THE VALUE OF URINE ANALYSIS PREDICTING ACUTE KIDNEY INJURY AND MORTALITY IN COVID-19 PATIENTS

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Abstract

ABSTRACT Purpose Kidney involvement is frequent among patients with coronavirus disease 2019 (Covid-19). However, kidney involvement is varied and mild kidney injury can easily go unnoticed. We aimed to investigate the urinalysis data of Covid-19 patients on admission and to explore the value of urinalysis in the prediction of AKI and in-hospital mortality in patients with Covid-19. Methods The demographic, clinical and laboratory data of patients with confirmed Covid-19 were collected from the electronic health records of the hospital. The outcomes were development of AKI and in-hospital mortality. Results 244 patients were included in the analysis. Mean age was 59.6 ± 13.7 and 65.2% of patients were male. Median SCr on admission was 0.86 (0.72-1.05) mg/dL. Glucosuria, proteinuria and hematuria were found in 36.1%, 22.9% and 22.1% of patients, respectively. AKI was detected in 63 patients (25.8%) on any time of hospitalization. According to multivariate binary logistic regression analayses; AKI development was associated with higher WBC and decreased eGFR as well as with proteinuria on admission. During median 8 (IQR, 5-12) days of follow-up, 33 patients (13.5%) died. Older age, higher CRP levels and proteinuria on admission were also independent predictors of in-hospital mortaliy. Conclusion Proteinuria on admission is associated with development of AKI and in-hospital mortality in patients with Covid-19. Urinalysis can be useful for the evaluation of COVID-19 progression and early diagnosis of kidney damage before SCr rise.

of hospitalization. According to multivariate binary logistic regression analayses; AKI development was associated with higher WBC and decreased eGFR as well as with proteinuria on admission. During median 8 (IQR, 5-12) days of follow-up, 33 patients (13.5%) died. Older age, higher CRP levels and proteinuria on admission were also independent predictors of in-hospital mortaliy.

Conclusion

Proteinuria on admission is associated with development of AKI and in-hospital mortality in patients with Covid-19. Urinalysis can be useful for the evaluation of COVID-19 progression and early diagnosis of kidney damage before SCr rise.

Key Words: Acute kidney injury, Covid-19, proteinuria, urinalysis.

INTRODUCTION

In December 2019, a new strain of coronavirus was identified and officially named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. Clinical presentations of coronavirus disease 2019 (Covid-19) can range asymptomatic infection, self-limited influenza like symptoms, and acute pneumonia to severe respiratory failure. Besides lungs, kidney involvement is also well defined [2].

Kidney involvement, defined both as urinary abnormalities and changes in kidney function, has been described among patients with Covid-19 and it might be present in up to 75% of cases [3].Because of the expression of the membrane-bound peptidase angiotensin-converting enzyme 2 (ACE2) in tubular epithelia and podocytes and the known property of ACE2 as a facilitator of cell entry for SARS-CoV-2, it has been proposed that direct viral infection into the kidneys may account for some of the acute kidney injury (AKI) pathogenesis for patients with Covid-19 [4]. However, kidney involvement during Covid-19 disease may have a broad clinical spectrum, and mild kidney injury can easily go unnoticed.Several studies have found a significant association between AKI and death among Covid-19 infected patients Early detection of AKI would be beneficial to identify the patients to improve the clinical status of Covid-19 patients [4,5].

Urine analysis may be useful to predict the development of AKI and mortality in Covid-19 patients.Multiple observational studies have reported the presence of proteinuria and hematuria in Covid-19 patients [6-12]. However to date, there have been relatively few studies focussed on urinalysis parameters except hematuria and proteinuria in Covid-19 patients [6,9,11].

In this study, we aimed to investigate the urinalysisdataof Covid-19 patients on admission and to explore the value of urinalysis in the prediction of AKI and in-hospital mortality in patients with Covid-19.

MATERIALS AND METHODS

Patients hospitalized with diagnosis of Covid-19 between October 2 and December 25, 2020were enrolled. The diagnosis of Covid-19 was confirmed with at least one positive real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test result in cases admitted with symptoms, signs and findings (laboratory/radiological) suggestive of Covid-19, according to the national guidelines [13]. We excluded the following patients; patients who were on regular hemodialysis, pregnant, who were transferred from intensive care unit (ICU), who had urinary tract infection or who had uretheral catheters. For patients who had multiple qualifying hospital admissions, we included only the first hospitalization however outcomes were recorded according to the last hospitalization.

