ORIGINAL ARTICLE

Electrolyte Disturbances in COVID-19 Patients

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ABSTRACT

Keywords: Electrolyte Disturbances - COVID-19

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Background: COVID-19 is respiratory pandemic that emerged in 2020. COVID-19 manifestations ranged from asymptomatic to severe ones and death. Majority of cases have a mild self-limited presentation (81%), but severe respiratory symptoms (14%) as dyspnea, tachypnea, and hypoxia require hospital admission. **Aim of the Work:** To estimate incidence and types of electrolyte disturbances in positive COVID-19 patients. **Patients and Methods:** This cross-sectional study, 200 adult patients with proved COVID-19 by PCR for SARS- CoV2 RNA with nasopharyngeal specimens. admitted in isolation department at Aswan University Hospital, from October 2021 till April 2022. Patients were homogenized with regard to age, gender, and underlying electrolytes. The study was conducted under the approval of the Ethics Committee of the Aswan University Hospital and written informed consent forms were obtained from all patients. **Results:** The mean potassium, calcium and magnesium of the included patients were was statistically significant difference, but sodium and chloride were statistically non-significant difference. **Conclusion:** Electrolyte disturbances are complications in COVID-19 patients which lead to death, measure disease status and progression. Dysnatremia, hypokalemia, hypocalcemia, hypochloremia are the most common electrolyte disorders in SARS-CoV-2 infection. If these disorders are observed, definitive and immediate treatment should be started.

INTRODUCTION

The lung is the principal target of the novel coronavirus, and atypical pneumonia is the most common clinical presentation**.** Previous studies have shown that in COVID-19, in addition to the respiratory system, the disease and its complications also affect the gastrointestinal (GI) tract, and urogenital system. Because the GI tract and kidneys play an essential role in fluid and electrolyte balance in the body, disturbance can lead to an imbalance of fluid and electrolytes. Impaired fluid and electrolyte balance can be dangerous if left unchecked. [1]

Patients with COVID-19 can experience a long hospital stay. They usually undergo multiple treatments varying from delivering ventilatory support to the administration of experimental agents for SARS-CoV-2 infection. In this setting, fever, hyperventilation, Sweating, medication-related side effects and dietary changes may cause concerning electrolyte imbalances. [2]

Some studies showed that SARS-CoV-2 infection is associated with a high prevalence of hypokalemia as a frequent lab abnormality. [3] Low plasma potassium (K+) levels were reported in 55% of COVID 19 patients. [4]

Notably, the degree of hypokalemia has been strongly associated with the severity of COVID19 and a high mortality rate. In addition, COVID-19 patients are susceptible to pro- arrhythmic events related to electrolyte imbalance. [5]

Possible causes of hypokalemia in the context of SARS-CoV2 infection may result from hyper-activation of the renin- angiotensin-aldosterone system (RAAS), gastrointestinal losses, anorexia secondary to concurrent illness, and tubular damage caused by ischemia or nephrotoxic agents. Concerning this latter hypothesis, tubular damage may be linked to the direct cytotoxic effect of SARS-CoV-2, since the virus has been associated to diffuse tubular damage. [6]

Covid-19 patients may develop hypomagnesemia; the prevalence of hypomagnesemia was higher than that of hypokalemia; this may be the reason why hypomagnesemia precedes hypokalemia. [1, 7, 8]

In early COVID-19 studies, some evidence has been provided that electrolyte disorders may also be present in patients' presentation, including sodium, potassium, chloride, and calcium abnormalities. Such electrolyte disturbances have important implications not only for patient management but also for identifying potential pathophysiologic mechanisms underlying COVID-19 that could drive novel therapeutic opportunities. [1, 7, 9]

It was found that the electrolytes levels in the blood circulation have important roles to alleviate or increase the severity of the disease and thus the mortality rates of the patients are affected. [8]

PATIENTS AND METHODS

Study design and Study Setting:

In this cross sectional study, 200 patients were enrolled, diagnosed as COVID-19 and entered Isolation department in Aswan University Hospital between (October 2021 till April 2022).

