

Electrolyte Abnormalities in Patients Hospitalised with COVID-19 in the Southern Gaza Strip, Palestine: A Retrospective Case-control Study

MAHMOUD I ELHABIBY¹, AYMAN ABU MUSTAFA², ABDELMAROUF HASSAN MOHIELDEIN³

(cc) BY-NC-ND

ABSTRACT

Introduction: Coronavirus Disease-2019 (COVID-19), has caused, nearly 18 million deaths worldwide, many more hospitalisations, and severe economic and social disruption, as of March 2022. Malnutrition and electrolyte imbalance can lead to immune system dysfunction, which can increase the risk of infection.

Aim: To evaluate the electrolyte imbalance and other biomarkers in COVID-19 patients and also, to compare these parameters with healthy individuals.

Materials and Methods: A retrospective case-control study was conducted in the Department of Medical Laboratory Sciences at European Gaza Hospital, Southern Gaza Strip, Palestine. The duration of the study was four months, from February 2022 to May 2022. A total of 200 participants were included in the study, out of which 100 patients were diagnosed with COVID-19 infection by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) test and 100 healthy individuals were recruited from blood bank donors and comprehensive Screening Department. Biochemical profile; Fasting Blood Glucose (FBG), urea, Creatinine (Cr), Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), total Creatinine Kinase (CK-total), Creatine Kinase (CK)

isoenzyme CK and electrolytes (Na, K, phosphorous, and Mg, ionised calcium, total calcium, and Cl) were assayed. Data were statistically analysed using Student's t-test and Chi-square test.

Results: The mean age of the study participants was 54.1 ± 12.2 years for cases and 54.3 ± 12.4 years for controls. A total of 200 subjects, both the groups had 34 (34.0%) males and 66 (66.0%) females, which was not statistically significant (p-value >0.05). COVID-19 patients had significantly higher values of Na (141.9\pm4.6 vs 139.7\pm3.1; p<0.001), K (4.6\pm0.9 vs 4.3 ± 0.5 ; p-value=0.001), Cl (108.7±5.3 vs 101.1±4.0; p<0.001), P (4.6\pm0.6 vs 4±1.4; p<0.001), and Mg (2.1\pm0.2 vs 1.7\pm0.3; p<0.001). However, they had lower Ca ionised (1.0±0.1 vs 1.1±0.1; p<0.001) and total Ca (8.4±0.9 vs 9.1±1.1; p<0.001). Furthermore, COVID-19 patients had significantly higher levels of biomarkers of other biochemical profiles compared to healthy controls.

Conclusion: As compared to healthy individuals, patients hospitalised with COVID-19, exhibited alterations in their electrolyte balance and other biochemical markers. Management of these parameters to get homeostasis warrant opportunities to reduce morbidity and mortality of disease.

Keywords: Biomarkers, Coronavirus disease-2019, Manifestations, Multiorgan injury, Pandemic

INTRODUCTION

The number of COVID-19 infection cases, grew exponentially throughout the world. Over 14.9 million confirmed cases and more than 610,000 deaths attributed to COVID-19 have been recorded globally as of July 2020 [1]. The proportion of severe and critical COVID-19 cases increased nearly two fold in the Gaza Strip, Palestine [2]. Additionally, the elderly and those with preexisting conditions such as, diabetes, hypertension, cardiovascular disease, and cancer are at a greater risk of contracting the COVID-19 [3]. COVID-19 infect their hosts via Angiotensin-Converting Enzyme 2 (ACE2) receptors [4]. Since, ACE2 receptors are expressed in the kidneys and Gastrointestinal (GI) tract, the virus can cause damage to these organs, which can lead to acute kidney injury and digestive problems [1]. COVID-19 disease may also affect the respiratory, nervous, cardiovascular, and urogenital systems [5-7]. Electrolytes plays a critical role in homeostasis, including fluid and acid-base balance regulation, oxygen delivery, and neurological function [8]. Since, the GI tract and kidneys plays a crucial roles in fluid and electrolyte balance, patients with COVID-19 disease, may experience fluid and electrolyte imbalances, which, if untreated, may result in adverse events [9]. In addition, electrolyte disorders (hyponatraemia, hypernatraemia, hypokalaemia, hyperkalaemia, and hypomagnesaemia) are prevalent among older subjects (55 years or older) in general population [10].

The prognosis of COVID-19 disease appears to be affected by various electrolyte imbalances, according to the findings of several

Journal of Clinical and Diagnostic Research. 2023 Jul, Vol-17(7): BC05-BC09

investigations [11,12]. This is the first research to evaluate COVID-19 related electrolyte abnormalities in hospitalised patients, in the southern Gaza Strip. Possible advantages and applicability of such a study will enhance the patient outcomes, guiding clinical decision making and public health policy, and adding to the existing body of information on COVID-19. Hence, the present study was conducted to compare the electrolyte imbalance and biomarkers among patients hospitalised with COVID-19 and healthy subjects in the southern Gaza Strip of Palestine.

MATERIALS AND METHODS

This retrospective case-control study was conducted in the Department of Medical Laboratory Sciences at European Gaza Hospital, a Government Hospital directed and owned by the Palestinian Ministry of Health (MOH), southern Gaza Strip. The duration of the study was four months, from February 2022 to May 2022. The Medical Laboratory Department at Al-Aqsa University in Gaza, approved the study. In addition, permission was obtained from the MOH's General Directorate of Human Resources Development (GDHRD) to conduct the present study (approval no. 931180). The confidentiality of participants was maintained as all of the data were used anonymously.