The source of medical records was OCTOMED (Kartal Dr.Lutfi Kirdar City Hospital Automation Program) electronic database system. The National Public Health Data Management System database was also used as an external data source, particularly to track the RT-PCR test results and to obtain data on previous creatinine values. We collected data for patient demographics, comorbidities, vital signs and laboratory test results on admission. Laboratory data consisted of measurements of white blood cell (WBC), lymphocyte, hemoglobin (Hb), platelet count (PLT), serum glucose, urea, creatinine (SCr), albumin, sodium, potassium, chloride, calcium, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), C-reactive protein (CRP), ferritin, fibrinogen, D-dimer and creatinine kinase (CK) levels.The first

value of laboratory data within 48 hours of hospital admission was taken. Additionally, peak and discharge creatinine values were also collected. IL-6 was taken once as the highest value during hospitalization. Furthermore, medications used for the treatment of Covid-19 were also recorded.

We additionally collected urinalysis with automated microscopy that were obtained within 48 hours after admission. The urine samples were collected in containers, transported and analysed within 2 h of collection. The analyses were carried out on H-800 and FUS-200 automatic modular urine analysers (Dirui Industry, Changchun, China). A further microscopic analysis of sediments was performed, if required.

Outcomes data were retrieved until January 10, 2020. By the time of this analysis, all patients had either died or had been discharged from the hospital. The primary outcome was the development of AKI and secondary outcome was in-hospital mortality.

Definitions

The date of hospital admission was accepted as the first day. Patients using antihypertensive drugs were accepted as hypertensive, while those using antidiabetic drugs were accepted as diabetic.

The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [14]. Decreased eGFR was defined as < 60 mL/min/1.73 m^2.

AKI on admission or during hospital stay was defined according to Kidney Disease: Improving Global Outcomes (KDIGO) criteria as follows: stage 1, as an increase in SCr level by 0.3 mg/dL within 48 hours or 1.5 to 1.9 times increase in SCr from baseline within 7 days; stage 2, as 2 to 2.9 times increase in SCr within 7 days; stage 3, as 3 or more times increase in SCr within 7 days or initiation of renal replacement therapy (RRT) [15]. Patients were stratified according to the highest AKI stage attained during their hospital stay. Available baseline value for each patient was taken as the mean outpatient value 7-365 days prior to admission [16]. If baseline value of SCr was not available, the lowest value during hospitalisation was taken [15]. We did not use the urine output criteria to define AKI as the documentation of urine output in the electronic health record was unavailable.

Renal glycosuria was defined in a person if blood glucose level rises higher than 170–200 mg/dL who doesn't have diabetes or if blood glucose level rises higher than 200–250 mg/dL who has type 2 diabetes mellitus and the filtered glucose load exceeds the capacity for tubular glucose reabsorption [17]

Proteinuria was defined as the presence of ?1+ on dipstick urinalysis. Trace proteinuria was considered as negative. Microscopic hematuria was accepted as the presence of three or more erythrocytes per high-power field. Pyuria was also accepted as the presence of five or more leukocytes per high-power field.

The follow-up period started from the date of hospitalization and ended the day of discharge or in-hospital mortality.

Statistical analysis

Continuous data are presented as mean with standard deviation (SD) or as median and interquartile range (IQR) in case of non-normal distribution. Categorical data are presented as percentages. For multiple group comparisons of categorical variables, the Chi-square test was used. Continuous variables were first analyzed for normality using the Kolmogorov-Smirnov test and then were compared using the independent sample t-test or the Mann-Whitney U test, when appropriate. To explore the risk factors associated with AKIwe performed logistic regression models, with adjustment for risk factors that differed between subjects who developed AKI and those who did not. Also multivariate logistic regression analysis were used to estimate the risk factors associated with in-hospital mortality. We did not include associates of decreased eGFR (urea, creatinine, eGFR) and hematuria (Hburia) in our prediction models.Kaplan-Meier survival curve analysis was done to determine the correlation between proteinuria and in-hospital mortality and log rank test was used for survival analysis.All tests were performed using SPSS for Windows, version 17.0 software (SPSS Inc., Chicago, IL, USA).P values of less than 0.05 were considered statistically significant.