Inclusion criteria:

1. Patients with confirmed positive COVID-19(positive PCR).
2. No restriction of race, gender, or occupation.
3. Patient > 18 years.

Exclusion criteria:

Any condition, which may directly affect electrolyte balance, had been excluded such as:

- Hypokalemic periodic paralysis.
- Adrenocortical insufficiency.
- Cushing syndrome. ▪ Acute renal failure.
- Chronic renal failure.

Sample Size:

The sample size was calculated at 167, considering $P = 70.4\%$ and $q = 29.6\%$, based on the study by ***Wan et al.*** [10], the significance level of 0.05, and power 80%. The researcher enrolled the eligible patients (according to the inclusion criteria stated above) using the census method; before enrollment, the researcher explained the research objectives to the patients and asked them to read and sign the written informed consent sheets.

Methods:

All eligible individuals for this study were subjected to:

History:

1) The data included demographics (age, gender, smoking history).
2) History of symptoms of COVID-19

3) Clinical examination

- Blood pressure, pulse, temperature, respiratory rate (vital signs).
- Any signs of covid-19.

Laboratory investigation:

- HRCT chest.
- Electrolytes (K, Na, Ca, Cl, Mg).
- ECG.
- Complete blood count.
- Kidney function test (blood urea and Serum Creatinine).
- Liver function tests (SGPT, SGOT, Total& direct bilirubin)

Patients were evaluated regarding to;

Incidence and Types of electrolyte imbalance in covid-19 patients. One venous blood sample was taken from the brachial vein of all patients at admission and sent to the laboratory for measurement of lymphocyte count, C-reactive protein (CRP), electrolytes, including sodium (Na), calcium (Ca), phosphorus (P), potassium (K), and magnesium (Mg).

The EDTA-containing tubes were used for lymphocyte count, measured using cell counter Sysmex KX-21 (with a normal range of 1360 – 3740) and serum was used for the rest of serum parameters. CRP, Na, K, Ca, Mg, P, and LDH were measured using Chemistry Analyzer Spectrophotometry BT3000; the normal range of CRP is < 10 mg/L in adults, Na is 135– 145 meq/L, K is 3.5 – 5.3 meq/L, Ca is 8.6 – 10.3 mg/dL, Mg is 1.5 – 2.6 mg/dL, P is 2.5 – 5 mg/dL in adults, and LDH is 225– 500U.

The collected information included demographics (age and gender) and the information needed to classify patients based on disease severity, including clinical symptoms (such as shortness of breath, fever, cough, loss of consciousness, gastrointestinal symptoms), computed tomography (CT) scan findings, respiratory rate (RR) per minute, oxygen saturation (SpO2) at rest, mean arterial blood oxygen pressure to respiratory oxygen concentration ratio (PaO2/FiO2), respiratory failure requiring mechanical ventilation, admission to ICU, and shock.

Accordingly, the severity of the disease was categorized into four classes: mild (mild clinical symptoms and no imaging), moderate (fever and/or respiratory symptoms, or imaging evidence of pneumonia), severe ($RR \geq 30$ per minute, $SpO2 \leq 93\%$, or $PaO2/FiO2 \leq 300$ mmHg), and critical (respiratory failure requiring mechanical ventilation, shock, multiple organ dysfunction or need for monitoring and treatment in the ICU). Mild cases did not require hospitalization and were not included in the present study.

