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Renal Impairment
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RENAL IMPAIRMENT: IS THERE A NEED FOR MONITORING RENAL FUNCTIONS IN COVID INFECTION

Asma Hayat, Numan Majeed, Shabana Abbas, Farhan Akhtar, Sunila Tashfeen, Amna Siddique

Army Medical College/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To determine association of renal function derangement with disease severity in COVID-19 patients
Study Design: Cross sectional study.
Place and Duration of Study: Department of Pathology, Army Medical College and Pak Emirates Military Hospital, Rawalpindi, from April 2020 to May 2020.
Methodology: All the confirmed COVID-19 patients admitted in the hospital over a period of 5 weeks were included in the study. Patients having diabetes, hypertension, or history of any renal abnormality were excluded from the study. Patients were categorized as mild, moderate, or severe according to the symptoms as well as the location of the patient in different wards admitted.
Results: A total of 105 patients were included in the study. The study population had 99 (94.2%) males and 6 (5.8%) females. Serum creatinine (p=0.027), urea (p≤0.001), potassium (p≤0.001) were found to be significantly associated with disease severity while serum sodium levels (p=0.091) showed a non-significant association with the infection. Whereas all of these had a positive correlation with COVID-19, serum potassium levels had a negative correlation with the severity of the disease.
Conclusion: COVID-19 patients show renal function impairment at all levels of disease severity; hence vigilant monitoring of these patients is required. As certain drugs used in treatment of COVID-19 have renal clearance, dose adjustment should be considered for better patient outcome.

Keywords: COVID 19, Disease severity, Renal impairment.

INTRODUCTION

In December 2019, there was an outbreak of an unknown epidemic in Wuhan, China, after research and taxonomic studies, the virus was identified to be from of the SARS family and thus named 2019-nCoV[1] and the disease associated with the virus as COVID-19 by the World Health Organization (WHO) on 30th January, 2020[2,3].

There was a sheer rise in the number of cases worldwide and was declared as endemic, still in some countries such as USA, Iran and India etc. the number is yet on surge with a total number of cases to be 19,259,391 and a death toll of 717,687 [4], but in Pakistan the cases are declining after reaching a maximum of almost 6825 cases per day from mid-June to about 650 cases per day by 1st week of August. The total number of cases reported to date are 280152 with a total mortality of 5,851[5].

Until now, seven strains of coronaviruses have been identified that are known to cause respiratory tract infection in human. Out of these seven, 3 had caused almost similar pandemic pattern[6]. Having anasymptomatic state is the major cause of concern in all these infections, making it harder to contain and prevent[7]. The peculiar pattern of the Corona virus from the other viruses belonging to this family is that it not only causes respiratory manifestation but also has extra-pulmonary manifestations such as involving liver, kidneyand even pancreas in some cases[8].

An explanation of renal involvement by Valizadeh *et al*, proposed dehydration as the cause of renal derangement. They suggested that fever or decreased intake of fluids may lead to dehydration which has various consequences on the kidney leading to reduction of glomerular filtration rate and acute kidney injury. If volume

Correspondence: Dr Asma Hayat, Associate Professor of Pathology, Army Medical College, Rawalpindi Pakistan
Email: asma.hayat72@gmail.com
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depletion is not severe, it is reversible with hydration, however if ischemia persists, acute tubular necrosis may happen. Other proposed mechanisms comprise sepsis by COVID-19, which leads to cytokine storm syndrome. Furthermore, rhabdomyolysis and hypoxia are other possibilities. Additionally, direct virus invasion of the renal tubular cells and interstitium or glomeruli is possible, since the direct cytopathic effect of virus on various renal cells have been detected in previous studies[9].

A more likely and logical explanation was given by Pan *et al*, suggesting that Co-localization analysis of ACE2 and TMPRSS genes showed a relatively high co-expression in podocytes and proximal straight tubule cells. The TMPRSS 2 gene, one of the most important mediators of SARS-CoV-2 entry into host cells, was found to be co-expressed with ACE2 in podocytes suggesting that SARS-CoV-2 induces acute kidney injury[10]. Objective of the study was to assess the association of renal function derangement due to COVID infection as well as to establish its correlation with the severity of the disease.

METHODOLOGY

It was a cross sectional study, conducted at Pak-Emirates Military Hospital, Rawalpindi. Data collection was done for 5 weeks, for the patients admitted in the hospital form 15th April to 20th May 2020. A total of 105 patients with a positive COVID-19 RT-PCR, admitted in the hospital during this period. Patients with a history of any renal disorder, hypertension or diabetes mellitus were excluded from the study. Patients were categorized as mild, moderate or severe according to the symptoms as well as the location of the patient in different wards. Patients in regular wards were considered as mild, while those in High Dependency Unit (HDU) were considered to have moderate disease. Patients admitted to intensive care unit (ICU) were considered as cases with Severe disease. Clinical data was obtained from wards and 3cc of venous blood sample was drawn in Vacctue TMGel tubes by trained staff nurse under aseptic measures and were sealed and sent to lab. The samples were analyzed for renal functions including serum urea and creatinine, using Roche Cobas 6000 based on spectrophotometric technique while serum sodium and potassium levels were assayed by indirect ISE using the same platform. Serum ferritin levels were assayed on Roche Cobas e411 by electrochemiluminescence. All patients were followed for the outcome.

Ethical approval (ERC/ID/34) was sought from the institutional review board, written informed consent was taken from the patients to use their medical data for research purposes. Anonymity of each participant was ensured, and data was entered using specific codes designated to each patient rather than by names.