Ethics

The study protocol was approved by the Clinical Research Ethics Committee of Kartal Dr. Lutfi Kirdar City Hospital (approval date: 14.10.2020, approval number: 2020/514/187/15) and the Scientific Committee of the Ministry of Health (approval no: 2020-10-08T16_20_20). The study was conducted in accordance with the 1975 Declaration of Helsinki, as revised in 2013.

RESULTS

695 patients have been hospitalized in infectious clinics with Covid-19 diagnosis in study time. Of these 695 patients, 244 patients were included in the analysis. Flow chart of study is shown in Figure 1.

Mean age was 59.6 +- 13.7 and 65.2% of patients were male. The median time from diagnosis to hospital admission was 5.5 (IQR, 1-8) days. 130 patients (53.3%) had hypertension and 91 patients (37.3%) had diabetes mellitus. Thirty-seven (15.7%) patients admitted with fever and 164 (67.2%) of patients admitted with oxygen saturation (SaO_2)[?] 93% in a resting state.

On admission of the 244 patients, median serum urea and SCr were 34 (IQR, 26.8-48) and 0.86 (0.72-1.05) mg/dL, respectively. eGFR<60 mL/min per 1.73 m2 was reported in 44 (18%) of patients. During hospitalization, median peak SCr was 0.95 (IQR, 0.80-1.25) mg/dL. Mean HbA1c of diabetic patients was 7.91 +- 1.99%. Most of the patients (98.8%) admitted with elevated CRP values. IL-6 was available in 96 patients with a median value of 28.3 (IQR, 7.03-113.6) pg/mL.

Thirty-three patients (13.5%) admitted with AKI. AKI was detected in 63 patients (25.8%) on any time of hospitalization including stage 1 in 41/63 (65.1%) patients, stage 2 in 7/63 (11.1%) patients, and stage 3 in 15/63 (23.8%) patients. Table 1 shows the baseline demographic and clinical characteristics and laboratory values of all patients and comparison of the patients grouped according to the presence of AKI. Compared with patients without AKI, patients who developed AKI were significantly older, had more comorbidities; hypertension and diabetes mellitus and admitted to emergency in a shorter time after Covid-19 diagnosis. Moreover patients with AKI had higher leukocytes, CRP and D-dimer values than patients without AKI. Median value of serum urea, SCr, eGFR and percentage of decreased eGFR on admission were significantly higher in patients who developed AKI than patients who did not.

Urinalysis data of study patients are shown in Table 2. The median pH value was 6 (IQR, 5.5-6) and the median urine-specific gravity was 1019.5 (IQR, 1012-1028). After excluding glycosuric patients, the median urine-specific gravity was 1017 (IQR, 1010-1023) in 156 patients. Glycosuria was found in 88 (36.1%) patients and median blood glucose level at the time of urinalysis was 268 (IQR, 210.5-321.5) (data regarding blood glucose at the time of urinalysis in glucosuric patients were available in 48 patients). Only six patients of glucosuric patients(6/48, 12.5%) had a bloodglucose value under renal threshold defined.By urine dipstick, 189 patients (77.5%) had no heme and 188 patients (77.1%) had no proteinuria. The percentage of patients with proteinuria, hematuria and pyuria were significantly higher in patients with AKI. In contrast, urine pH was significantly lower in patients with AKI than patients without AKI.

Most patients received antiviral therapy (favipiravir, 93.4%; remdesivir, 5.3%), low-molecular-weight heparin (LMWH) (93.4%) and corticosteroid therapy (dexamethasone, 82.4%, pulse methylprednisolone, 33.6%). Patients with AKI received hydroxychloroquine treatment less frequently than those without AKI, however patients with AKI received more antibacterial therapies than patients without AKI. The treatments of the study patients; all patients and patients grouped according to the presence of AKI are shown in Table 3.

According to multivariate logistic regression analyses of risk factors on admission associated with the development of AKI in patients with Covid-19 are shown in Table 4. AKI development was associated with higher WBC and decreased eGFR as well as with proteinuria on admission.