Inclusion criteria: All patients with confirmed diagnosis of COVID-19 infection with or without electrolyte imbalance were included in the study. The control group consisted of age and gender matched healthy individuals. To ensure that, no one in the control group ever had a COVID-19 infection, they were chosen from newly employed and healthy donors recruited prior to the COVID-19 pandemic.

Exclusion criteria: Missing data files, patients who were not enrolled in COVID-19 department, patients with kidney disease, those with additional underlying illnesses, or those, who had received certain drugs, that might have an impact on their biochemical or electrolyte levels were excluded from the study.

Sample size calculation: The Epi Info programme calculator was used to calculate sample size. The total population with complete data on the study's parameters was 5000 patients, with expected frequency 50% and margin error 6.8% at 95% Confidence Interval (CI), the total sample size calculated was 200 (100 cases and 100 controls).

The European Gaza Hospital diagnoses COVID-19, using World Health Organisation (WHO) and Palestinian Ministry of Health guidelines. The WHO recommends diagnosing COVID-19 with RT-PCR. Nasopharyngeal and oropharyngeal swabs are tested for virus genetic material [13,14].

Study Procedure

The European Gaza Hospital diagnoses COVID-19, using World Health Organisation (WHO) and Palestinian Ministry of Health guidelines. The WHO recommends diagnosing COVID-19 with RT-PCR. Nasopharyngeal and oropharyngeal swabs are tested for virus genetic material [13,14]. The data concerning results of electrolytes and biochemical profile were extracted from the electronic archive system of European Gaza Hospital for patients with COVID-19 disease from February 2022 to May 2022, while the controls' data were extracted from November 2017 to February 2018, from the system of blood bank donors and comprehensive screening department for new employees before the COVID-19 epidemic. Using a Mindray BS-480 clinical chemistry analyser, commercial kits were used to measure FBG, urea, Cr, AST, ALT, CK-total, isoenzyme Creatine Kinase-Myocardial Band (CK-MB), Phosphorous (P), and Magnesium (Mg). In addition, Ion-selective Electrode (ISE) analysers Erba Lyte 90 were used to assay the serum electrolytes sodium (Na), potassium (K), ionised calcium (Ca ionised), total calcium (total Ca), and chloride (Cl). The cut-off range for all the parameters, investigated in the present study, along with their respective references shown in [Table/Fig-1].

Biochemical parameters	Normal range	Manufactures for the assayed parameters			
FBG (mg/dL)	70-100 mg/dL	AMS kit			
Urea (mg/dL)	15-45 mg/dL	Lab kit			
Cr (mg/dL)	0.6-1.2 mg/dL	Chroma kit			
AST (IU/L)	10-40 IU/L	AMS kit			
ALT (IU/L)	10-40 IU/L	AMS kit			
CK-total (IU/L)	40-250 IU/L	Elic kit			
CK-MB (IU/L)	0-25 IU/L	Biosystem kit			
Na (mmol/L)	135-145 mmol/L	Erba kit			
K (mmol/L)	3.5-5.0 mmol/L	Erba kit			
Ca ionised (mmol/L) 1	0.15-1.30 mmol/L	Erba kit			
Total Ca (mg/dL)	8.5-10.5 mg/dL	Erba kit			
CL (mmol/L)	96-106 mmol/L	Erba kit			
P (mg/dL)	2.5-4.5 mg/dL	Lab kit			
Mg (mg/dL)	1.8-2.4 mg/dL	Lab kit			
[Table/Fig-1]: The cut-off range for all the parameters along with the reference.					

STATISTICAL ANALYSIS

The data was analysed using Statistical Package for Social Sciences (SPSS) version 25.0. Results were summarised using mean and Standard Deviation (SD) or number (percentage), and comparison between patients and controls, between genders were done by

Student's t-test and Chi-square test. Pearson's correlation test was used to investigate the relationship between age and selected parameters. A (p-value <0.05) was considered statistically significant.

RESULTS

The present study included 200 subjects (100 COVID-19 patients as cases and 100 healthy individuals, as controls). Regarding gender, both groups' cases and controls had equal numbers of males 34 (34.0%) and females 66 (66.0%) and there was no statistically significant difference (p>0.05). Patients with COVID-19 showed significantly higher levels of Na (p<0.001)), K (p=0.001), Cl (p<0.001), P (p<0.001), Mg (p<0.001) than healthy controls. In contrast levels of Ca ionised (p<0.001) and total Ca (p<0.001) were significantly lower in patients with COVID-19 characterised by significantly higher levels of biomarkers of other biochemical profiles compared to healthy controls; FBG (p<0.001), Urea (p<0.001), Cr (p<0.001), AST (p<0.001), ALT (p=0.001), CK-total (p<0.001), CK-MB (p<0.001) [Table/Fig-2].

