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ORIGINAL ARTICLE

Renal Profile of patients Diagnosed with Corona Virus Disease (Covid-19) admitted in Tertiary Care Hospital

HUMA AMIN[1], FATIMA TUR ZUHRA[1], NADIA WALI[2], FARHANA SHAUKAT[3], MUHAMMAD SOHAIL ASLAM[2], ATIKA MASOOD[2]
[1]Department of Pathology, Rawalpindi Medical University, Rawalpindi. Pakistan.
[2]Department of Pathology, Akhtar Saeed Medical & Dental College, Lahore, Pakistan.
[3]DHQ Hospital, Rawalpindi, Pakistan.
Correspondence to Dr. Huma Amin, Email: humaamin2000@hotmail.com, Cell: +923334331490

ABSTRACT

Aim: To assess the baseline renal profile of patients with COVID-19.
Methods: It was a cross sectional study, conducted in hospitals of Rawalpindi Medical University from March to August 2020. Consecutive 169 confirmed cases of COVID-19 were enrolled. Patients with history of kidney disease were not included. Peripheral blood samples were analysed for renal functions on fully automated chemistry analyser. Estimated glomerular filtration rate (eGFR) for every patient was calculated using two equations for chronic kidney disease epidemiology collaboration (CKD-EPI) and modification of diet in renal disease (MDRD).
Results: Out of total 169 COVID-19 patients, 97(57%) were males 72(43%) were females. The mean age was 54.1±16.30 (18 to 92) years. A total of 96(57%) patients were below 60 years of age. Mean Urea, serum creatinine (Scr) and blood urea nitrogen (BUN) were found to be elevated in this study cohort with no statistically significant difference with respect to age and gender (P value >0.05). Scr was raised in 46(27%) while 113(67%) and 103 (62%) patients had elevated serum Urea and BUN respectively. eGFR of <60mL/min/1.73m^2 was observed in 50(30%) of patients.
Conclusion: Elevated mean Urea, Scr and BUN were observed in COVID 19 patients without any significant difference according to age and gender. Moderate to severe derangement in eGFR was noted in one third of COVID 19 patients.
Keywords: COVID-19, Renal function test, Estimated glomerular filtration rate

INTRODUCTION

Coronavirus disease 2019 (COVID-19) was declared a global pandemic by World Health Organization on 11th March 2020[1]. It is a recently encountered infectious disease caused by the SARSCoV-2 virus[2]. COVID-19 has brought forward new challenges for the entire world[3].

The Coronavirus presents with an altered pattern of illness when compared with other viruses of the same family. This virus not only causes respiratory manifestation but also involves the liver, kidneys and even pancreas[4]. In most of the severe cases of COVID-19, an exaggerated immune response triggers the overproduction of cytokines resulting in circulatory failure and multi-organ dysfunction. One of the organs commonly targeted by this virus is the kidney[5]. Initially it was considered that kidney involvement in COVID-19 patients was negligible. However recently there is growing evidence that severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) specifically invades the kidneys and acute kidney injury (AKI) is common in COVID-19 patients[6]. Angiotensin converting enzyme 2 (ACE2) is deemed to be a functional receptor of SARS CoV-2. ACE2 receptors are expressed in lung tissue as well as in the kidneys, primarily in afferent arterioles, proximal tubules, collecting ducts, and ascending limb of Helen[2]. Kidney dysfunction is characterized by an increased in Scr along with abnormalities in the urinary sediments[6]. The presence of Viral nucleic acid in urine of 6.9% pts with this disease also advocate kidneys as a target of virus[2].

The evaluation of kidney function should be taken into account timely in every COVID patient at risk. [5] Impaired renal function results in obstruction in excretion of metabolites and toxins from the body, adversely affecting the electrolyte and acid-base balance. Uremia will be an additional factor endangering the life of already sick patients[7]. Abnormal kidney function as a consequence of injured glomerular epithelium is one of the considerable risk factors of death in severely ill COVID-19 patients particularly with diabetes[5]. Acute kidney injury (AKI) is frequently noticed in critically ill COVID but can occur in all stages of infection.[6] Clinical awareness, early detection, diagnosis of renal injury and timely and efficient interventions are indispensable for reducing complications and improving prognosis[7,8].