During median 8 (IQR, 5-12) days of follow-up, thirty-five patients (14.3%) were admitted to the ICU and 33 patients (13.5%) died. Patients with AKI had significantly higher ICU admission and in-hospital mortality

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rates than patients without AKI (39.5% vs. 5.5%, P =0.000; 38.1% vs. 5%, P =0.000). Five patients (7.9% of patients with AKI) required continuous renal replacement therapy (CRRT).

Comparison of the demographic, clinical, and laboratory characteristics on admission between patients who survived and who died are shown in Table 5. Compared to the patients who survived, deceased patients were older and they had significantly higher SCr, CRP, ferritin, D-dimer and lower SaO2, lymphocyte and urine pH levels. Moreover, patients who died had significantly higher percentages of AKI, decreased eGFR, proteinuria andhematuriathan patients who survived. According to the multivariate logistic regression analysis; older age, higher CRP levels and proteinuria were independent predictors of in-hospital mortaliy (Table 6). Kaplan-Meier analysis revealed a significantly higher AKI and in-hospital mortality rate for patients with proteinuria (P =0.013) (Figure 2).

DISCUSSION

In this retrospective analysis, we investigated the urinalysis data of Covid-19 patients, incidence and risk factors of AKI development, and mortality in-hospital in patients with Covid-19.

The importance of urine to show the severity of Covid-19 was firstly reported by Liu et al. They found significantly higher positive rates of hematuria, and proteinuria and higher urine pH in Covid-19 patients compared to healthy controls [41.2% vs. 22.2%, 28.6% vs. 11.1%, 6.27 +- 0.6 vs. 5.94 +-0.7, respectively],however in contrast urine specific gravity was found significantly lower in Covid-19 patients than healthy controls (1020 +- 0.007 vs. 1023 +- 0.007) [6]. Hirsch et al. found median value of urine specific gravity as 1020 (IQR, 1010-1020) [8]. We found urine specific gravity lower than previous reports especially in patients without glucosuria. Urine ph value was similar to the values reported previously [8,10]

Notably, glucosuria was found in 36.1% of patients similar to a previous report [12]. In our study most of the patients received corticosteroids. However; in only six patients (12.5%), renal glucosuria was found without serum glucose level not exceeding renal threshold for glucose similar to a previous report [18].It may be a result of proximal tubule injury in patients with Covid-19.

The rates of other urine parameters such as ketonuria and pyuria were found in our study as 15.6% and 9%, respectively. These changes had not been focussed in previous reports mostly. We found lower rates of pyuria than other studies [6,9]. Hirch et al. had found the frequency of pyuria more than our study in Covid-19 patients with AKI (36.5% vs. 15.9%) [8].

The high frequency of renal abnormalities including proteinuria and hematuria were reported in previous reports ranging between 20.3-89.8% and 6-81%, respectively [3,6-12,19]. Our study detected an incidence of proteinuria of 22.9% and hematuria of 22.1% on admission among the hospitalized patients with Covid-19.

The quantification and characterization of proteinuria were began to be investigated in recent studies. Huart et al. found proteinuria over 500 mg/g in 68 patients (44%) and they also found urine α_1-microglobin (a marker of tubular injury) concentration higher than 15 mg/g in 89% patients suggesting tubular proteinuria [20]. In a recent analysis, Karras et al. found urine protein-creatinine ratio at admission [?] 1g/g in 84 patients (42%) with a urine albumin-protein ratio <50% in 92% of patients. They also found urine retinol binding protein concentrations as [?] 0.03 mg/mmol in 62% patients suggesting that Covid-19 associated proteinuria reflected low-molecular weight proteins, which cannot be reabsorbed by the proximal kidney tubule due to acute tubular damage [21].

Among our study population, we observed an incidence of AKI of 25.8% similar to other reports [11,22-24]. The reported rates of AKI are extremely variable; however, available evidence suggests that it likely affects >20% of hospitalized patients and >50% of patients in the ICU [25]. In a recent meta-analysis; the incidence of AKI was reported as 13.28% (162/1220) in all included studies [26].Differences may have resulted from definitions of AKI and the populations studied. The pathogenesis of AKI in patients with Covid-19 is likely multifactorial, involving both the direct effects of the SARS-CoV-2 virus on the kidney such as collapsing glomerulopathy, endothelial damage, coagulopathy, complement activation, and inflammation and the indirect mechanisms resulting from systemic consequences of viral infection or effects of the virus