	Cases	Controls	Statistical test			
General characteristics	(n=100)	(n=100)	t/χ²	p-value		
Age (years)	54.1±12.2	54.3±12.4		0.877		
Gender (M:F)	34: 66	34:66	0	1		
FBG (mg/dL)	109.2±43	88.4±11.5	4.673	<0.001*		
Urea (mg/dL)	38.7±15.5	28.6±5.1	6.158	<0.001*		
Cr (mg/dL)	1.0±0.1	0.8±0.3	5.388	<0.001*		
AST (IU/L)	48.9±39	29.9±7.7	4.785	<0.001*		
ALT (IU/L)	41.4±41	26.7±12.1	3.417	0.001*		
CK-total (IU/L)	437.5±864.8	106.8±56.9	3.815	<0.001*		
CK-MB (IU/L)	34.5±25.8	13.8±2.7	7.984	<0.001*		
Na (mmol/L)	141.9±4.6	139.7±3.1	3.875	<0.001*		
K (mmol/L)	4.6±0.9	4.3±0.5	3.400	0.001*		
Ca ionised (mmol/L)	1.0±0.1	1.1±0.1	-5.507	<0.001*		
Total Ca (mg/dL)	8.4±0.9	9.1±1.1	-4.665	<0.001*		
CI (mmol/L)	108.7±5.3	101.1±4.0	11.415	<0.001*		
P (mg/dL)	4.6±0.6	4±1.4	3.993	<0.001*		
Mg (mg/dL)	2.1±0.2	1.7±0.3	10.256	<0.001*		

[Table/Fig-2]: General characteristics and laboratory findings of the study population. Data represented as mean±SD; *p≤0.05: significant, n: Number of the subjects; SD: Standard deviation; t: Student's t-test; χ²: Chi-square test; FBG: Fasting blood glucose; Cr: Creatinine; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; CK: Creatine kinase; CK-MB: Creatine kinase isoenzyme MB; Na: Sodium; K: Potassium; Ca: Calcium; P: Phosphorus; Mg: Magnesium

In the cases, data analysis revealed that, males had significantly higher levels of CK-MB than females (41.6±26.6 vs 30.9±24.8, p=0.048). However, there was no statistically significant difference found in the levels of other studied parameters between males and females (p>0.05) [Table/Fig-3]. In present study, there was no significant correlation between age and electrolytes and other biochemical parameters among patients hospitalised with COVID-19, indicating that, age is not a major contributing factor to changes in these parameters. However, Na in cases was positively correlated with K, CK total and isoenzyme (p<0.05). In addition, the correlation between the ionised and total Ca levels and the CI. Lastly, the CI in cases correlated positively with Ca total and Ca ionised (p<0.05) [Table/Fig-4].

DISCUSSION

Coronaviruses have spread throughout the world, resulting in nearly 18 million deaths, many more hospitalisations and significant economic and social disruption as of March 2022 [15]. Monitoring clinical, haematological, and biochemical parameters is essential for COVID-19 patient management. Severity and outcome categorisation based on biochemical parameters is important [16]. A total of 100 patients with COVID-19 were recruited for this age- and gender-matched

	Male (n=34)	Female (n=66)	Statistical test			
Parameters	Mean±SD	Mean±SD	t-value	p-value		
Age (in years)	54.9±12	53.7±12.3	0.459	0.647		
Na (mmol/L)	142.5±4.6	141.6±4.6	0.922	0.359		
K (mmol/L)	4.8±0.9	4.6±0.9	0.989	0.325		
Ca ionised (mmol/L)	1±0.1	1.1±0.1	0.983	0.328		
Total Ca (mg/dL)	8.4±0.5	8.4±1	-0.082	0.935		
CI (mmol/L)	108.3±5.5	108.8±5.2	-0.444	0.658		
P (mg/dL)	4.6±0.6	4.7±0.6	-0.996	0.322		
Mg (mg/dL)	2.1±0.2	2.1±0.2	0.266	0.791		
Glucose (mg/dL)	106.6±43.8	110.5±42.8	-0.423	0.673		
Urea (mg/dL)	38.5±14.9	38.8±15.9	-0.097	0.923		
Cr (mg/dL)	1.0±0.3	1±0.4	0.190	0.850		
AST (IU/L)	46.6±42	50.1±37.7	-0.418	0.677		
ALT (IU/L)	42.7±44.1	40.7±39.7	0.236	0.814		
CK total (IU/L)	418.2±652	447.4±960.8	-0.159	0.874		
CK-MB (IU/L)	41.6±26.6	30.9±24.8	1.999	0.048*		
[Table/Fig-3]: Compar	ison between b	iochemical parameter	s among ma	ales and		

females in cases. Data represented as mean±SD.

*p<0.05: Significant, n: Number of the subjects; SD: Standard deviation; t: Student's t-test. FBG: Fasting blood glucose; Cr: Creatinine; AST; Aspartate aminotransferase; ALT; Alanine aminotransferase; CK: Creatine kinase; CK-MB: Creatine kinase isoenzyme MB; Na: Sodium;