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Serum creatinine levels are mainly affected by kidney function but few other factors such as age, sex, ethnicity and muscle mass also influence it. Therefore to estimate glomerular filtration rate (eGFR) based on creatinine formulas biological variations are also taken into consideration[9]. For estimation of GFR, CKD EPI equation is now used as worldwide standard instead of the MDRD equation used formerly[10]. MDRD is commonly used to estimate GFR by clinical laboratories because it only requires knowledge of a serum creatinine level, age, gender, and race of a person[9]. Whereas eGFR based on the CKD-EPI equation provides better risk prediction in patients with heart failure, end stage renal disease and diabetes as compared to the eGFR values calculated using the MDRD equation[11].

Involvement of lungs in COVID-19 patients is well recognized but its effect on kidney function is yet to be explored. [9] The exact incidence of acute kidney failure and its prognosis in these patients are still not known and information regarding clinical impact of kidney involvement is not available[12]. In this study, we present the details of renal function of patients with laboratory confirmed SARS-CoV-2 infection.

The aim is to observe the effect of COVID-19 on renal profiles of these infected patients at the time of admission at tertiary care teaching hospital and to compare the eGFR measurements by two commonly used formulas.

MATERIALS AND METHODS

This cross sectional study was conducted for six months from March 2020 to August 2020. A total of 169 admitted patients of COVID-19 in two different hospitals of Rawalpindi Medical University were enrolled by consecutive sampling in this study. All adult patients with confirmed COVID-19 by Real time PCR irrespective of disease severity were included. Patients with previous history of renal disease and other co-morbidities were excluded. Written informed consent for publishing their medical data for research purposes was obtained from each patient and the study was approved by institutional research ethical committee.

Laboratory data of renal function tests were obtained at the time of admission in this study cohort by drawing 3cc of venous blood sample in Gel tubes (BD, America) under aseptic measures. These tubes were then sealed and sent to the laboratory. The samples were analyzed for renal functions including serum urea and creatinine, using Beckman coulter AU480 (fully automated

chemistry analyzer) based on photometric technique. Blood urea nitrogen was calculated for every patient. The cut off criteria for elevated levels was: Serum Creatinine more than 1. 2mg/dL, Urea levels more than 40mg/dL, and/ or BUN more than 20mg/dL. Other information like demographic data and medical history were obtained on proforma.

We calculated estimated glomerular filtration rate (eGFR) in this study according to the two equations (MDRD and CKD-EPI).

MDRD study equation [11]

eGFR = 186.3 ×(Scr)$^{-1.154}$ × (age)$^{-0.203}$ × (0.742 for female)× (1.210 for black race).

eGFR in (mL/min/1.73 m^2), Scr: serum creatinine in (mg/dL), age in years

CKD-EPI equation[11]

Female with Scr ≤0.7 mg/dl: eGFR = 144 × (Scr/0.7)$^{-0.328}$ × (0.993)^{Age}

Female with Scr >0.7mg/dl: eGFR = 144 × (Scr/0.7)$^{-1.210}$ × (0.993)^{Age}

Male with Scr ≤0.9 mg/dl: eGFR = 141 × (Scr/0.9)$^{-0.415}$ × (0.993)^{Age}

Male with Scr >0.9mg/dl: eGFR = 141 × (Scr/0.9)$^{-1.210}$ × (0.993)^{Age}

eGFR in (mL/min/1.73 m^2)

Patients were divided into three groups according to the values of estimated glomerular filtration rate (eGFR) obtained at the time of admission. Group 1 include patients with GFR > 60 mL/min/1.73 m2. They were considered to have no significant renal failure. Group II included patients having GFR values between 30–60 mL/min/1.73 m^2 and were considered to have moderate renal failure while group III included patients with GFR < 30mL/min/1.73m^2 and were considered to be suffering from severe renal failure. SPSS 25.0 statistical software was used for all statistical analysis. Frequencies and percentages were used for categorical data, while quantitative data was expressed as mean± SD. The independent t-test was used to compare the differences in the means of Scr, Urea and BUN between patients in different age and gender while Paired t test was used to compare means of eGFR calculated by two different equations. P-value of < 0.05 was considered as statistically significant.

RESULTS

Total of 169 patients identified as laboratory confirmed novel Coronavirus (nCoV-19) infection were studied. The age range varied from 18 to 92 years for all the patients. A total of 97(57%) of the study population were males and 72(43%) were females. Ninety six (57%) patients were below 60 years of age while 73(43%) were more than 60 years.

