidney transplants and 87 with CKD. Median duration of hospitalization was 6 (1 to 38) days. The comorbidities were hypertension (HTN) in 282 (42.8%), diabetes mellitus (DM) in 236 (35.8%), ischemic heart disease (IHD) in 145 (22%), chronic lung disease in 40 (6.1%), malignancy in 23 (3.5%) and rheumatologic disease in 33 (5%) patients. Forty- five patients (6.8%) were receiving immunosuppressive medications (Table 1).

Coronavirus disease 19 was diagnosed with positive PCR and typical chest CT compatible with COVID-19 in 145 patients (22%), only typical chest CT scan compatible with COVID-19 in 411 patients (62.3%) and only positive PCR for COVID-19 in 53 patients (8%). Fifty patients (7.5%) were diagnosed according to clinical findings associated with atypical chest CT for COVID-19, with or without a history of recent close contact with definite case of COVID-19 (Table 2).

The most common symptoms at presentation were dyspnea (73.4%), followed by cough (64.9%) and fever (63.3%) (Table 3).

The administered therapies are shown in table 4. Due to retrospective and non- randomized nature of our study, comparison of the efficacy of various

Table 1. Demographic and Clinical Conditions of 659 Patients with COVID-19

Age (median, range)	62 (17, 95)
Male / Female	369 / 290
Duration of Hospitalization, Days (Median, Range)	6 (1, 38)
Diabetes Mellitus	236 (35.8%)
Hypertension	282 (42.8%)
Ischemic Heart Disease	145 (22%)
Chronic Lung Disease	40 (6.1%)
Malignancy	23 (3.5%)
Rheumatologic Disease	33 (5%)
Non-kidney Group*	451 (68.4%)
Kidney Group**	208 (31.6%)
CKD	87 (13.2%)
ESKD	86 (13%)
Kidney Transplant	35 (5.3%)

Abbreviations: COVID-19, coronavirus disease 19; CKD, chronic kidney disease; ESKD, end stage kidney disease.
*Patients with No History or Evidence of Underlying Kidney Disease
**Patients with History of any of the Mentioned Underlying Kidney Diseases

Table 2. Diagnostic Characteristics of Patient with COVID-19

	Positive PCR	Negative PCR	PCR Not Checked
Typical Chest CT Scan	145	176	235
Atypical Chest CT Scan	53	34*	16*
Total	198	210	251

*Diagnosis made according to clinical findings consistent with COVID-19 and atypical abnormalities in chest CT scan.
Abbreviations: COVID-19, coronavirus disease 19; CT, computed tomography; PCR, polymerase chain reaction.

Table 3. Clinical Signs and Symptoms of Patients with COVID-19

Dyspnea	73.4%
Cough	64.9%
Fever	63.3%
Chills	40.5%
Body Pain	27.8%
Nausea / Vomiting	16.8%
Sore throat	12%
Diarrhea	8%
Anosmia	3.8%

Abbreviations: COVID-19, Coronavirus disease 19.

Table 4. Medications Administered for COVID-19 Patients

Main Regimens	Number (%)
No Specific Treatment	39 (5.9)
Hydroxychloroquine + Lopinavir / Ritonavir	418 (63.4)
Hydroxychloroquine Alone	64 (9.7)
Hydroxychloroquine + Azithromycin	106 (16.1)
Adjunctive Medications	**Number (%)**
IVIG	47 (7.1)
Methylprednisolone	65 (9.8)
Ribavirin	19 (2.8)
Oseltamivir	57 (8.6)

Abbreviations: IVIG, intravenous immunoglobulin.

therapeutic modalities was not included in this study.

Totally, 178 patients (27%) died during hospitalization or within 30 days after discharge, including 63 patients with refractory respiratory failure and 115 patients with other complications of COVID-19. Mortality rate was significantly higher in patients with CKD vs. non-kidney patients (50.6% vs. 23.4%, $P < .001$) but in the kidney transplant and ESKD patients the mortality rate was close to non-kidney patients (25.7%, 23.3%, and 23.3%; respectively) (Table 5).

Ninety-two patients (14%) needed mechanical ventilation. The incidence of AKI was significantly higher in ventilator dependent vs. non-ventilator dependent patients (62.9% vs. 38.2%, respectively; $P < .001$). The mortality rates were 81.5% in ventilator dependent and. 18.1% in non-ventilator dependent patients ($P < .001$).

Acute kidney injury occurred in 239 (41.8%) patients. The incidence of AKI was significantly higher in patients with CKD and kidney transplant, compared to patients with no history of kidney disease ($P < .001$) (Table 5). Acute kidney injury was associated with high mortality rate in all ($P < .001$), non-kidney ($P < .001$), and transplant patients ($P < .01$). However, such an association was not found in CKD patients ($P > .05$) (Table 5).