K: Potassium; Ca: Calcium; P: Phosphorus; Mg: Magnesium

Mahmoud I Elhabiby et al., Electrolyte Abnormalities in Patients Hospitalised with COVID-19

blood of COVID-19 patients were reported [21-23]. Hypocalcaemia was significantly associated with severity of the disease, mortality in patients with COVID-19, number of hospitalisation days and admission to the intensive care unit [24-26]. In contrast to these findings, a number of published studies have documented that, patients diagnosed with COVID-19 infection and while they were hospitalised, exhibited symptoms of hyponatraemia, hypochloraemia and hypokalaemia [27-30]. Sarvazad H et al., reported from a cross-sectional study that, 38% hyponatraemia, 7.3% hypokalaemia and 32% hypomagnesaemia were found in patients with COVID-19 [31]. Moreover, hypophosphataemia was reported in 33 patients diagnosed with COVID-19 with an incidence of 7.6% [32]. [Table/Fig-5] demonstrates discrepancy in reporting findings of electrolytes in patients diagnosed with COVID-19. The present study's data analysis revealed that, patients diagnosed with COVID-19 had significantly higher FBG levels than healthy controls. In line with the findings of the present study, the mean value of FBG has been found to be higher in patients with COVID-19, and there has been an association between the severity of COVID-19 and blood glucose level [31]. Rao S et al., found that, COVID-19 infected hospitalised patients who died, had higher admission glucose levels than those who lived [33].

In the present study, COVID-19 patients had significantly higher levels of urea and creatinine, when compared to healthy controls.

	Age (in	years)	Na (m	mol/L)	K (mr	nol/L)	Ca ionise	ed (mmol/L)	Ca (m	ng/dL)	CI (mi	nol/L)	P (m	g/dL)	Mg (n	ng/dL)
Parameters	r- value	p- value	r- value	p- value	r- value	p- value	r-value	p-value	r- value	p- value	r- value	p- value	r- value	p- value	r- value	p- value
Age (years)	-	-	-0.015	0.881	0.151	0.134	-0.053	0.597	-0.087	0.387	-0.008	0.939	-0.053	0.597	0.132	0.189
Glucose (mg/dL)	0.050	0.620	-0.016	0.878	-0.037	0.713	0.009	0.927	-0.013	0.897	-0.051	0.616	-0.150	0.137	0.055	0.590
Urea (mg/dL)	0.033	0.742	0.074	0.466	-0.028	0.781	0.006	0.951	-0.026	0.794	0.155	0.124	-0.007	0.941	-0.014	0.886
Cr (mg/dL)	0.120	0.234	-0.162	0.107	0.135	0.182	0.052	0.609	0.022	0.827	-0.121	0.230	-0.002	0.982	0.121	0.230
AST (IU/L)	0.058	0.563	0.073	0.470	0.194	0.052	0.109	0.280	0.164	0.103	0.131	0.193	-0.034	0.738	-0.007	0.947
ALT (IU/L)	0.090	0.375	0.058	0.568	0.182	0.070	0.070	0.490	0.149	0.140	-0.099	0.325	0.005	0.958	0.001	0.990
CK total (IU/L)	-0.012	0.904	0.317	0.001*	0.151	0.133	0.195	0.051	0.218	0.029*	-0.058	0.564	-0.002	0.987	0.052	0.604
CKMB (IU/L)	0.099	0.325	0.267	0.007*	0.130	0.196	0.148	0.142	0.193	0.055	0.041	0.683	-0.056	0.582	0.157	0.118
Na (mmol/L)	-0.015	0.881	-	-	0.238	0.017*	-0.051	0.617	-0.010	0.924	0.063	0.535	0.026	0.794	-0.125	0.214
K (mmol/L)	0.151	0.134	0.238	0.017*	-	-	-0.184	0.067	-0.065	0.524	-0.072	0.477	0.038	0.705	0.071	0.484
Ca ionised (mmol/L)	-0.053	0.597	-0.051	0.617	-0.184	0.067	-	-	0.921	<0.001	0.304	0.002*	-0.094	0.352	0.074	0.463
Ca (mg/dL)	-0.087	0.387	-0.010	0.924	-0.065	0.524	0.921	<0.001	-	-	0.240	0.016*	-0.139	0.167	0.121	0.231
CL (mmol/L)	-0.008	0.939	0.063	0.535	-0.072	0.477	0.304	0.002*	0.240	0.016*	-	-	-0.103	0.309	-0.140	0.164
P (mg/dL)	-0.053	0.597	0.026	0.794	0.038	0.705	-0.094	0.352	-0.139	0.167	-0.103	0.309	-	-	0.090	0.372
Mg (mg/dL)	0.132	0.189	-0.125	0.214	0.071	0.484	0.074	0.463	0.121	0.231	-0.140	0.164	0.090	0.372	-	-
[Table/Fig-4]: C	Table/Fig-4]: Correlation between the studied parameters among cases.															

*p≤0.05: Significant, n: Number of the subjects; r: Pearson correlation. FBG: Fasting blood glucose; Cr: Creatinine; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; CK: Creatine kinase CK-MB: Creatine kinase isoenzyme MB; Na: Sodium; K: Potassium; Ca: Calcium; P: Phosphorus; Mg: Magnesium

case-control study, representing the cases, and 100 healthy individuals served as the controls.

Reports of electrolyte abnormalities in COVID-19 patients are heterogeneous and controversial. Data from the present study revealed that, Na, K, Cl, P, and Mg levels in the blood were significantly higher in COVID-19 patients than in healthy controls. However, Ca ionised and total Ca significantly decreased in cases compared to controls. In previous studies, hypernatraemia and hyperkalaemia were found to be significantly more common in COVID-19 patients than in Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) negative patients [17-19], which is in line with the findings of the current research.