Table 1 summarizes the baseline renal function test and estimated GFR by two equations. Mean Urea, Scr and BUN were found to be elevated in this study population of COVID 19. Mean Urea and BUN was found to be insignificantly elevated in patient above sixty years of age when compared with a younger group. However Mean Scr 2.06±3.83 was although elevated in younger patients (< 60 years) but this difference in both groups was not found to be statistically significant. No significant difference in mean Scr, Urea and BUN were observed in both gender (Table 1).

The eGFR was calculated by using the MDRD and CKD-EPI equations (Table1) from Scr and other factors in study population at the time of presentation. Although two different equations were used for calculating eGFR but no significant difference was observed in eGFR values according to age groups and gender. Significantly reduced eGFR were observed in an elderly group by both equations (Table 1).

Out of total 169 patients 46 (27%) had raised serum Creatinine. Elevated serum Urea levels were observed in 113 (67%) patients while abnormal blood urea nitrogen (BUN) were observed in 103 (62%) patients (Figure1).

We categorized the patients into three groups according to eGFR on admission. Table 2 summarizes the data of patients according to groups based on eGFR. When we compared these groups, the Majority (70%) of patients were placed in normal eGFR > 60 mL/min/1.73 m^2 group. Thirty percent of patients were included in moderate to severe renal failure group (18% were included in moderately reduced eGFR30–60 mL/min/1.73 m^2 and 12% patients in severely reduced eGFR <30mL/min/1.73 m^2 group). It was noted that higher mean age was found in moderately reduced eGFR group. Furthermore, male predominance was also observed in similar group as compared to other groups. Group with severely reduced eGFR on admission had higher proportion (66%) of young patients and equal number of male and female patients (Table 2).

Figure 2 demonstrate the mean eGFR calculated by CKD-EPI and by MDRD equations in three groups. When comparing the eGFR by two equations it was observed that mean values in all three group calculated by CKD EPI equation were slightly lower as compared with the mean values by MDRD equation in the same groups. However this difference was not statistically significant. (P value 0.052)

Table 1: Mean values for baseline renal function test and eGFR in COVID 19 patients according to different age groups and gender

	Mean±SD Urea	**Mean±SD Serum Creatinine**	**Mean±SD BUN**	**Mean±SD eGFR CKD-EPI**	**Mean±SD e GFR MDRD**
Total (n=169)	72.8±67.2 (15-436)	1.84±3.14 (0.30-23.5)	33.9±31.36 (7-203)	79.17 ±38.55 (2-192)	82.37 ±51.02 (2-382)
<60 years	68.40±75.56 (15-436)	2.06±3.83 (0.3-23.50)	31.9±35.08 (7-203)	87.36 ±42.77 (2-192)	91.17 ±59.42 (2-382)
>60 years	78.46± 55.0 (25-370)	1.56 ± 1.92 (0.5-10.2)	36.6±25.67 (11.6-172)	68.4±29.09 (5-119)	70.80±34.2 (5-166)
P value	0.33	0.30	0.33	0.001	0.005
Males	76.96± 51.7 (15-436)	1.85 ± 2.95 (0.3-23.5)	35.9±30.5 (7-203.4)	77.2 ±36.2 (2-192)	81.22±51.7 (2-382)
Females	67.26± 69.7 (16-424)	1.83 ± 3.4 (0.4-21.9)	31.3±32.5 (7.32-197.8)	81.72 ±41.6 (2-170)	83.93±50.3 (2-240)
P value	0.35	0.9	0.35	0.46	0.73

BUN: Blood Urea Nitrogen, eGFR: estimated Glomerular Filtration Rate, CKD EPI: Chronic Kidney Disease Epidemiology Collaboration , MDRD: Modification of Diet in Renal Disease, S.D: Standard Deviation

Table 2: Demographic and laborotory characteristics of different groups according to the estimated glomerular filtration rate (eGFR)

Variables	**Group I**	**Group II**	**Group III**
n% <60 years >60 years	120 (70%) 75 (62%) 45 (38%)	28(18%) 9 (30%) 21 (70%)	21 (12%) 14 (66%) 7 (33%)
Mean ±S.D Age (Years)	51.9±15.8	65.5±14	50.05±15.5
Age range years	18-87	26-92	26-74
Male	68 (57%)	19 (68%)	10 (50%)
Females	52(43%)	9 (32%)	10 (50%)
Mean ±S.D Urea	45.61±20.7	93±30.1	205.8± 09.4
Mean ±S.D Creatinine	0.81±0.23	1.5±0.34	8.4 ± 5.8