Ethical considerations:

- Approval of the ethical committee of Faculty of Medicine, Aswan University to the final study was obtained.
- Verbal and Written consent was obtained from all cases or their relatives before getting them involved in the study.
- The steps of the study, the aim of the study, the potential benefit and hazards, all were discussed with the patients.
- Confidentiality of all data was ensured.
- Patients had the right to withdraw from the study at any time without giving any reason.
- All patients had the right to refusal to participate in the study with no negative effect on service delivered to them. \

Statistical analysis:

The collected data was revised, coded, tabulated, and introduced to a PC using Microsoft excel. All statistical analysis was done using R version 4.1.1 software (R Core Team). Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

Descriptive statistics:

- Median and Interquartile range (IQR) for numerical data.
- Frequency and percentage for categorical data.

Analytical statistics:

A logistic regression model was conducted to assess whether different variables of COVID19 patients are related to electrolyte disturbances.

P- value: level of significance ▪

P>0.05: Non-significant (NS).

- P< 0.05: Significant (S).
- P<0.01: Highly significant (HS).

RESULTS

In this cross sectional study, 200 were enrolled **COVID-19** patients who enter Isolation department in Aswan University Hospital between) October 2021 till April 2022 for the investigation of electrolyte imbalance, clinical changes. **I. Demographic Data:**

Demographic data of the included patients were statistically calculated and tabulated. 52% of our patients (104/200 patients) were males and 48% (96/200 patients) were females. Their ages ranged between 18 years old as minimum age and 78 years old as maximum age with median as 46 years old. More than one third of the patients (35.5%) (71/200 patients) were smokers and 64.5% of our patients were non-smokers (129/200 patients).

Table (1): Demographic data of the included patients.

Demographic Data	Mean±SD	Min. - Max.	Median	P value
Age (Years-Old)				
Age	45.61±13.84	18 – 78	46	< 0.0001*
Gender (Male / Female)				
	Percentage (N = %)			
Male	104 (52%)			
Female	96 (48 %)			
Smoking				
Non – Smoking	129 (64.5 %)			
Smoking	71 (35.5 %)			

SD: Standard deviation, **N:** Number, **%:** Percentage, ***:** highly significant,
<0.05: statistically significant; **>0.05:** statistically Non-significant.

II. Clinical Symptoms of our COVID-19 patients:

All the clinical symptoms of the included patient were calculated. **Abdominal Pain:** 51.5% of our patients had abdominal pain which included (103/200 patients) and 48.5% of our patients didn't have

abdominal pain which included (97/200 patients) in our study. **Ageusia (loss of taste):** 51% of our patients had ageusia which included (102/200 patients) and 49% of our patients didn't have ageusia which included (98/200 patients) in our study. **Cough:** 39.5% of our patients had cough which included (79/200 patients) and 60.5% of our patients didn't have cough which included (121/200 patients) in our study. **Diarrhea:** 47.5% of our patients had diarrhea which included (95/200 patients) and 52.5 % of our patients didn't have diarrhea which included (105/200 patients) in our study. **Dyspnea:** 54.5% of our patients had dyspnea which included (109/200 patients) and 45.5% of our patients didn't have dyspnea which included (91/200 patients) in our study. **Fever:** 52.5% of our patients had fever which included (105/200 patients) and 47.5% of our patients didn't have fever which included (95/200 patients) in our study. **Nausea:** 54.5% of our patients had nausea which included (109/200 patients) and
45.5% of our patients didn't have nausea which included (91/200 patients) in our study. **Vomiting:** 41.5% of our patients had vomiting which included (83/200 patients) and 58.5% of our patients didn't have vomiting which included (117/200 patients) in our study. **Weakness:** 48% of our patients had weakness which included (96/200 patients) and 52% of our patients didn't have weakness which included (104/200 patients) in our study.

Table (2): Clinical Symptoms of our COVID-19 patients.

