ORIGINAL ARTICLE

SPECTRUM OF BIOCHEMICAL ALTERATIONS IN PATIENTS WITH COVID-19

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Background: The COVID-19 pandemic has claimed millions of lives around the globe. In addition to respiratory involvement, multi organ failure has also been noted in these patients. We tried to assess the biochemical abnormalities in these patients to have a better understanding of this disease and its complications. **Methods:** Adult patients (n=107) who tested positive for COVID-19 by RT-PCR were included in this study. Blood was analysed for Urea, Creatinine, Ferritin, Lactate Dehydrogenase (LDH), Calcium, Magnesium and Phosphorus in Cobas C501 (Roche Diagnostics) using spectrophotometric technology. Sodium, Chloride, Potassium and Bicarbonate were analysed on NOVA electrolyte analyser using ion-selective electrodes. **Results:** Urea and creatinine were elevated in 33.6% and 22.4% patients respectively. Ferritin and LDH were high in 88.8% and 93.5% patients respectively. Reduced levels of electrolytes was observed , i.e., Sodium in 44.9%, Potassium in 22.4%, Bicarbonate in 53.3%, Calcium in 48.6%, and Phosphorus in 23.4% patients. There were no significant differences in abnormalities in the different age groups (p>0.05). **Conclusion:** COVID-19 patients suffer from pulmonary disease as well as multi-organ involvement as seen by the biochemical alterations, and this should be kept in mind while treating these patients.

Keywords: COVID-19, Pandemic, Biochemical, Multi-organ failure, Electrolytes

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INTRODUCTION

Since December 2019, Severe Acute Respiratory Syndrome Corona Virus-2 (SARS COV-2) started spreading from Wuhan, China, and on 11th March 2020, World Health Organization[1] declared COVID-19 disease. Many of the patients are asymptomatic or have mild disease with upper respiratory tract infection, but diffuse alveolar damage and acute respiratory failure is also seen.[1,2] Multiple organ failure has been seen to cause the morbidity and mortality in COVID-19 patients.[3]

The SARS COV-2 virus interacts with angiotensin-converting enzyme 2 (ACE2) via its spike protein. It invades the human cell by binding with (ACE2) on the cell membrane. Therefore, cells with ACE2 expression such as type II alveolar cells (AT2) in the lung may act as target cells and be susceptible to COVID-19 infection.[4] ACE2 protein has been proved to have an abundant expression in many cells, such as intestinal epithelial cells, renal tubular epithelial cells, alveolar epithelial cells, heart, arterial smooth muscle cells, and gastrointestinal system.[5] That is why we can assume that SARS COV-2 may invade the lung, upper respiratory tract, ileum, heart and kidney, causing Acute Kidney Injury (AKI), acute heart injury, dyspnoea and diarrhoea especially in patients with a high viral load.[6,7]

The binding of SARS COV-2 to ACE2 can cause angiotensin dysregulation, activation of innate and adaptive immunity, and a hypercoagulable state leading to AKI.[8] The hypercoagulability could cause acute tubular necrosis, progressing to cortical necrosis and irreversible kidney failure.[8]

The ACE2 is main counter regulator of the Renin-Angiotensin System (RAS), which is critical for blood pressure and electrolyte control. SARS COV-2 binds with ACE2 and causes its degradation and so reduces the counteraction of ACE2 on RAS. This causes increased reabsorption of sodium and water, excretion of potassium and increased blood pressure. Severe hypokalemia can cause ventricular arrhythmias and respiratory muscle dysfunction which can cause severe morbidity and mortality.[9] Very few studies with small sample sizes have been conducted regarding the biochemical abnormalities associated with COVID-19 disease, especially in Pakistan. We aim to observe the biochemical parameters to assess the presence of multi organ derangement in these patients.

METHODOLOGY

This cross-sectional study was conducted in the Department of Chemical Pathology, Liaquat National Hospital, Karachi. A total of 107 adult patients who tested positive for COVID-19 by RT-PCR from 1st January 2021 to 28th February 2021 were included in the study after approval by the Ethical Review Committee. Non-probability consecutive sampling was done. Patients who were less than 18 years were not included in the study.