Group I: Absence of significant renal failure: GFR more than 60mL/min/1.73 m^2

Group II: Moderate renal failure: GFR between 30–60 mL/min/1.73 m^2

Group III: Severe renal failure : GFR less than 30 mL/min/1.73 m^2

Figure 1: Number of COVID 19 Patients with deranged renal function test Scr: Serum Creatinine, BUN: Blood Urea Nitrogen, eGFR: estimated Glomerular Filtration Rate

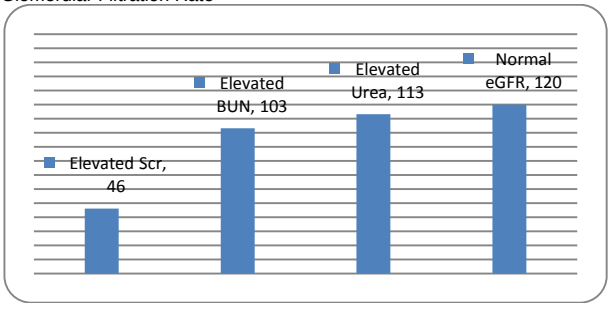
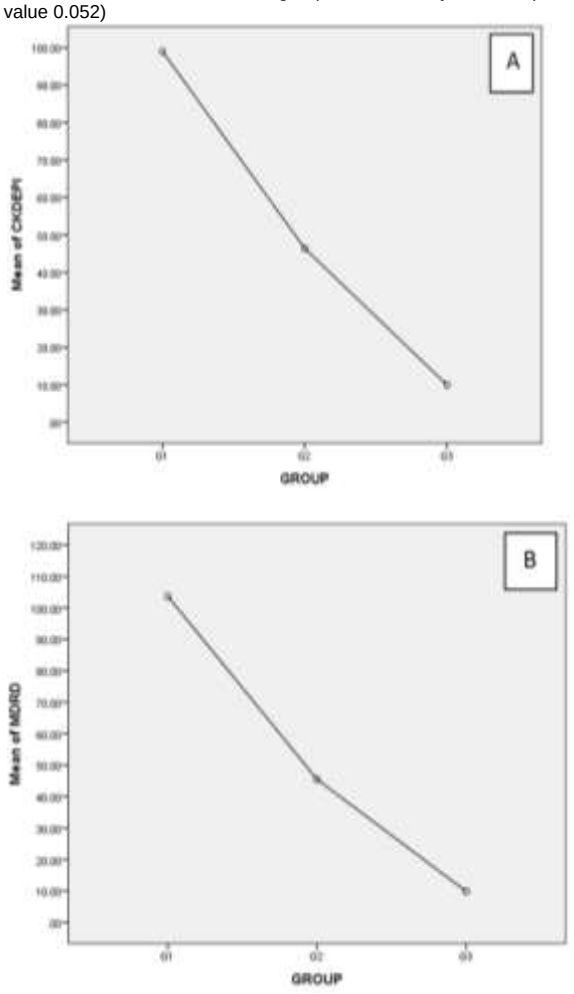


Figure 2: Mean eGFR of three groups according to eGFR calculated by two equations.
A: Mean eGFR in three different groups calculated by CKD-EPI equation, B: Mean eGFR in three different groups calculated by MDRD equation. (P value 0.052)



DISCUSSION

Widespread alveolar injury and respiratory failure are well known characteristics of COVID-19 but damage to other vital organs must also be investigated[6]. Renal involvement in such patients is not much known so the present study was focussed to summarize the baseline renal laboratory profile of patients admitted in hospital with COVID 19.

The mean age of study cohort was 54.10±16.3 years, which was almost in accordance with early reports[1,13]. Male predominance was observed in COVID 19 patients as demonstrated in previously published studies[13,14]. This predominance may be due to increased foreign travel or exposure by males. The study revealed that majority of the patients was less than 60 years of age as shown previously[1,15].

While analysing the kidney function test of COVID 19 patients at the time of admission, it was found that 27% of the patients exhibited elevated serum creatinine levels while 62% and 67% of patients had an increased level of BUN and urea levels respectively. Similar results were observed in a international registry carried out in America and Europe showing almost 30% of the patients on admission had raised serum creatinine levels[12]. Another study reported 19% and 27% of the Covid 19 patients had more than normal levels of Scr and BUN, respectively[7]. A study from India revealed that after infection with the virus 18.6% patients without chronic kidney disease (CKD) showed a mild increase of BUN or serum creatinine levels[1].

