

Assessment of changes in blood urea and creatinine levels in patients with coronavirus disease 2019 (COVID-19)

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Abstract

Background Coronavirus disease 2019 (COVID-19) is new respiratory tract infections disease with an evolving understanding of its epidemiology and clinical appearances. Kidney defect seems to be common in patients with Covid-19. Urea and creatinine level often occurs at the beginning or during the infection. This evidence shows that Covid-19 also attacks the kidneys. The aim of this study was to evaluate changes in biochemical parameters associated with kidney function, including urea and creatinine in patients with COVID-19.

Methods We conducted a retrospective analysis of the plasma creatinine and urea levels of the 100 COVID-19 patients with normal plasma creatinine and urea at first clinical presentation of COVID-19.

Results Among these 100 patients with COVID 19, total of 35 (35%) patients, increased BUN and creatinine levels occurred at duration of 2–4 days after the onset of viral infection. The mean serum urea level in first clinical presentation and at duration of 2, 3 and 4 days after the onset of viral infection were 34.75 ± 0.10 and 37.64 ± 0.32 , 39.81 ± 0.10 , 42.56 ± 0.35 mg/dl, respectively. The mean of creatinine concentration in first clinical presentation and at duration of 2, 3 and 4 days after the onset of viral infection were 1.50 ± 0.026 and 1.51 ± 0.016 , 1.99 ± 0.012 , 2.58 ± 0.020 mg/dl, respectively.

Background

On December 31, 2019 a cluster of cases of pneumonia of unknown origin was reported in Wuhan city, in the Hubei province of China. After a short time, Chinese health authorities confirmed that this cluster was associated with a Novel Coronavirus 1 and was named coronavirus disease 2019 (COVID-19) in February, 2020, by World Health Organization (WHO). From the beginning of the coronavirus COVID-19 outbreak until now, COVID-19 has affected more than 2,536,673 patients in 210 countries and has become a major global health concern. 175,759 people have died so far from the coronavirus COVID-19 outbreak as of April 07, 2020. The highest number of mortality from coronavirus COVID-19 is in the United States, Italy and Spain, respectively (1–7). Coronavirus COVID-19 has rapidly spread across China and many other countries, therefore, the WHO declared the COVID-19 outbreak as the sixth public health emergency of international concern. So, health workers, governments and the public requires a coordinated international response to prevent the spread of the disease (5–7). Among patients with confirmed coronavirus COVID-19, we encountered a significant number of patients with changes in biochemical parameters associated with kidney function (8). According to a recent study, Shi et al., reported that severe acute respiratory syndrome coronavirus 2 interacts with human angiotensin converting enzyme-II (ACE2) molecules through its Spike protein. In addition to lungs and heart the expression of ACE2 receptor has also been observed in kidneys (9–12). We retrospectively analyzed the clinical laboratory information on kidney function from 100 cases of coronavirus COVID-19 who were admitted into the Ayatollah Alimoradiyan Hospital in Nahavand, Hamadan Province, from February 17, 2020 to April 21, 2020.

Methods

Patients and Data collection

We conducted a retrospective analysis of the plasma creatinine and urea levels in blood of the 100 COVID-19 patients with normal plasma creatinine and urea at first clinical presentation of COVID-19 in Ayatollah Alimoradiyan Hospital in Nahavand, Hamadan Province, from February 17, 2020 to April 11, 2020 were collected and retrospectively analyzed. Initial laboratory investigations included complete blood count (CBC), erythrocyte sedimentation rate (ESR), arterial blood gas (ABG), lactate dehydrogenase (LDH), creatine phosphokinase (CPK), C-reactive protein (CRP) liver, and renal function tests. Serial monitoring of the laboratory profile was performed according to the clinical progress of individual patient. All the patients were laboratory-confirmed positives for COVID-19 by use of quantitative RT-PCR (qRT-PCR) on throat swab samples. We reviewed clinical laboratory findings for all the COVID-19 patients. All information was obtained and curated with a customized data collection form.

Results

Patient demographic data

During the survey period, 100 patients with approved COVID-19 were admitted the Ayatollah Alimoradiyan Hospital in Nahavand, Hamadan Province. Among 100 patients, 35 patients (and 11 females 24 males) (35%) with an average age of 51 years (20 to 82) were subsequently found to have elevated plasma creatinine and urea levels during the later clinical course. Most of these 31 (88.57%) patients had fever on appearance. High temperature ($\geq 38.5^\circ\text{C}$) was observed in 87% of patients. The details are shown in table 2.

Laboratory test findings

All patients had raised levels of high-sensitivity CRP and ESR (100 %). In addition, mean serum LDH (350-450 U/l) was increased, especially in those with high baseline serum creatinine and urea levels (Figure 1-Table 2).

On the other hand, urea and creatinine levels did not differ between male and female of patients. But, But, old Patients who developed impaired kidney function has higher urea and creatinine levels ($P < 0.001$) Figure 2.