Clinical Examination		
	Had Percentage (N = %)	**Didn't have Percentage (N = %)**
Abdominal Pain	103 (51.5 %)	97 (48.5 %)
Ageusia(loss of taste)	102 (51 %)	98 (49 %)
Cough	79 (39.5 %)	121 (60.5 %)
Diarrhea	95 (47.5 %)	105 (52.5 %)
Dyspnea	109 (54.5 %)	91 (45.5 %)
Fever	105 (52.5 %)	95 (47.5 %)
Nausea	109 (54.5 %)	91 (45.5 %)
Vomiting	83 (41.5 %)	117 (58.5 %)
Weakness	96 (48 %)	104 (52 %)

N: Number; **%:** Percentage

III. Clinical Examination (Vital Signs):

Clinical examination (vital signs) of the included patients were statistically calculated and tabulated. **Respiratory rate (12 - 18 breaths/minute):** The mean breathing of the included patients were 15.63 ± 4.03 breaths/minute, ranged between 8 breaths/minute as minimum breathing and 22 breaths/minute as maximum breathing with median 17 breaths/minute, p value < 0.0001*. **Blood Pressure (90/60 mm/Hg):** The mean blood pressure of the included patients were 96.2 ± 26.80 mm/Hg, ranged between 75/50 mm/Hg as minimum blood pressure and 150/120 mm/Hg as maximum blood pressure with median 90/50 mm/Hg, p value 0.1563. **Pulse (60 - 100 beats/minute):** The mean pulse of the included patients were 99.38 ± 22.12 beats/minute, ranged between 53 beats/minute as minimum pulse and 141 beats/minute as maximum pulse with median 97 beats/minute, p value 0.1723. **Temperature (37 ^{o}C):** The mean temperature of the included patients was 38.91 ± 1.61 ^{o} C, ranged between 35.5 ^{o} C as minimum temperature and 44.5 ^{o} C as maximum temperature with median 38.5 ^{o} C, p value < 0.0001*.

Table (3): Clinical Examination (Vital Signs).

Vital Signs	Mean±SD	Min. - Max.	Median	P value
Respiratory rate (Breaths/Minute) (12 - 18)	15.63±4.03	8 - 22	17	< 0.0001*
Blood Pressure (mm/Hg) (90/60)	96.2±26.80	75/50 - 150/120	90/50	0.1563
Pulse (Beats/Minute) (60 - 100)	99.38±22.12	53 - 141	97	0.1723
Temperature (37 °C)	38.91±1.61	35.5 - 44.5	38.5	< 0.0001*

SD: Standard deviation; **N:** Number, **%:** Percentage, ***:** highly significant, **<**0.05: statistically significant, >0.05: statistically Non-significant **IV. Electrolytes:**

Electrolytes of the included patients were statistically calculated and tabulated. **Potassium:** The mean potassium of the included patients was 4.54±1.74 mmol/L, ranged between 1.8 mmol/L as minimum potassium and 9.1 mmol/L as maximum potassium with median 4 mmol/L, p value< 0.0045. **Sodium:** The mean sodium of the included patients was 125.42±35.50 mmol/L, ranged between 54 mmol/L as minimum sodium and 261 mmol/L as maximum sodium with median 136.5 mmol/L, p value 0.229. **Calcium:** The mean calcium of the included patients weas 9.72±2.70 Mg/dL, ranged between 1.2 Mg/dL as minimum calcium and 20.2 Mg/dL as maximum calcium with median 9.2 Mg/dL, p value 0.012. **Chloride:** The mean chloride of the included patients was 95.41±18.21 mmol/L, ranged between 42 mmol/L as minimum chloride and 201 mmol/L as maximum chloride with median 98 mmol/L, p value<0.170. **Magnesium:** The mean magnesium of the included patients was 3.61 ±2.65 Mg/dL, ranged between 0.3 Mg/dL as minimum magnesium and 10 Mg/dL as maximum magnesium with median 2.1 Mg/dL, p value 0.002.

Table (4): Incidence of Electrolytes.