It was demonstrated in a previous study that patients with elevated serum creatinine levels on admission had a higher incidence of acute kidney injury (AKI) and increased incidence of admission to intensive care units (ICU), mechanical ventilation and hospital mortality irrespective of severity of disease and patients physical condition. [3] Therefore in such patients even with mild respiratory symptoms, kidney functions should be monitored and special care must be given to patients with altered results.

A much higher frequency of COVID 19 patients with elevated Urea and BUN level were noticed in the present study. Both these parameters are not the sole indicator of kidney dysfunction. The temporary derangement in renal function in these patients could also be due to nitrogen equilibrium, inflammation, sepsis, hypovelemia leading to renal hypoperfusion, or reduced cardiac output, secondary injury due to vomiting, diarrhoea or associated comorbidities. [1, 16] The present study did not take into account any of these confounding factors or the severity of presentations in COVID 19 patients. This could be the reason for observing such high Urea and BUN levels. It was however studied earlier that raised BUN at 24 hours of hospitalization in COVID 19 patients was associated with multiple clinical outcomes and therefore active monitoring of BUN has its importance in the treatment of these patients[17].

Scr, Urea and BUN are routine but not very sensitive indicator of renal function. Higher values are usually noticed with considerable damage of kidneys.[7] Similarly plasma creatinine level within the normal reference range does not mean normal functioning renal system. Therefore, for the assessment of renal function, measurement of plasma creatinine level should not be used exclusively[18]. Calculation of eGFR which rely on age, gender, weight, and Scr gives better reflection of the renal function impairment at an early stage[7].

The study also calculated the eGFR among COVID-19 patients on admission. The study presented the eGFR by CKDEPI and with the MDRD equation in COVID 19 patients. When comparing the eGFR by two equations it was reported that no striking divergence between the two equations has been observed in this study, the CKD EPI equation however gave a slightly lower mean eGFR compared with the MDRD equation (Table 2 and Figure 2) but the difference was statistically insignificant. There are previous studies in which the MDRD equation predicted a higher level of GFR[11] but contrary findings are also reported by other researchers[9,10]. It was concluded in a study that using the CKD-EPI equation can over represent CKD prevalence as compared to MDRD equation. This difference could be because of participant age, population studied or due to the precision of the creatinine method used[10]. It was observed that the level of eGFR was lower in the older patients which is in accordance to previous report. [15] The reason being that there is a likely decline in GFR with advancing age[9] therefore this finding of declined eGFR with age was not surprising according to both these equations[11].

The eGFR > 60 mL/min per 1.73m^2 was found in most (70%) people in this study cohort, while 30% had baseline eGFR under 60mL/min/1.73m^2 (18% of patient had moderate, while 12% had severely decreased eGFR) Previous study demonstrated that 18% of patient had baseline eGFR under 60 mL/min/1.73m^2.[13]. Analysis from the international HOPE-Registry (NCT04334291) reports 30% of patient with under 60mL/min eGFR in COVID 19 patients[12].

Patients were placed in 3 different groups based on eGFR values (eGFR>60 mL/min/1.73 m2 [n=120], eGFR 30–60 mL/min/1.73 m2 [n=28] and eGFR<30 mL/min/1.73 m2 [n=21] all three group showed no significant predilection to age and gender. However a previous study reported that higher mean age was reported in groups having eGFR<60 mL/min/1.73 m^2. [12]

CONCLUSION

Patients of COVID 19 generally presented with deranged levels of Scr Urea and BUN at the time of admission. No significant difference in these variables was observed according to age groups and gender. The calculation of eGFR in COVID-19 patient revealed 30% had reduced glomerular filtration rate. A statistically significant difference in eGFR values calculated using the MDRD and CKD-EPI equations were not demonstrated in this study.

Limitations: Viral load of patients was not evaluated, which is a potentially valuable marker associated with organ damage.

Ethics approval: Approval for the study was obtained from the research and ethical committee of Rawalpindi Medical University and Allied Hospitals,(Ref No. 82/REF/RMU/2020)

Data availability statement: Available on reasonable request from the corresponding author

Contribution of authors: **HA:** Design, manuscript writing, data evaluation, statistical analysis, **FTZ:** Concept, definition of intellectual content, data collection, **NW:** Critical evaluation of manuscript, technical assistance, **FS:** Data entry, data evaluation and data collection

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