Discussion

COVID-19 is a new respiratory tract infections disease with a challenging morbidity and mortality in world. As of February 22, 2020, COVID-19 has killed 96,000 people worldwide. The initial phase in Coronavirus COVID-19 infection is to attach to the host cell receptor and enter the host cells. A varied range of non-respiratory symptoms has consequently been described suggesting other organ involvements including the liver, heart and kidney during the course of the

COVID-19 (1, 2, 3, 9–10). Corona viruses have a structure of spike protein, which is closely bound to human cell receptor ACE2. So, the cells with ACE2 expression may act as target cells and be sensitive to COVID-19 infection. Recently, Lin W et al., reported that ACE2 receptors expression in human kidneys reveals a potential route of coronavirus COVID-19 infection (10). Also in another study, Fan et al., showed that ACE2 receptors are expression in human kidneys. Yan et al., reported that 63% of COVID-19 patients had a raised level of proteinuria. These results demonstrate that coronavirus COVID-19 mediated impaired kidney function may be one of the main causes final death in COVID-19 patients (11). Luwen Wang et al., reported that 12 (10.8%) patients showed increase of BUN or creatinine after 2 days. In this study, we found that 35 (35%) of patients with COVID-9 had increase in creatinine and urea levels (Table 1). Over time, the creatinine and urea levels rate increased further (13). Guan et al. showed also the data of clinical characteristics of 1,099 patients confirmed with COVID-19. From this study, the renal function showed that the patients' number of creatinine $\geq 133 \mu\text{mol/L}$ were (1.6%). These laboratory tests findings suggesting that impaired kidney function are comparatively common following COVID19 infection. Recently, some investigators have reported they have successfully isolated coronavirus COVID-19 particles from the sample urine of COVID-19 patients, showing that kidney-originated viral particles may penetrate the urine via glomerular filtration. According to our and other study, these findings confirm that the human kidney is also a place of coronavirus COVID-19 infection and replication outside of the lungs (12–13, 15). However, the kidney function of patients with COVID-19 requirements to be monitored regularly, particularly in patients with elevated plasma creatinine and urea.

Conclusion

Analysis of creatinine and urea levels in patients at the onset of the disease and after (2 to 4 days) showed that impaired kidney function is occurs in COVID-19 patients, it is one of the leading causes of death in these patients.

Abbreviations

COVID-19
coronavirus disease 2019
ACE2
angiotensin converting enzyme-II
WHO
World Health Organization
CBC
complete blood count
ESR
erythrocyte sedimentation rate
ABG
arterial blood gas
LDH
lactate dehydrogenase
CPK
creatine phosphokinase
CRP
C-reactive protein

Declarations

Ethics approval and consent to participate

All procedures were approved by Hamadan University of Medical Sciences, Hamadan, Iran (IR.UMSHA.REC.1399.095). All research was performed in accordance with the relevant guidelines and regulations.

Consent for Publication

Person identifiable data was not collected as part of this study and no individual level data are presented within this publication.

Availability of data and material

The datasets used and analyzed in the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

HM designed the study. HM performed the experiments. NMT and HM performed the data analysis. HM drafted the manuscript. HM supervised the project. All authors contributed to the interpretation of the results, provided critical feedback, contributed to the writing of the manuscript and have approved the final version.

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Tables

Table 1 Clinical Characteristics of COVID-19 patients

Groups	Patients without	changes in urea and creatinine levels	Patients with changes in urea and creatinine levels	P value
All Patients (n=100)	N (n=65)		N (n=35)	
Age years				
≥55yr	42 (64.61%)		29 (82.85%)	0.001
<55yr	23 (35.39%)		6 (17.15%)	
Sex				
Male	45 (69.23%)		24 (68.57%)	0.398
Female	20 (30.77%)		11(31.43%)	
Symptoms				
Fever	56 (86.15%)		31 (88.57)	0.0023
palpitation	55 (84.61%)		33(94.28%)	0.0035
cough	40(61.53%)		23(65.71%)	0.0017
chills	37(59.92%)		26(4.28%)	0.0051
malaise	35 (53.84%)		31 (88.57)	0.0075
dyspnea	34(52.30%)		20(57.14%)	0.002
anorexia	2(3.07%)		0(0)	0.075
headache	4(6.15%)		1(2.58%)	0.014
myalgia	3(4.61%)		2(5.71%)	0.034

Table 2 Changes in urea and creatinine levels in 100 COVID-19-confirmed patients

P values indicate differences between patients without changes in urea and creatinine levels and patients with changes in urea and creatinine levels. *P* < 0.05 was considered statistically significant. Abbreviation: BUN, blood urea nitrogen; COVID-19, coronavirus disease 19