on distant organs including the lung, in addition to mechanisms relating to the management of Covid-19 [27]. Some studies reported the presence of viral particles within both the tubular epithelium and podocytes on electron microscopy, implying the direct infection of the kidney [28,29], others failed to demonstrate the presence of virus in the kidney [30-32]. In addition to direct pathophysiological mechanisms, renal dysfunction in the context of Covid-19 may also arise through the systemic effects of SARS-CoV-2 infection and critical illness. Volume depletion, exposure to nephrotoxins, increase in renal ven pressure and reduced filtration due to positive end expiratory pressure (PEEP), the release of cytokines, vasoactive substances and damage associated molecular patterns (DAMPs) from lung injury are also other mechanisms for kidney injury [27].

Risk factors of AKI in Covid-19 are diverse and multifactorial. A number of previous studies have suggested that the development of AKI in Covid-19 patients may be affected by multiple risk factors, such as older age, male sex, black race, comorbidities, increased CRP, proteinuria at admission, the need for ventilator support, use of vasopressor drug treatment [3,8,20,23,25]. On the basis of our multivariate logistic regression analysis; higher leukocytes, decreased eGFR and presence of proteinuria were independent predictors of AKI. As reported previously, we observed a high prevalence of hematuria and proteinuria in Covid-19 patients with AKI [3,12,19,21,22]. However in a recent study, they found no significant differences in proteinuria, hematuria and leukocyturia among patients with AKI compared with non-AKI patients [24].

Several mortality risk scores have been proposed to predict mortality in Covid-19 patients [33-35], most of which did not include an evaluation of kidney status. However, kidney indicators seem to be the main predictors of mortality. We found the highest mortality frequencies in patients with AKI compared to patients without AKI (38.1% vs. 5%,P =0.000) consistent with previous reports [19,23,36]. In a recent meta-analysis, Covid-19 patients with AKI had a significantly increased risk of death compared patients without AKI (OR 30.46, 95% CI 9.29-15.19) [26]. We also found that proteinuria were independently associated with mortality similar to previous reports [11,12]. Pei et al. showed higher overall mortality in the patients with renal involvement, including hematuria, proteinuria, and AKI, compared with that of patients without renal involvement (11.2% vs 1.2%,P =0.006) [3]. Cheng et al. reported the incidence of mortality in-hospital in the patients with elevated baseline serum creatinine on admission was 33.7%. They also found that proteinuria of any degree, hematuria of any degree, elevated baseline BUN, elevated baseline SCr, peak SCr> 133 mmol/l, and AKI over stage 2 were independently associated with mortality [7]. In another study Portoles et al. confirmed that elevated baseline SCr, previous chronic kidney disease, hematuria, and in-hospital AKI were independent risk factors for mortality in-hospital after adjusting for age, sex and comorbidity [9]. However; in a recent study, Ouahmi et al. reported that proteinuria was not found as an independent predictor for in-hospital mortality [24].

This study has several limitations. First, the number of patients included in this study is limited, and there were some missing data. Second, an accurate baseline serum creatinine and urine output was not available, which may have led to an under or overestimation of AKI or erroneous associations. We also were unable to distinguish patients who had preexisting proteinuria and hematuria prior to presentation from those who had it new-onset on admission due to lack of previous urinalysis in most patients. Third, disease severity was not defined because of missing data. Fourth, quantification of proteinuria could not be investigated.

Our study has some strengths. Mostly previous reports had urinalysis data based on dipstick results [3,7,9]. Our urinalysis results based on both dipstick and automatic sediment analyzers. Also we did not include patients with urinary catheterization, so hematuria may reflect more kidney involvement rather than urinary tract abnormalities.

In conclusion, proteinuria on admission is associated with development of AKI and in-hospital mortality in patients with Covid-19. We hence reinforce the suggestion that urinalysis may be useful for the evaluation of COVID-19 progression and early diagnosis of kidney damage before SCr rise. Early detection and effective intervention of kidney involvement may help to reduce development of AKI and to improve the vital prognosis of Covid-19.

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Table 1. The demographic, clinical and laboratory characteristics of the study patients on admission; all patients and patients grouped according to the presence of acute kidney injury (AKI).

