Assessment of Serum Urea and Serum Creatinine Level in Covid-19 Patients

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Abstract
Aim & Objectives: The aim of this study is to estimate the levels of Serum Urea and Creatinine in COVID-19 patients and healthy controls.
Materials And Methods: In this study, 50 COVID-19 patients and 50 healthy controls of both gender matching in age and sex were included. The analysis of biochemical parameters was done by using autoanalyzer using diagnostic reagent kit.
Results: In the present study Mean of Serum Urea and Creatinine was higher in COVID-19 patients than controls. ($P < 0.001$)
Conclusion: Significant changes were observed in Serum Urea and Creatinine. They are favourable prognostic biomarkers with high accuracy for predicting the in-hospital mortality in patients with COVID-19

Introduction

At the winter of 2019, Coronavirus Disease 2019 (COVID-19), an emerging infectious disease with unclear etiology broke out in Wuhan City, Hubei Province, China [1]. Later, this unknown virus was clarified and named as severe acute respiratory syndrome coronaviruse-2 (SARS-CoV-2) [2, 3]. Now, it has been pandemic across the world. Up to January 1st, 2021, there were approximate 90 million accumulated confirmed patients of SARS-CoV-2 infections in 220 countries, of them about one million cases have died [4]. All humanity is sustained huge disaster from SARS-CoV-2 [5, 6].
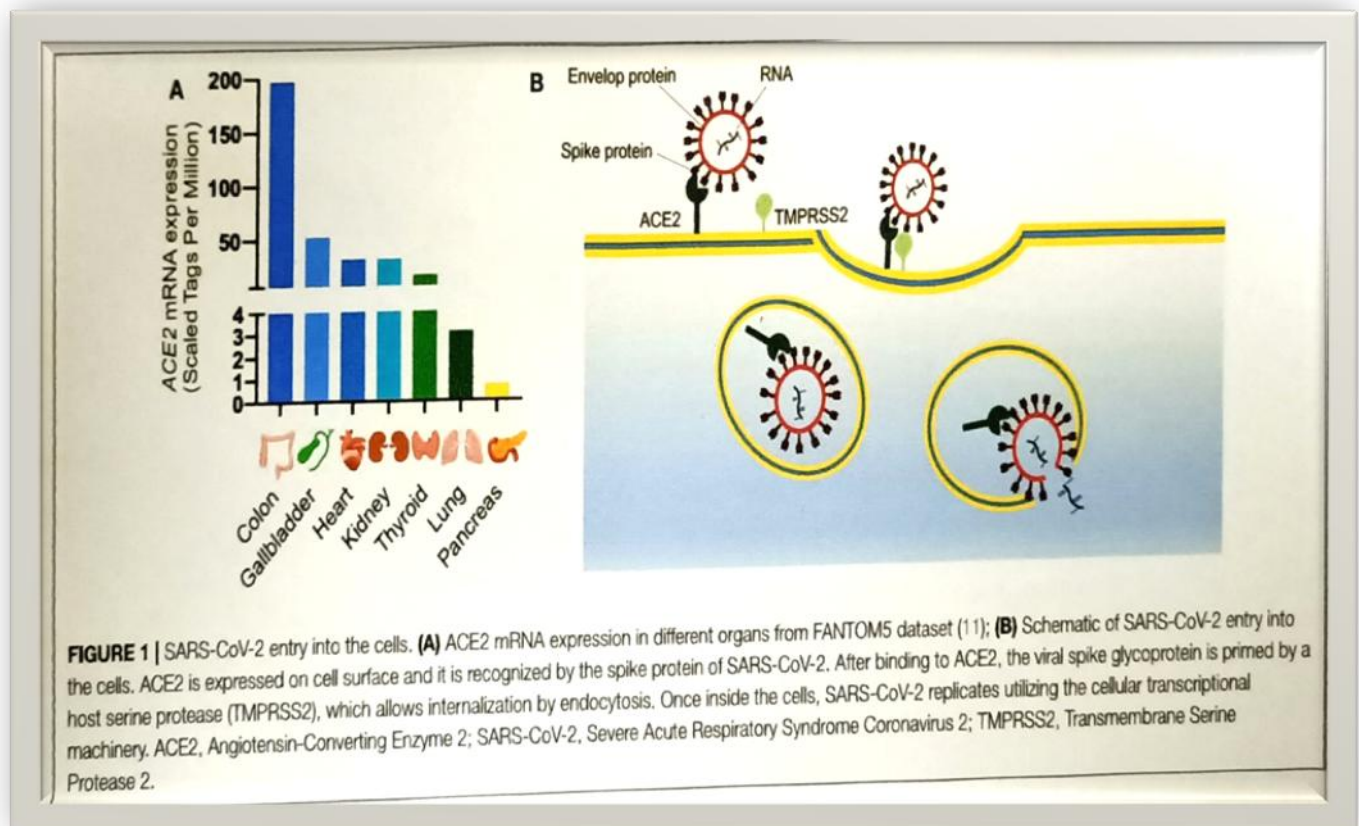
Previous studies have demonstrated that COVID-19 patients mainly accompanied with fever, diarrhea, dry cough, lymphocyte reduction and radiographic evidence of pneumonia [7].