Blood was collected in yellow top tube (BD Vacutainer) containing gel and allowed to clot. Serum was separated and stored at -20 °C. Dilutions and aliquots were prepared where needed. Blood was analysed for urea, creatinine, ferritin, lactate dehydrogenase (LDH), calcium, magnesium and

phosphorus in Cobas C501 (Roche Diagnostics) using spectrophotometric technology. Sodium, chloride, potassium and bicarbonate were analysed on NOVA electrolyte analyser using ion-selective electrodes. The reference intervals used for urea and creatinine were <50 mg/dL and 0.5–1.5 mg/dL respectively. As regards Ferritin and LDH the gender based reference intervals were, Ferritin M: 30–400 ng/ml, F: 15–150 ng/ml, LDH M: 135–225 U/L, F: 135–214 U/L respectively. For chloride, sodium, potassium and bicarbonate, the reference intervals were 94–110 mmol/L, 136–145 mmol/L, 3.5–5.3 mmol/L and 22–34 mmol/L respectively. The values were 8.6–10.2 mg/dl, 1.7–2.55 mg/dl and 2.5–4.5 mg/dl respectively for calcium, magnesium and phophorus.

Data was analysed using SPSS-25. Frequency and percentage of the abnormalities of the different parameters was calculated. The frequency of the abnormalities of these parameters in the different age groups were also calculated using Chi-square and $p<0.05$ was taken as significant.

RESULTS

Out of a total of 107 patients of age 18–90 (Mean 56.6) years, 69 (64.5%) were males and 38 (35.5%) were females. There were 13, 20, 18 and 56 patients in the age groups of ≤40 years, 41–50, 51–60 and >60 years respectively. The frequency of abnormalities of the different parameters in the patients is shown in Table-1.

There were high levels of urea and creatinine signifying the presence of renal disease in COVID patients. Ferritin and LDH are also increased as they are acute phase reactants. There were greater percentage of low levels of electrolytes in these patients that is low sodium, potassium, bicarbonate, chloride, calcium, magnesium and phosphorus. We looked at the abnormalities of the parameters according to the age groups (Table-2). It shows that when the patients are divided in different age groups, the analyte abnormalities are still the same and there are no significant differences in abnormalities in the different age groups ($p>0.05$). Low bicarbonate only was seen with $p=0.036$ which was significance.

The frequency of abnormalities of the different analytes is shown in Table-3. Significant differences are seen in case of sodium and calcium ($p=0.029$ and 0.025 respectively). In the rest of the parameters there were no significant gender differences seen.

Table-1: Frequency of patients with abnormalities of different parameters

Analyte	Abnormality	Frequency	%
Urea	**High**	36	33.6
Creatinine	**High**	24	22.4
Ferritin	**High**	95	88.8
Lactate Dehydrogenase	**High**	100	93.5
Chloride	**Low**	9	8.4
	High	4	3.7
Sodium	**Low**	48	44.9
	High	3	2.8
Potassium	**Low**	24	22.4
	High	2	1.9
Bicarbonate	**Low**	57	53.3
Calcium	**Low**	52	48.6
	High	1	0.9
Magnesium	**Low**	12	11.2
	High	3	2.8
Phosphate	**Low**	25	23.4
	High	9	8.4

Table-2: Frequency of patients with abnormalities of the analytes in the different age groups [n (%)]