Many studies reported significantly higher serum concentrations of Mg (hypermagnesaemia) and P (hyperphosphataemia) in patient diagnosed with COVID-19 and its association with the severity of the disease [18-20]. While Low levels of total and ionised Ca in

Journal of Clinical and Diagnostic Research. 2023 Jul, Vol-17(7): BC05-BC09

In agreement with the findings from present study, a retrospective, single-centre study found that, the serum creatinine and blood urea nitrogen levels of COVID-19 patients increased substantially during the disease's peak compared to the recovery period [34]. In addition, liver enzymes AST and ALT in COVID-19 patients were significantly higher than in the healthy controls. Medetalibeyoglu A et al., reported high mean values of liver enzymes AST and ALT for COVID-19 patients on admission [35]. Moreover, Wu Y et al., found that, elevated liver enzymes AST and ALT in COVID-19 patients may have multiple causes, including direct liver injury, associated inflammatory responses, congestive hepatopathy, haepatic ischaemia, and drug-induced liver injury [36,37]. Lastly, the results from the preset study revealed that, COVID-19 patients had statistically significantly higher mean values of CK-total and CK-MB than controls. Yang J et al., evaluated cardiac function in patients with COVID-19 infections and found that, among hospitalised

Studies [Ref. No.]	Place and year of the study	Sample size	Findings
Present study	Palestine, February 2022 to May 2022	100 patients, diagnosed with COVID-19 infection	COVID-19 patients had significantly higher values of sodium (141.9 \pm 4.6 vs 139.7 \pm 3.1; p-value <0.001), potassium (4.6 \pm 0.9 vs 4.3 \pm 0.5; p-value=0.001), chloride (108.7 \pm 5.3 vs 101.1 \pm 4.0; p-value <0.001), phosphorus (4.6 \pm 0.6 vs 4 \pm 1.4; p-value <0.001), and magnesium (2.1 \pm 0.2 vs 1.7 \pm 0.3; p-value <0.001). However, they had lower Ca ionised (1.0 \pm 0.1 vs 1.1 \pm 0.1; p-value <0.001) and total Ca (8.4 \pm 0.9 vs 9.1 \pm 1.1; p-value <0.001).
Sodium			
Machiraju PK et al., [27]	India, June 2020 to September 2020	113 patients hospitalised with COVID-19	Hyponatraemia was present in 50 out of 113 (44%) patients in the present study, and it was generally mild. There were more male patients in hyponatraemia group (p-value=0.006), and hyponatraemic patients were older than normonatremic patients (p-value=0.001).
Malieckal DA et al., [28]	USA, March 2020 to April 2020	10,385 patients hospitalised for COVID-19,	Hyponatraemia was the most commonly identified disorder (37.5%), followed by hypochloraemia (26.0%) and hypocalcaemia (18.3%). Among patients with an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m ² , 30.3% had hyponatremia, 11.1% had hyperkalaemia and 19.7% had hypochloraemia.
Chloride	•		
Malieckal DA et al., [28]	USA, March 1, 2020, to April 27, 2020	10,385 patients hospitalised for COVID-19,	Overall, hyponatraemia was the most commonly identified disorder (37.5%), followed by hypochloraemia (26.0%) and hypocalcaemia (18.3%). Among patients with an estimated Glomerular Filtration Rate (eGFR) <60 mL/min/1.73 m ² , 30.3% had hyponatremia, 11.1% had hyperkalaemia and 19.7% had hypochloraemia.
Potassium	·		
Chen D et al., [29]	China, January 2020 to February 2020	175 COVID-19 patients	Severe hypokalaemia {31 patients (18%)}, hypokalaemia {64 patients (37%)}, and normokalaemia {80 patients (46%)}.
Alfano G et al., [30]	Italy, February2020 to April 2020	290 non ICU admitted patients with COVID-19	Hypokalaemia was detected in 119 out of 290 patients (41%) during hospitalisation. Mean serum potassium was 3.1±0.1 meq/L. The majority of patients (90.7%) patients experienced only a mild decrease in serum potassium level (3-3.4 mEq/L).
Magnesium	·		
Sarvazad H et al., [31]	Iran, April 2020 to July 2020	134 COVID-19 patients	From all included patients, 49.1% hyperglycaemia, 38% hyponatraemia, 7.3% hypokalaemia, and 32% hypomagnesaemia were observed. For the blood potassium levels, 85% of patients were in the normal range, 1.8% were hypokalaemic, 7.3% were severely hypokalaemic and 5.5% were hyperkalaemic.
Phosphorus			
Wang R et al., [32]	China, January 2020 to February 2020	435 COVID-19 patients	Hypophosphataemia at admission occurred in 33 patients, with an incidence of 7.6%. The hypophosphataemia group had a significantly higher incidence of respiratory failure (54.5% vs 32.6%, p=0.013) and mortality (57.6% vs 15.2%, (p-value <0.001). Hypophosphataemia at admission is associated with increased mortality in COVID-19 patients.

COVID-19 patients, the prevalence of myocardial injury is high and is associated with a significant elevation of related cardiac biomarkers [38]. In addition, abnormalities in myocardial enzymes, including cardiac troponin I, creatine kinase, lactate dehydrogenase, and CK-MB have been reported to be associated with the severity and fatal outcomes of COVID-19 [39].