The spike protein is key to its high-virality as the RNA virus enters cells through binding between the S protein and its host receptor. The virus efficiently binds to the angiotensin converting enzyme 2 (ACE2) receptor which is highly expressed in many organs including the bronchus and lung parenchyma, heart, kidney, and gastrointestinal tract (Figure 1A). Zhao et al. demonstrated that ACE2 is highly expressed in the alveolar epithelial type II cells (AECII), suggesting that these cells could be the reservoir for the virus. Other studies have showed that the AECII cells have several genes related to the viral process, replication, life cycle and assembly, therefore facilitating the viral replication in the lung.

After binding to ACE2, the cellular transmembrane protease, and serine 2 (TMPRSS2) mediates the S protein priming allowing the virus to enter the host

cells through clathrin-dependent endocytosis (Figure 1B). The endosomal entry way for the virus requires a low inner pH, and once inside, the virus exploits the cellular transcriptional machinery to replicate itself and spread throughout the host. By hijacking the endogenous transcriptional machinery, the virus alters the behavior of the host cells and tissue making them unable to fulfill their normal function.[8].

FIGURE 1 | SARS-CoV-2 entry into the cells. **(A)** ACE2 mRNA expression in different organs from FANTOM5 dataset (11); **(B)** Schematic of SARS-CoV-2 entry into the cells. ACE2 is expressed on cell surface and it is recognized by the spike protein of SARS-CoV-2. After binding to ACE2, the viral spike glycoprotein is primed by a host serine protease (TMPRSS2), which allows internalization by endocytosis. Once inside the cells, SARS-CoV-2 replicates utilizing the cellular transcriptional machinery. ACE2, Angiotensin-Converting Enzyme 2; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; TMPRSS2, Transmembrane Serine Protease 2.

Recently, Cheng et al., have reported that some COVID-19 patients had an elevated level of proteinuria, suggesting SARS-CoV-2 infection might result in acute kidney injury (AKI).[9] SARS-CoV-2 can also directly infect human kidney organoids via the ACE2 receptor.[10] However, no evidence has demonstrated that SARS-CoV-2 can directly infect human kidney leading to AKI.

In this work, we analyse the clinical data on renal function from 50 cases of COVID-19 who were admitted in Shivatej Arogya Seva Santhas Govt. Covid Care Centre, Khed, Maharashtra, India. To elucidate the mechanism of renal injury caused by SARS-CoV-2 infection.

Material And Methods

This study was carried out on COVID-19 patients admitted in Shivtej Arogya Seva Sansth's Govt. covid care center. Fifty patients with confirmed COVID-19 according to ICMR guidelines and fifty healthy age and sex matched non covid-19 controls were included in the study often obtaining their informed consent. The study was conducted on with age group between 20 to 60 years. The analysis of biochemical parameters was done using standard grade reagent chemicals. Serum Urea and Serum Creatinine were assayed by autoanalyzer using diagnostic reagent kit.

The exclusion criteria included subjects of any systemic or metabolic disease, liver disease, vascular diseases, renal artery stenosis, alcoholics, pregnant female and those who were taking any kind of medication last few years. A record was maintained containing current history, diet along with laboratory investigations and previous history of any disease.

Distribution Of Study Subjects:

Group I	N = 50 COVID-19 patients.
Group II	N= 50 Healthy controls

Collection Of Blood Samples:

Blood was collected from each subject under aseptic conditions by using vacutainers. The blood samples were allowed to clot at room temperature for 20–30 minutes & serum was separated from cells by centrifugation for analysis of biochemical parameters. The analysis of biochemical parameters was done by using standard grade reagents and chemicals. Serum reagent as per the manual provided by the manufacturer.

Results

Table no. 1: The mean value of Serum Urea and Creatinine in COVID-19 patients and controls

Name Of the Parameters	Covid-19 Patients (N=50)		Controls (N==50)		Significance
	Mean ±SD	Std. Error of Mean	Mean ±SD	Std. Error of Mean	
Urea	35.86±8.80 ***	1.245	26.32±4.70	0.66	**P =< 0.001**
Creatinine	1.65±0.32 ***	0.466	0.79±0.18	0.25	**P = <0.001**

The statistical method uses to compare data was unpaired 't' test

*P> 0.05……Not Significant

**P<0.05……...Significant

***P<0.001…...Highly Significant

There is highly statistically significant difference in means of serum Urea and Creatinine (P < 0.001) as compare to controls.

Discussion

COVID-19 is a new respiratory tract infectious 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 COVID-19.[11,12,13,14,15]

Recently Luwen Wang et al., reported that 12 (10.8%) patients showed increase of BUN or creatinine after 2 days.[16] Also in another study we found that 35 (35%) of patients with COVID-9 had increase in creatinine and urea levels.[17] Li et al. analysed kidney function in 193 COVID-19 patients and found that 31% of patients had an elevated level of blood urea nitrogen (BUN) and 22% had increased serum creatinine.[18]

In Our study we also found that highly significant (P <0.001) Serum Urea and serum Creatinine level in COVID-19 patients compared to controls . According to our and other study, these findings confirmed that the human kidney is also a place of COVID-19 infection and replication outside of the lungs. These laboratory tests finding 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. [16,19,20] However, the kidney function of patients with COVID- 19 requirements to be monitored regularly, particularly in patients with elevated serum creatinine and urea.

Conclusion

We conclude that renal dysfunction is positively correlated with the severity of covid-19 patients. These easily available biomarkers can direct physician worldwide to effectively priority resources for patients at high risk of mortality and to implement more aggressive treatments at an earlier phase to save patients' lives.

This study could help healthcare workers to identify those patients at an early stage for early treatment. However, a large sample size and multicentre studies are needed in order to confirm this study.

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