In evaluation of clinical conditions with univariate logistic regression, sex was not associated with mortality ($P > .05$). Age, IHD, DM, HTN AKI, and CKD had a significant association with mortality ($P < .01$). However, in multivariate logistic regression, IHD had a marginal association with mortality rate (odds ratio [OR]: 1.55, 95% confidence interval [CI]: 0.97 to 2.49; $P = 0.065$ (marginal association)) and age (OR = 1.03, 95% CI: 1.02 to 1.05), AKI (OR = 2.58, 95% CI: 1.7 to 3.92), and CKD (OR = 1.71, 95% CI: 1 to 2.92) had a significant association with mortality ($P < .05$) (Table 6).

Hematuria and proteinuria were checked only in 263 patients and were not associated with mortality ($P > .05$) (Table 7)

Lymphocyte count less than 1100/µL, low level of GFR at admission and during hospitalization, elevated CRP, LDH, and INR, D-dimer more than 1000 ng/mL and hyponatremia were associated with mortality ($P < .05$), in univariate logistic regression. Vitamin D levels were checked in only 87 patients, that showed vitamin D level less than 20 ng/mL (vitamin D deficiency) was marginally associated

Table 5. Acute Kidney Injury and Mortality in Kidney and Non-kidney Patients with COVID-19

	Incidence of AKI (%)	*P* value (for AKI)	Mortality Rate (%)	*P* value (for Mortality)	*P* value (for Association of AKI with Mortality)
Non-kidney Group (451)*	34.7	< .001	23.3	< .001	< .001
Kidney Group (208)**	68		35		> .05
Kidney Tx	51.4		25.7		< .05
CKD	74.7		50.6		> .05
ESKD	–	–	23.3		–
Total	41.8		27		< .001

Abbreviations: AKI, acute kidney injury; Tx, transplant; CKD, chronic kidney disease; ESKD, end stage kidney disease.
*Patients with no History or Evidence of Underlying Kidney Disease
**Patients with History of any of the Mentioned Underlying Kidney Diseases

Table 6. Evaluation of Association of Clinical Conditions with Mortality (Univariate / Multivariate Logistic Regression)

	Univariate				Multivariate			
	OR	95% CI		*P*	OR	95% CI		*P*
		Upper	Lower			Upper	Lower	
Age	1.047	1.034	1.060	< .001	1.036	1.021	1.051	< .001
Sex	1.021	0.722	1.444	> .05				
Diabetes Mellitus	1.595	1.121	2.267	< .01	1.135	0.724	1.78	> .05
Hypertension	1.69	1.196	2.39	< .01	1.062	0.678	1.664	> .05
Ischemic Heart Disease	2.563	1.738	3.78	< .001	1.559	0.973	2.499	> .065
AKI	3.62	2.463	5.321	< .001	2.588	1.707	3.925	< .001
CKD	3.345	2.106	5.312	< .001	1.711	1	2.927	< .05

OR: odds ratio; CI: confidence interval; AKI: acute kidney injury; CKD: chronic kidney disease

Table 7. Evaluation of Association Between Biomarkers and Mortality (Univariate / Multivariate Logistic Regression)

	Univariate				Multivariate			
	OR	95% CI		*P*	OR	95% CI		*P*
		upper	lower			upper	lower	
First GFR	0.973	0.966	0.981	< .001				
First GFR < 44.2 mL/min	5.156	3.462	7.677	< .001	4.004	2.246	7.140	< .001
Lowest GFR	0.963	0.954	0.971	< .001				
Lowest GFR < 45.204 mL/min	8.041	5.163	12.523	< .001				
Lymphocyte count ≤ 1100 /µl	2.511	1.682	3.748	< .001	1.538	0.825	2.865	> .05
Maximum CRP	1.007	1.005	1.010	< .001	1.005	1.001	1.009	< .05
LDH at admission, U/L	1.002	1.001	1.003	< .001	1.002	1	1.003	< .01
Maximum LDH, U/L	1.001	1.001	1.002	< .001				
D-dimer > 1000 ng/mL	4.664	1.5	14.54	< .05				
Vitamin D < 20 ng/mL	2.620	0.946	7.257	> .064				
Sodium < 135 meq/L	1.838	1.288	2.623	< .001	1.275	0.695	2.339	> .05
Potassium < 3.5 meq/L	1.246	0.831	1.870	> .05				
Phosphorus < 2.5 mg/dL	0.695	0.369	1.309	> .05				
Magnesium < 1.9 mg/dL	0.832	0.521	1.328	> .05				
Maximum INR	1.515	1.076	2.134	< .05	1.842	0.696	4.873	> .05
Hematuria	1.551	0.822	2.928	> .05				
Proteinuria	1.709	0.915	3.194	> .05				

Abbreviations: OR, odds ratio; CI, confidence interval; GFR, glomerular filtration rate; CRP, C-reactive protein; LDH, lactate dehydrogenase; INR, international normalized ratio.

with death ($P = 0.064$ (marginal association)) (Table 7).