Variables
Age (years)
Gender (male,%)
HT (%)
DM (%)
Time diagnosis to admission (day)
Fever on admission (%)
sBP (mmHg)
dBP (mmHg)
SaO2 (%)
ΩB" (ξ10³/μΛ)
Λψμπηοςψτε (ξ10³/μΛ)
Hemoglobin (g/dL)
Πλατελετ (ξ10³/μΛ)
Glucose (mg/dL)
Urea (mg/dL)
Creatinine (mg/dL)
eGFR (ml/min/1.73m²)
Decreased eGFR (%)
Albumin (g/L)
Sodium (mEq/L)
Potassium (mEq/L)
Chloride (mEq/L)
Calcium (mg/dL)
AST (U/L)
ALT (U/L)
LDH (U/L)
CRP (mg/L)
Ferritin (ng/mL)
Fibrinogen (mg/dL)
Δ-Διμερ (μγ/Λ)
CK (U/L)

ALT: alanine aminotransferase; **AST:** aspartate aminotransferase; **CK:** creatinine kinase; **CRP:** C-reactive protein; **dBP:**

Table 2 . Urinalysis data obtained within 48 hours in patients with COVID-19.

Variables	All patients n=244	No AKI n=181	AKI n=63	P
pH, median (IQR)	6 (5.5-6)	6 (6-6.5)	5.8 (5.5-6)	**0.000**
Specific gravity, median (IQR)	1019.5 (1012-1028)	1020 (1011-1028)	1018 (1013-1027)	0.977

Variables	All patients n=244	No AKI n=181	AKI n=63	P
Protein, n (%) 0, negative or trace 1+ 2+˜3+	188 (77.1) 29 (11.9) 27 (11)	150 (82.9) 16 (8.8) 15 (8.3)	38 (60.3) 13 (20.6) 12 (19.1)	**0.000**
Blood, n (%) 0, negative or trace 1+ 2+˜3+	189 (77.5) 26 (10.7) 29 (11.8)	153 (84.5) 17 (9.4) 11 (6.1)	36 (57.1) 9 (14.3) 18 (28.6)	**0.000**
Glucosuria, n (%)	88 (36.1)	64 (35.4)	24 (38.1)	0.697
Ketonuria, n (%)	38 (15.6)	28 (15.5)	10 (15.9)	0.939
Urine microscopy automated, n (%) White blood cells [?] 5/hpf Red blood cells [?] 3/hpf Epithelial cells* Yeast cells*	22 (9) 54 (22.1) 39 (15.9) 9 (3.7)	12 (6.6) 27 (14.9) 31 (17.1) 8 (4.6)	10 (15.9) 27 (42.9) 9 (14.3) 3 (4.8)	**0.027 0.000** 0.600 0.783

AKI: acute kidney injury; hpf: high power field. *if [?] 1 element/hpf is present.

Table 3. The treatments of the study patients; all patients and patients grouped according to the presence of acute kidney injury (AKI).

Variables	All patients n=244	No AKI n=181	AKI n=63	P
Treatment	Treatment	Treatment	Treatment	Treatment
Antiviral, %	98.4	98.3	98.4	0.998
LMWH, %	93.4	95	88.9	0.091
Corticosteroid, %	91.4	90.6	93.7	0.605
O2, %	74.2	72.9	77.8	0.449
Colchicine, %	34.8	33.7	38.1	0.528
Antibacterial, %	29.1	24.9	41.3	**0.014**
Hydroxychloroquine, %	27.5	30.9	17.5	**0.039**

LMWH: low-molecular-weight heparin.

Table 4. Multivariate logistic regression analyses of risk factors on admission associated with

the development of acute kidney injury in patients with Covid-19.

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Variables	Multivariate	Multivariate	Multivariate
	OR	**95% CI**	P
Age, years	1.026	0.995-1.059	0.105
Hypertension	0.640	0.274-1.495	0.302
Diabetes	0.863	0.393-1.897	0.714
Time diagnosis to admission, day	0.958	0.873-1.051	0.367
ΩΒˆ (ξ10³/μΛ)	1.000	1.000-1.000	**0.028**
Decreased eGFR	0.210	0.087-0.508	**0.001**
CRP (mg/dL)	1.003	0.999-1.008	0.174
Urine pH	0.468	0.215-1.019	0.056
Proteinuria	0.405	0.181-0.906	**0.028**
Hematuria	0.500	0.205-1.219	0.127
Pyuria	0.920	0.259-3.264	0.897

CRP: C-reactive protein; **eGFR:** estimated glomerular filtration rate; **WBC:** white blood cell.