Liu J et al., studied the association of sex with clinical outcomes in COVID-19 patients and they discovered males of all ages had greater levels of organ function parameters (such as ALT, AST, and CK-MB) than did age-matched females, according to age group stratification [40]. Pearson's correlation analysis revealed no significant relationship between the ages in the COVID-19 patients. Tezcan ME et al., found that, there was no statistically significant relationship between the age of the cases and the examined variables [41]. Findings of the present study could conclude that, the age was not a confounding factor and had no contribution in alteration of the investigated parameters during the study. This could suggest that, the severity of the illness and the presence of co-morbidities are more significant factors in determining the development of electrolyte abnormalities than previously thought.

However, Pearson's correlation analyses showed positive correlations between Na and ionised Ca in one hand and K and cardiac biomarkers, CK total and CK-MB in other hand. These results agreed with Sjöström A et al., who found that, there is a relation between the electrolyte and biochemical parameters among COVID-19 cases [42]. However, there was no significant association between the K and the other studied chemistry parameters. In contrast to present study's findings, hypokalaemia was associated with hypocalcaemia in subjects with COVID-19, which was detected in 50% of subjects [30].

Limitation(s)

The researchers of the present study, did not have access to the patients' complete medical history, which could have an impact on the interpretation of laboratory results. Also, focusing on a specific set of laboratory tests or abnormalities could limit the overall understanding of the effect that COVID-19 has on electrolyte abnormalities and other aspects of the biochemical profile.

CONCLUSION(S)

In conclusion, the results of the present study showed that, patients with COVID-19 had significantly higher Na, K, Cl, P, and Mg values. In addition, COVID-19 patients had higher levels of biomarkers of other biochemical profile including glucose, kidney function, liver enzymes AST and ALT, and cardiac enzymes than normal individuals. The author's findings suggested that, hospitalise COVID-19 patients manifest significant alteration in electrolytes and other biochemical profile. Management of these parameters to get homeostasis, could that warrant opportunities to reduce morbidity and mortality of disease. In future research, the long term impacts of COVID-19 on electrolyte abnormalities and other aspects of survivors' biochemical profiles could be investigated. Also, it might be possible to investigate how the various COVID-19 variants may influence electrolyte abnormalities and other aspects of a person's biochemical composition.

Acknowledgement

The authors would like to extend their gratitude to the members of the JCDR editorial for the assistance they provided in restructuring the results.

REFERENCES

 Kordzadeh-Kermani E, Khalili H, Karimzadeh I. Pathogenesis, clinical manifestations and complications of coronavirus disease 2019 (COVID-19). Future Microbiol. 2020;15:1287-305. Doi: 10.2217/fmb-2020-0110.