Data was entered in SPSS, frequencies and percentages were calculated for categorical data, while mean and SD was calculated for quantitative data. ANOVA was applied to test the association of parameters under observation with disease severity; Post Hoc Tukey's test was applied to test the intragroup association with various test parameters. Pearson's Correlation was used to assess the relative change in the levels of these parameters using serum ferritin as a marker of severity of disease.

RESULTS

A total of 105 COVID patients were included in the study. The study population had 99 males and 6 females (table-I). Mean age of the study participants was found to be 46.62 ± 13.86 years, while average admission duration of the patients discharged was 14.34 ± 5 days. Mean admission duration of the Severe cases is less as most of the patients were under treatment at the time of data collection (table-II). To determine the association of renal function tests with severity of the disease, one-way ANOVA was applied. Results of ANOVA along with mean and SD of the parameters included are as shown in table-II. Post-Hoc analysis was used to assess the association of the significantly associated parameters with different severity levels of the disease (table-III). To assess the relative change in these parameters,

Pearson's correlation was applied considering ferritin as maker of severity of the disease (table-IV).

patients affected with COVID is directly associated with age[1,12].

COVID-19 manifests as seasonal flu or viral pneumonia, which in later stages leads to

Table-I: Gender distribution and outcome of study participants.

		Mild	Moderate	Severe
Gender	Male	64 (61%)	19 (18.1%)	16 (15.2%)
	Female	3 (2.9%)	-	3 (2.9%)
Outcome	Recovered and discharged	7 (6.7%)	19 (18.1%)	7 (6.7%)
	Ongoing treatment	-	-	9 (8.6%)
	Expired	3 (2.9%)	-	3 (2.9%)

Table-II: Result of ANOVA along with Mean and SD for the analytes of interest.

	Mild	Moderate	Severe	*p*-value
Age (years)	38.94 ± 9.97	51.83 ± 13.71	57.79 ± 14.17	<0.001
Admission duration (days)	14.45 ± 4.37	15.81 ± 5.01	11.3 ± 7.81	0.79
Urea (mmol/L)	4.4 ± 1.4	7 ± 7.4	12.4 ± 10.5	<0.001
Creatinine (µmol/L)	93.4 ± 13.8	104.3 ± 40.1	128.4 ± 106.1	0.027
Sodium (mmol/L)	139.1 ± 4.2	136.7 ± 4.7	139.7 ± 5.7	0.091
Potassium (mmol/L)	4.54 ± 0.47	4.35 ± 0.47	4 ± 0.6	<0.001
Ferritin (ng/mL)	150 ± 83	1227 ± 3378	2374 ± 4687	0.002

Table-III: Post- Hoc analysis of significant variables.

Analyte	Condition	Comparative condition	*p*-value
Urea (mmol/L)	Severe	Moderate	0.010
		Mild	<0.001
	Moderate	Mild	0.166
Creatinine (µmol/L)	Severe	Moderate	0.301
		Mild	0.020
	Moderate	Mild	0.685
Sodium (mmol/L)	Severe	Moderate	0.086
		Mild	<0.001
	Moderate	Mild	0.327
Ferritin (ng/mL)	Severe	Moderate	0.322
		Mild	0.002
	Moderate	Mild	0.209

Table-IV: Pearson's correlation of lab values with disease severity.

		Urea	Creatinine	Sodium	Potassium
Ferritin	Pearson Correlation	0.671	0.49	0.023	-0.160
	p-value	<0.001	<0.001	0.822	0.109

DISCUSSION

Our study had a predominant male population i.e.only 6 females, indicating that males are affected more. This can be due to the fact that males have to go out from home thus increasing the risk of exposure. Similar gender distribution is shown by other studies as well[11]. Similarly, the severity of symptoms as well as number of

respiratory failure as well as involving other organs such as liver, kidney and GIT. The best mechanism regarding viral entry in the host cells so far understood is wide distribution of Angiotensin converting enzyme 2 (ACE2) receptors which the virus uses to invade the cell[13].

Elevation of levels of serum creatinine as well as of those of urea or BUN was found to be

associated significantly with all the stages of COVID. While for creatinine levels, there was a significant association in mild and severe stage of the disease only, but the correlation was found to be positive and highly significant with severity of the disease. Similar results were reported by Li *et al*[14]. Similarly, Wang *et al* suggested that COVID infection is not significantly associated with COVID-19[15].

Our study suggested a non-significant association of serum sodium levels as well as non-significant positive correlation with disease severity. Non conclusive results regarding change in serum sodium levels were seen, some studies suggest a non-significant association while some suggest significant one[16,17]. A meta-analysis by Lippi *et al*, suggested that there was an inverse correlation with COVID severity[18].

Unlike serum sodium levels, in case of serum potassium levels, there was a consensus found in all the studies reporting serum potassium levels. An inverse relationship with the disease severity, i.e. with increase in severity of the disease, there was a decline in serum potassium levels. Our findings are in concordance with previously reported results by Cheng *et al*, and Lippi *et al*[16,18]. NICE guidelines (UK) suggest that AKI is not only more common in COVID but also is associated with increased risk of mortality, suggesting volume depletion to be a cause of AKI in COVID[19].

CONCLUSION

COVID-19 patientsshow renal function impairment at all levels of severity for disease; hence vigilant monitoring of these patients is required. As certain drugs used in treatment of COVID-19 have renal clearance, dose adjustment should be considered for better patient outcome.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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