By plotting ROC Curve, first GFR less than 44.21 mL/min could predict mortality with a sensitivity of 72.8%, specificity of 65.8 %, and C statistics of 0.703 (OR = 5.156, 95% CI: 3.462 to 7.677). Lowest GFR during hospitalization less than 45.2 mL/min predicted mortality with sensitivity of 66.4%, specificity of 80.3% and C statistics of 0.751(OR = 8.041, 95% CI: 5.16 to 12.52).

In multivariate logistic regression of laboratory findings, LDH at admission (OR = 1.002, 95% CI: 1 to 1.003), first GFR less than 44.2 mL/min (OR = 4.004, 95% CI: 2.246 to 7.14), lowest GFR less than 45.2 mL/min (OR = 6.24, 95% CI: 3.38 to 11.51), and CRP (OR = 1.005, 95% CI: 1.001 to 1.009) were significantly associated with outcome ($P < .05$) (Table 7).

In the multivariate analysis of clinical and laboratory characteristics, IHD, elevated CRP, LDH, and initial GFR less than 44.2 mL/min had significant association with mortality ($P < .05$ for IHD, elevated CRP, LDH, and $P < .001$ for initial GFR less than 44.2 mL/min) (Table 8).

DISCUSSION

In the present study, we retrospectively analyzed the outcome of 659 hospitalized COVID-19 patients in six centers of the country with high incidence of the disease, and compared the mortality rates between patients with or without previous underlying kidney disease. Overall, the 30 days mortality rate

Table 8. Multivariate Analysis of Biomarkers and Clinical Conditions in Association with Mortality

Variable	OR	95%CI		*P*
		Upper	Lower	
Diabetes Mellitus	1.345	0.725	2.495	> .05
Hypertension	1.472	0.78	2.78	> .05
Ischemic Heart Disease	2.305	1.192	4.458	< .05
Sodium < 135meq/L	1.205	0.649	2.240	> .05
Maximum CRP	1.005	1.001	1.009	< .05
LDH at Admission (U/L)	2.305	1	1.002	< .05
Lowest Lymphocyte Count ≤ 1100/μL	1.428	0.76	2.686	> .05
First GFR < 44.2 mL/min	3.03	1.642	5.59	< .001
Maximum INR	1.932	0.704	5.304	> .05

Abbreviations: OR, odds ratio; CI, confidence interval; GFR, glomerular filtration rate; CRP, C-reactive protein; LDH, lactate dehydrogenase; INR, international normalized ratio.

was 27% that was significantly higher in patients with history of CKD (50.6%). The mortality rate of hospitalized COVID-19 patients has been variable between 16% to 28% depending on the admission criteria and clinical settings.[14-16] Mortality rates as low as 4% has been reported by Wu *et al.*, which could have been due low threshold level for patient's admission.[17] The reported mortality rate in our study, which included a high number of patients with underlying kidney disorders, seems to be acceptable, in comparison to other studies.

Underlying clinical conditions such as age, DM, HTN and IHD have been shown to affect the mortality of COVID-19 patients in various studies.[18,19] In the report published by the Center of Control and Prevention of disease in China old age, DM, HTN, and cardiovascular disease were mentioned as risk factors for death in COVID-19 patients.[18] However, in the studies by Wang *et al.* and Zhou *et al.*, DM and HTN were not significantly associated with increased mortality.[14,18] In a systematic review by Sepandi *et al.* on 13 published papers, old age, male gender, DM, HTN, and underlying kidney, lung and heart disease were the risk factors for mortality in patients with COVID-19, and the highest odds ratio was 4.38 for heart disease.[20]

In our study, age had a significant association with mortality, however, DM and HTN lost their association with mortality in multivariate analysis and IHD had a marginal association with mortality.

We further analyzed the effect of these three clinical conditions in the kidney and non-kidney group, to rule out the possibility of co-linearity with kidney disease (data not shown). In the both kidney and non-kidneys groups, only IHD was strongly associated with mortality and this may be explained by the reported cardiac injury in COVID-19 patients through various mechanisms including hypercoagulable and proinflammatory states and direct virus damage to cardiomyocytes and endothelial cells, which may affect the patients with underlying IHD more severely.[21]

In our study the mortality rate of kidney transplant patients with COVID-19, was not significantly higher than non-kidney patients. In a study on 104 kidney transplant patients with COVID-19, mortality rate was 27%.[22] In another study, in 318 kidney transplant patients, the mortality rate was 17.9%.[19] Similar mortality rate of kidney transplant patients with COVID-19 to other patients may point to the importance of cytokine storm in mortality of COVID-19 patients, which may be less severe in patients receiving immunosuppressive medications especially calcineurine inhibitors.[23-25] These medications may also prevent viral replication.[23-25]