- [2] Ministry of Health (MOH-PHIC) daily reports on COVID-19 in gaza strip. COVID-19 cases in the Gaza strip. Monthly epidemiological bulletin from (16/10 TO 15/11 2021) AND from (16/11 TO 15/12 2021).
- [3] Boukhris M, Hillani A, Moroni F, Annabi MS, Addad F, Ribeiro MH, et al. Cardiovascular implications of the COVID-19 pandemic: A global perspective. Can J Cardiol. 2020;36(7):1068-80. Doi: 10.1016/j.cjca.2020.05.018.
- [4] Magrone T, Magrone M, Jirillo E. Focus on receptors for coronaviruses with special reference to angiotensin- converting enzyme 2 as a potential drug targeta perspective. Endocr Metab Immune Disord Drug Targets. 2020;20(6):807-11. Doi: 10.2174/1871530320666200427112902.
- [5] Xu J, Xiao W, Liang X, Shi L, Zhang P, Wang Y, et al. A meta-analysis on the risk factors adjusted association between cardiovascular disease and COVID-19 severity. BMC Public Health. 2021;21(1):1533. Doi: 10.1186/s12889-021-11051-w.
- [6] Hashim M, Athar S, Gaba WH. New onset adrenal insufficiency in a patient with COVID-19. BMJ Case Rep. 2021;14(1):e237690. Doi: 10.1136/bcr-2020-237690.
 [7] Zheng KI, Feng G, Liu WY, Targher G, Byrne CD, Zheng MH. Extrapulmonary
- complications of COVID-19: A multisystem disease? J Med Virol. 2021;93(1):323-35. Doi: 10.1002/jmv.26294.
- [8] Balc AK, Koksal O, Kose A, Armagan E, Ozdemir F, Inal T, et al. General characteristics of patients with electrolyte imbalance admitted to emergency department. World J Emerg Med. 2013;4(2):113-16. Doi: 10.5847/wjem.j.issn.1920-8642.2013.02.005.
- [9] Pourfridoni M, Abbasnia SM, Shafaei F, Razaviyan J, Heidari-Soureshjani R. Fluid and electrolyte disturbances in COVID-19 and their complications. Bio Med Research International. 2021;2021:6667047.
- [10] Liamis G, Rodenburg EM, Hofman A, Zietse R, Stricker BH, Hoorn EJ. Electrolyte disorders in community subjects: Prevalence and risk factors. Am J Med. 2013;126(3):256-63. Doi: 10.1016/j.amjmed.2012.06.037.
- [11] Panimathi R, Gurusamy E, Mahalakshmi S, Ramadevi K, Kaarthikeyan G, Anil S. Impact of COVID-19 on renal function: A multivariate analysis of biochemical and immunological markers in patients. Cureus. 2022;14(2):e22076. Doi: 10.7759/ cureus.22076.
- [12] Tang CF, Ding H, Jiao RQ, Wu XX, Kong LD. Possibility of magnesium supplementation for supportive treatment in patients with COVID-19. Eur J Pharmacol. 2020;886:173546. Doi: 10.1016/j.ejphar.2020.173546.
- [13] Palestinian Ministry of Health (2020): Diagnosis and management & treatment of patients with COVID-19.
- [14] Vandenberg O, Martiny D, Rochas O, van Belkum A, Kozlakidis Z. Considerations for diagnostic COVID-19 tests. Nat Rev Microbiol. 2021;19(3):171-83. Doi: 10.1038/ s41579-020-00461-z.
- [15] Mikolajek H, Weckener M, Brotzakis ZF, Huo J, Dalietou EV, Le Bas A, et al. Correlation between the binding affinity and the conformational entropy of nanobody SARS-CoV-2 spike protein complexes. Proc Natl Acad Sci USA. 2022;119(31):e2205412119. Doi: 10.1073/pnas.2205412119.
- [16] Sadiq A, Khurram M, Malik J, Chaudhary NA, Khan MM, Yasmeen T, et al. Correlation of biochemical profile at admission with severity and outcome of COVID-19. J Community Hosp Intern Med Perspect. 2021;11(6):740-46. Doi: 10.1080/20009666.2021.1974161.
- [17] Voets PJ, Frölke SC, Vogtländer NP, Kaasjager KA. COVID-19 and dysnatremia: A comparison between COVID-19 and non COVID-19 respiratory illness. SAGE Open Med. 2021;9:20503121211027778. Doi: 10.1177/20503121211027778.
- [18] Yasari F, Akbarian M, Abedini A, Vasheghani M. The role of electrolyte imbalances in predicting the severity of COVID-19 in the hospitalized patients: A cross-sectional study. Sci Rep. 2022;12(1):14732. Doi: 10.1038/s41598-022-19264-8.
- [19] Nakanishi H, Suzuki M, Maeda H, Nakamura Y, Ikegami Y, Takenaka Y, et al. Differential diagnosis of COVID-19: Importance of measuring blood lymphocytes, serum electrolytes, and olfactory and taste functions. Tohoku J Exp Med. 2020;252(2):109-19. Doi: 10.1620/tjem.252.109.
- [20] Quilliot D, Bonsack O, Jaussaud R, Mazur A. Dysmagnesemia in Covid-19 cohort patients: Prevalence and associated factors. Magnes Res. 2020;33(4):114-22. Doi: 10.1684/mrh.2021.0476.
- [21] Malinowska J, Małecka-Giełdowska M, Bałkowska D, Borecka K, Ciepiela O. Hypermagnesemia and hyperphosphatemia are highly prevalent in patients with COVID-19 and increase the risk of death. Int J Infect Dis. 2022;122:543-49. Doi: 10.1016/j.iijd.2022.06.057.
- [22] Sharma R, Heidari A, Johnson RH, Advani S, Petersen G. Serum magnesium levels in hospitalized patients with SARS-CoV-2. J Investig Med. 2022;70(2):409-14. Doi: 10.1136/jim-2021-001948.