Analyte	Abnormality	≤40 Years	41–50 Years	51–60 Years	>60 Years	*p*
Urea	**High**	5 (35.7)	6 (30.0)	5 (27.8)	20 (36.4)	0.905
Creatinine	**High**	1 (7.1)	3 (15)	3 (16.7)	17 (30.9)	0.211
Ferritin	**High**	12 (85.7)	17 (85)	18 (100)	48 (87.3)	0.384
LDH	**High**	13 (92.9)	18 (90)	17 (94.4)	52 (94.5)	0.934
Chloride	**Low**	2 (14.3)	0 (0)	2 (11.1)	5 (9.1)	0.4
Sodium	**Low**	7 (50)	8 (40)	9 (50)	24 (43.6)	0.687
Potassium	**Low**	1 (7.1)	5 (25)	5 (27.8)	13 (23.6)	0.575
Bicarbonate	**Low**	5 (35.7)	13 (65)	14 (77.8)	25 (45.5)	0.036
Calcium	**Low**	9 (64.3)	10 (50)	8 (44.4)	25 (45.5)	0.817
Magnesium	**Low**	4 (28.6)	1 (5)	2 (11.1)	5 (9.1)	0.135
Phosphate	**Low**	4 (28.6)	4 (20)	6 (33.3)	11 (20)	0.907

Table-3: Frequency of patients with abnormalities of the analytes in the different genders [n (%)]

Analyte	Abnormality	Male	Female	*p*
Urea	**High**	25 (36.2)	11 (28.9)	0.445
Creatinine	**High**	19 (27.5)	5 (13.2)	0.088
Ferritin	**High**	62 (89.9)	33 (86.8)	0.751
LDH	**High**	64 (92.8)	36 (94.7)	1.000
Chloride	**Low**	6 (8.7)	3 (7.9)	1.000
Sodium	**Low**	36 (52.2)	12 (31.6)	0.029
Potassium	**Low**	13 (18.8)	11 (28.9)	0.328
Bicarbonate	**Low**	41 (59.4)	16 (42.1)	0.086
Calcium	**Low**	39 (56.5)	13 (34.2)	0.025
Magnesium	**Low**	6 (8.7)	6 (15.8)	0.577
Phosphate	**Low**	14 (20.3)	11 (28.9)	0.548

DISCUSSION

In our study males were 65.5% as compared to 35.5% females. A study showed that more males were affected by the disease as compared to females probably because males were exposed more because they had to leave their homes.[10] In a study in Iran[11], 35% of patients with COVID-19 had impaired urea and creatinine levels suggesting that renal dysfunction is quite a common complication of this disease. Some researchers have found coronavirus COVID-19 particles in the urine of these patients showing that these viral particles

may have been present in the kidney, filtered in the glomerulus and passed into the urine.[11] Other studies stated that patients with COVID-19 pneumonia showed a rapid increase in urea and creatinine levels showing acute renal injury which could be due to muscle breakdown in these patients as there was associated hyperuricaemia and hypoalbuminaemia.[12,13] These findings are similar to our study where elevated urea and creatinine levels in 33.6% and 22.4% of patients respectively is reported, and the levels of these parameters are more in patients aged ≥60 years.

A study observed increased LDH and ferritin levels in COVID-19 patients.[14] A meta analysis showed elevated ferritin and LDH levels in COVID-19 patients suggesting use of serum ferritin level to monitor prognosis in these patients.[15] These findings are similar to our study. Another study pointed out a positive association between renal injury and acute renal failure with the risk of death.[16] A study from Iran reported a significant decrease in sodium levels in severe disease. It noted that for potassium levels the decrease was not significant.[17] A similar study showed the decline in serum sodium was non-significant with increase in disease severity, but there was a decline in serum potassium with disease severity.[10] We found hyponatremia and hypokalaemia in 44.9% and 22.4% patients respectively. Another study compared the electrolyte levels in severe and non-severe COVID-19 patients and found significantly low levels of sodium, potassium, and calcium in severe as compared to non-severe patients.[18] They say that COVID-19 patients especially with underlying heart or lung disease may have acute respiratory distress syndrome and acute cardiac injury which can be exacerbated by the prevalent hypokalemia.[18]

CONCLUSION

COVID-19 infection in addition to causing pulmonary disease also has multi-organ involvement evident by the biochemical alterations. Further research is required on the long term implications of these imbalances to counteract the complications of this disease.

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