There are few studies on the mortality rate of COVID-19 patients with underlying ESKD. In one study in China, the mortality rate of 49 hospitalized ESKD patients was higher than the control group (14% vs. 4%).[17] However in other studies mortality rates of 30.5%, 27.3%, and 16.2% have been reported in ESKD patients with COVID-19.[26-28] In our study the mortality rate of ESKD patients with COVID-19 was 23.3% and not higher than other patients. Low level of inflammatory cytokines in ESKD patients and inability to develop cytokine storm may have a role in this regard, despite the comorbidities and immune dysfunction in ESKD patients, as shown in a study by Ma *et al.*[28]

We found a significantly higher mortality rate in patients with history of CKD with an odds ratio

of 3.34 in univariate analysis There are few reports on COVID-19 patients with non-dialysis CKD in the literature. Henry *et al.* reported an association of CKD with more severe COVID-19 (OR = 3.03).[29] On the other hand, mortality rate of patients with CKD was not higher than non-CKD patients, in a study on 164 non-kidney solid organ transplant patients.[19] Overall, it seems that there has not been enough studies on the effect of CKD on mortality of COVID-19 patients and our findings, especially considering the high rate of observed AKI in our CKD patients, points to the need for more attention to CKD, as an important comorbidity in these patients.

In our study AKI occurred in 41.8% of all patients and 74.7% of CKD patients, pointing to the susceptibility of hospitalized and especially CKD patients to AKI. Overall, AKI was associated with death and its association with mortality was stronger than DM, HTN, and IHD. This association was not seen in CKD patients, in whom CKD itself may had been a better predictor of mortality.

In a study on 193 patients, AKI was observed in 28% of patients and increased the risk of death by 5.3 times.[30] In a review article on 23 studies, AKI was reported in 11% of total and 23% of critically ill patients.[31] In a systematic review including 24 studies, AKI was reported in 4.5% of all patients and in 36.4% of patients with severe COVID-19. In this review, AKI was associated with disease severity and disease prognosis.[3] In another meta-analysis the incidence of AKI was 4% that was significantly lower in non-severe group compared to deceased patients.[32] The variable incidence of AKI may depend on the admission criteria and disease severity. Due to recording the initial oxygen saturation of many of our patients under nasal oxygen, we were not able to accurately distinguish between severe and non-severe COVID-19 patients based on the given definition; however, considering the high incidence of dyspnea in our patients (73%), which may be a criterion for severe COVID-19, we assume a high frequency of patients with severe COVID-19 in our study population.[11] In addition, a high percentage of our patients had underlying kidney disease which may explain their general susceptibility to development of AKI.[22] We could also show the association between AKI and mortality, similar to other studies.[3,30]

In our study CRP, LDH and GFR had a strong association with mortality, and among all of the clinical and laboratory characteristics, the highest odds of mortality was related to GFR. Patients with D-dimer > 1000 ng/mL had very high odds of mortality in univariate analysis, however, because of the low number of patients in whom D-dimer had been checked, multivariate study was not performed. Lymphopenia was associated with mortality only in univariate analysis. In our study, low vitamin D level was also marginally associated with mortality. In previous studies vitamin D deficiency was significantly associated with the severity and mortality of COVID-19 patients, though in some studies, no association was found between vitamin D level and mortality of patients after adjustment for other variables.[33]

In a review on 34 studies, CRP, LDH, serum creatinine, and D-dimer were shown to be higher and lymphocyte and platelets counts to be lower in severe cases compared to non-severe cases.[34] In a pooled analysis on 1532 COVID-19 patients, a 6-fold increase in the risk of severe disease and a 16-fold increase in death rate in COVID-19 patients with elevated LDH was shown.[34] The relationship between kidney function, LDH, CRP, D-dimer and lymphopenia and mortality has been also shown in many other studies.[14, 30, 36]

Overall it seems that markers of kidney function, inflammation, coagulation, and tissue injury may all be associated with poor prognosis of COVID-19, as a disease with capability of multi-organ involvement.

CONCLUSION

Chronic kidney disease, AKI and low GFR at presentation or during the hospitalization course are important factors affecting the prognosis of COVID-19 and their impact on the mortality of these patients may be even greater than the usual risk factors such as age, diabetes, hypertension and ischemic heart disease. Close surveillance should be implied on patients with any underlying kidney disease, as a susceptible group of patients for COVID-19 complications. Moreover, CRP, LDH and D-dimer are useful biomarkers in determining the prognosis of COVID-19.

Future detailed prospective studies would help to further delineate the risk factors for mortality in COVID-19 patients.

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