- [23] Cappellini F, Brivio R, Casati M, Cavallero A, Contro E, Brambilla P. Low levels of total and ionized calcium in blood of COVID-19 patients. Clin Chem Lab Med. 2020;58(9):e171-73. Doi: 10.1515/cclm-2020-0611. PMID: 32459190.
- [24] Liu J, Han P, Wu J, Gong J, Tian D. Prevalence and predictive value of hypocalcemia in severe COVID-19 patients. J Infect Public Health. 2020;13(9):1224-28. Doi: 10.1016/j.jiph.2020.05.029.
- [25] Lippi G, South AM, Henry BM. Electrolyte imbalances in patients with severe coronavirus disease 2019 (COVID-19). Ann Clin Biochem. 2020;57(3):262-65. Doi: 10.1177/0004563220922255.
- [26] Alemzadeh E, Alemzadeh E, Ziaee M, Abedi A, Salehiniya H. The effect of low serum calcium level on the severity and mortality of Covid patients: A systematic review and meta-analysis. Immun Inflamm Dis. 2021;9(4):1219-28. Doi: 10.1002/iid3.528.
- [27] Machiraju PK, Alex NM, Safinaaz, Vadamalai V. Hyponatremia in coronavirus disease-19 patients: A retrospective analysis. Can J Kidney Health Dis. 2021;8:20543581211067069. Doi: 10.1177/20543581211067069.
- [28] Malieckal DA, Uppal NN, Ng JH, Jhaveri KD, Hirsch JS; Northwell Nephrology COVID-19 Research Consortium. Electrolyte abnormalities in patients hospitalized with COVID-19. Clin Kidney J. 2021;14(6):1704-07. Doi: 10.1093/ ckj/sfab060.
- [29] Chen D, Li X, Song Q, Hu C, Su F, Dai J, et al. Assessment of hypokalemia and clinical characteristics in patients with coronavirus disease 2019 in Wenzhou, China. JAMA Netw Open. 2020;3(6):e2011122-e.
- [30] Alfano G, Ferrari A, Fontana F, Perrone R, Mori G, Ascione E, et al. Modena Covid-19 Working Group (MoCo19). Hypokalemia in Patients with COVID-19. Clin Exp Nephrol. 2021;25(4):401-09. Doi: 10.1007/s10157-020-01996-4.
- [31] Sarvazad H, Cahngaripour SH, Eskandari Roozbahani N, Izadi B. Evaluation of electrolyte status of sodium, potassium and magnesium, and fasting blood sugar at the initial admission of individuals with COVID-19 without underlying disease in Golestan Hospital, Kermanshah. New Microbes New Infect. 2020;38:100807. Doi: 10.1016/j.nmni.2020.100807.
- [32] Wang R, He M, Kang Y. Hypophosphatemia at admission is associated with increased mortality in COVID-19 patients. Int J Gen Med. 2021;14:5313-22. Doi: 10.2147/JJGM.S319717.
- [33] Rao S, Ali K, Dennis J, Berdine G, Test V, Nugent K. Analysis of glucose levels in patients hospitalized with COVID-19 during the first phase of this pandemic in West Texas. J Prim Care Community Health. 2020;11:2150132720958533. Doi: 10.1177/2150132720958533.
- [34] Hong XW, Chi ZP, Liu GY, Huang H, Guo SQ, Fan JR, et al. Characteristics of renal function in patients diagnosed with COVID-19: An observational study. Front Med (Lausanne). 2020;7:409. Doi: 10.3389/fmed.2020.00409.
- [35] Medetalibeyoglu A, Catma Y, Senkal N, Ormeci A, Cavus B, Kose M, et al. The effect of liver test abnormalities on the prognosis of COVID-19. Ann Hepatol. 2020;19(6):614-21. Doi: 10.1016/j.aohep.2020.08.068.
- [36] Wu Y, Li H, Guo X, Yoshida EM, Mendez-Sanchez N, Levi Sandri GB, et al. Incidence, risk factors, and prognosis of abnormal liver biochemical tests in COVID-19 patients: A systematic review and meta-analysis. Hepatol Int. 2020;14(5):621-37. Doi: 10.1007/s12072-020-10074-6.
- [37] Moon AM, Barritt AS. Elevated liver enzymes in patients with COVID-19: Look, but not too hard. Dig Dis Sci. 2021;66(6):1767-69. Doi: 10.1007/s10620-020-06585-9.
- [38] Yang J, Liao X, Yin W, Wang B, Yue J, Bai L, et al. Study of 2019 Novel Coronavirus Pneumonia Infected Critically III Patients in Sichuan Province (SUNRISE) Group. Elevated cardiac biomarkers may be effective prognostic predictors for patients with COVID-19: A multicenter, observational study. Am J Emerg Med. 2020;39:34041. Doi: 10.1016/j.ajem.2020.10.013.
- [39] Zhang Q, Zheng Z, Zhang Y. Association of myocardial enzyme abnormality with clinical outcomes of patients with COVID-19: A retrospective study. Dis Markers. 2021;2021:3440714. Doi: 10.1155/2021/3440714.
- [40] Liu J, Zhang L, Chen Y, Wu Z, Dong X, Teboul JL, et al. Association of sex with clinical outcomes in COVID-19 patients: A retrospective analysis of 1190 cases. Respir Med. 2020;173:106159. Doi: 10.1016/j.rmed.2020.106159.
- [41] Tezcan ME, Dogan Gokce G, Sen N, Zorlutuna Kaymak N, Ozer RS. Baseline electrolyte abnormalities would be related to poor prognosis in hospitalized coronavirus disease 2019 patients. New Microbes New Infect. 2020;37:100753. Doi: 10.1016/j.nmni.2020.100753.
- [42] Sjöström A, Rysz S, Sjöström H, Höybye C. Electrolyte and acid-base imbalance in severe COVID-19. Endocr Connect. 2021;10(7):805-14. Doi: 10.1530/EC-21-0265.

PARTICULARS OF CONTRIBUTORS:

- 1. Associate Professor, Department of Medical Laboratory Sciences, Al-Aqsa University, Gaza.
- 2. Assistant Professor, Department of Continuing Academic Education, Palestine College of Nursing, Ministry of Health, Gaza.
- 3. Professor, Department of Medical Laboratory Sciences, College of Applied Medical Sciences, Qassim University, Buraidah, Qassim, Saudi Arabia.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Abdelmarouf Hassan Mohieldein, P.O. Box No. 6699, Buraidah-51452, Qassim, Kingdom of Saudi Arabia. E-mail: mabdelmarouf@hotmail.com

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA
- PLAGIARISM CHECKING METHODS: [Jain H et al.]
 Plagiarism X-checker: Feb 08, 2023
- Manual Googling: Mar 22, 2023

Maridal Googling: Mar 22, 2023 iThenticate Software: Apr 12, 2023 (8%)

Date of Submission: Jan 25, 2023 Date of Peer Review: Feb 23, 2023 Date of Acceptance: Apr 24, 2023 Date of Publishing: Jul 01, 2023

ETYMOLOGY: Author Origin

EMENDATIONS: 7