COVID-19-confirmed patients (<i>n</i> = 100)	Number	BUN, mg/dL 7 to 20	Creatinine, mg/dL 0.84 to 1.21
Patients without changes in urea and creatinine levels			
First clinical presentation (1 day)	65	10.63±0.02	0.86±0.012
2 day	65	9.62±0.09	0.94±0.032
3 day	65	10.40±0.10	0.91±0.030
4 day	65	9.84±0.09	0.85±0.016
Patients with changes in urea and creatinine levels			
First clinical presentation (1 day)	35	34.75±0.10	1.50±0.026
2 day	35	37.64±0.32	1.51±0.016
3 day	35	39.81±0.10	1.99±0.012
4 day	35	42.56±0.35	2.58±0.020
<i>P</i> value		<0.0001	< 0.0078

Figures

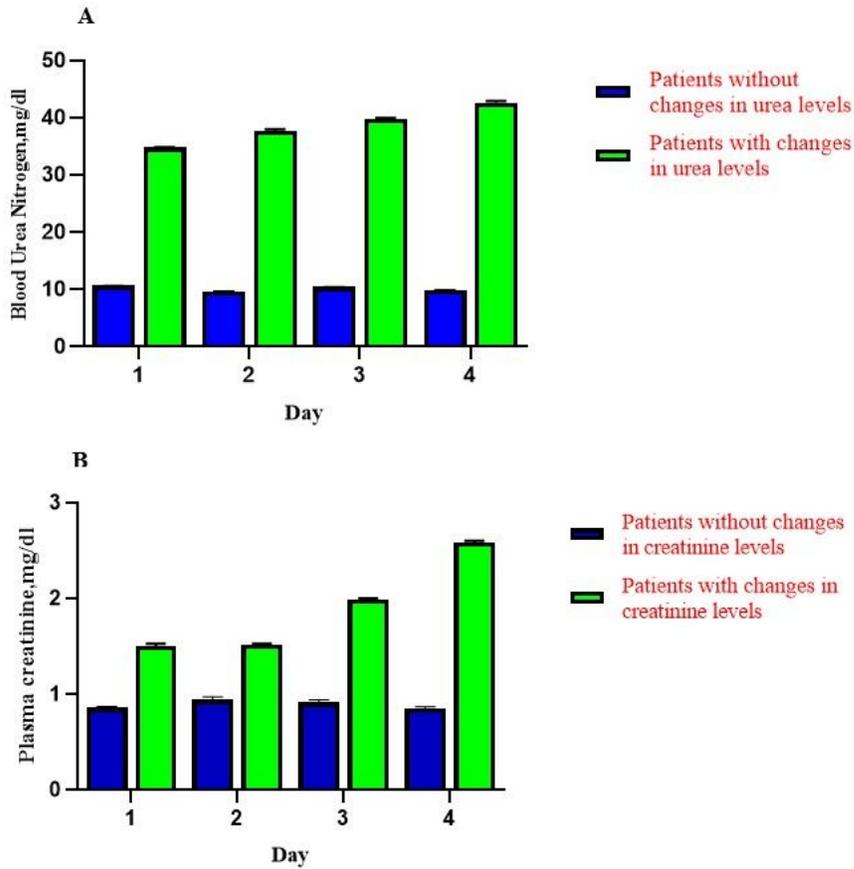


Figure 1

Differences between patients without changes in urea and creatinine levels and patients with changes in urea and creatinine levels

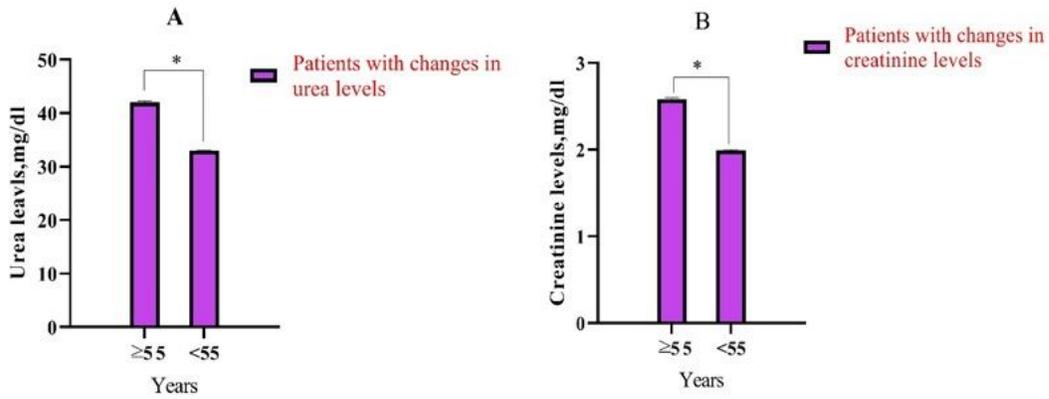


Figure 2

Differences between age year's patients with changes in urea and creatinine levels. * P < 0.05 was considered statistically significant.