Table 5. Comparison of the demographic, clinical and laboratory characteristics on admission between patients who survived and who died.

Variables	Patients who survived	Patients who survived	Patients who died	Patients who died	P
	n	**Summary**	**n**	**Summary**	
Age (years)	211	58.2 ± 13.6	33	68.5 ± 10.4	**0.000**
Gender (male,%)	211	63	33	78.8	0.077
HT (%)	211	51.2	33	66.7	0.097
DM (%)	211	35.5	33	48.5	0.153
sBP (mmHg)	203	120 (110-130)	33	120 (110-130)	0.476
dBP (mmHg)	203	70 (70-80)	33	120 (110-130)	0.529
SaO2 (%)	211	92 (89-94)	33	90 (87-92)	**0.006**
Λψμπηοςψτε (ξ10³/μΛ)	211	1.0 (0.7-1.4)	33	0.6 (0.5-1.1)	**0.001**
Hemoglobin (g/dL)	211	13.1 (12.3-14.1)	33	12.1 (11.1-13.9)	0.065
Πλατελετ (ξ10³/μΛ)	211	216 (161-278)	33	191 (144-289)	0.304
Creatinine (mg/dL)	211	0.83 (0.69-1.0)	33	1.09 (0.91-1.35)	**0.000**
eGFR < 60 mL/min/1.73m²	211	13.7	33	36.4	**0.001**
AKI	211	11.8	33	27.3	**0.017**
Albumin (g/L)	201	3.5 (3.3-3.7)	33	3.3 (2.9-3.6)	0.053
Sodium (mEq/L)	209	137 (134-139)	33	135 (132-140.5)	0.397

Variables	Patients who survived	Patients who survived	Patients who died	Patients who died	P
Potassium (mEq/L)	208	4.3 (3.9-4.6)	33	4.4 (4-4.7)	0.333
CRP (mg/L)	211	74.6 (38.8-129)	33	115 (77.4-204.5)	**0.000**
Ferritin (ng/mL)	210	489.3 (256.7-804.6)	33	520.3 (182.5-878.6)	0.828
Δ-Διμερ (μγ/Λ)	205	750 (505-1250)	33	1410 (845-3250)	**0.000**
Urine ph	211	6 (5.5-6)	33	5.5 (5.5-6)	**0.003**
Urine specific gravity	211	1020 (1012-1028)	33	1018 (1014-1029)	0.858
Proteinuria (%)	211	18.9	33	48.5	**0.000**
Glucosuria (%)	211	36.9	33	30.3	0.458
Ketonuria (%)	211	14.7	33	21.2	0.337
Urine microscopy automated, n (%) White blood cells [?] 5/hpf Red blood cells [?] 3/hpf	211	9.5 18	33	6 42.4	0.524 **0.000**

AKI: acute kidney injury;**CRP:** C-reactive protein;**dBP:** diastolic blood pressure; **DM:** diabetes mellitus;**eGFR:** estimated glomerular filtration rate; **HT:**hypertension; **SaO2:** oxygen saturation; **sBP:** systolic blood pressure.

Table 6. Risk factors associated with mortality in-hospital of Covid-19 patients.

Variables
Age, years
SaO2 (%)
Λψμπηοςψτε (ξ10^3/μΛ)
Decreased eGFR
AKI
CRP (mg/L)
Δ-Διμερ (μγ/Λ)
Urine pH
Proteinuria
Hematuria

AKI: acute kidney injury; **CRP:** C-reactive protein; **eGFR:** estimated glomerular filtration rate; **SaO2:** oxygen saturation

LEGENDS OF THE FIGURES

Figure 1. Flow chart of study cohort.

Figure 2. Kaplan-Meier survival analysis of patientswith Covid-19 subgrouped by proteinuria.

Hospital admissions for patients with Covid-19 diagnosis
between October 2nd and December 25th, 2020

n=695

Multiple admissions for one patient; only the first hospital episode
was included (n=19)

Patients transferred from intensive care unit (n=15)

Patients with urinary tract infections and urinary catheters (n=10)

Patients with dialysis (n=8)

Pregnant patients (n=1)

n=53 patients (excluded)

Urinalysis were
available
n=244