Electrolytes	Mean±SD	Min. - Max.	Median	P value
Potassium (3.7 - 5.1) mmol/L	4.54±1.74	1.8 - 9.1	4	< 0.0045
Sodium (136 - 144) mmol/L	125.42±35.50	54 - 261	136.5	0.229
Calcium (8.5 - 10.2) Mg/dL	9.72±2.70	1.2 - 20.2	9.2	<0.012
Chloride (96 - 106) Mmol/L	95.41±18.21	42 - 201	98	0.170
Magnesium (1.7 - 2.2) Mg/dL	3.61 ±2.65	0.3 - 10	2.1	<0.002

SD: Standard deviation, **N:** Number, **%:** Percentage, ***:** highly significance, **<0.05:** statistically significant, **>0.05:**
statistically non-significant

V. Hypo and Hyper Electrolytes:

Potassium:

The mean hypokalemia of the included patients was 2.81±0.60 were hypokalemia, ranged between "1.8 - 3.6" with median 2.8, p value 0.012. The mean normal range of potassium levels in included patients were 4.20±0.42, ranged between "3.7 - 5.1" with median 4, p value 0.020. The mean hyperkalemia of the included patients was 7.13±1.21 were hyperkalemia, ranged between "5.2 - 9.1" with median 6.5, p value 0.035. The percentage of potassium included in this study; (60/200patients), representing 30 % of all patients were hypokalemia, (82/200 patients), which represents 41 % of all patients were in the normal range and (58/200 patients), which represents 29 % of all patients were hyperkalemia.

Sodium: The mean hyponatremia of the included patients was 93.93±17.85 were hyponatremia, ranged between "54 – 135" with median 92, p value 0.525. The mean normal range of sodium levels in included patients were 139.74±2.51, ranged between "136 – 144" with median 140, p value 0.952. The mean hypernatremia of the included patients was 7.13±1.21 were hypernatremia, ranged between "145 – 261" with median 160, p value 0.050. The percentage of sodium included in this study; (91/200 patients), which representing 45.5 % of all patients were hyponatremia, (66/200 patients), which represents 33 %of all patients were in the normal range and (43/200 patients), which represents 21.5 % of all patients were hypernatremia.

Calcium: The mean hyponatremia of the included patients was 6.35±2.13 were hypocalcemia, ranged between "1.2 - 8.4" with median 6.8, p value 0.071. The mean normal range of calcium levels in included patients were 9.18±0.46, ranged between 8.5 - 10.2 with median 9.1, p value 0.020. The mean hypercalcemia of the included patients was 13.8±3.21 were hypercalcemia, ranged between 10.3 - 20.1 with median 12.7, p value 0.113. The percentage of calcium included in this study; (23/200 patients), which representing 11.5 % of all patients were hypocalcemia, (139/200 patients) which represents 69.5 % of all patients were in the normal range and (38/200 patients), which represents 19% of all patients were hypercalcemia

Chloride: The mean hypochloremia of the included patients was 78.20±11.19 were hypochloremia, ranged between "42 – 94" with median 79, p value 0.600. The mean normal range of chloride levels in included patients were 100.44±2.54, ranged between 96 - 10.6 with median 101, p value 0.450. The mean hypercalcemia of the included patients was 120.5±28.61 were hyperchloremia, ranged between 108 - 201 with median 110, p value 0.521. The percentage of chloride included in this study; (69/200 patients), which representing 34.5 % of all patients in hypochloremia, (109/200 patients), which represents 54.5 % of all patients in normal range and (22/200 patients), which represents 11 % of all patients were hyperchloremia.

Magnesium: The mean hypomagnesia of the included patients were 0.93±0.33 were hypomagnesia, ranged between 0.3 - 1.6 with median 0.9, p value 0.0006. The mean normal range of magnesium levels in included patients were 1.97±0.15, ranged between "1.7 - 2.2" with median 2, p value 0.0007. The mean hypermagnesia of the included patients were 5.79±2.36 were hypermagnesia, ranged between "2.3 – 10" with median 5.9, p value 0.0001. The percentage of magnesium included in this study; (30/200 patients), which represents 15 % of all patients were hypomagnesia, (81/200 patients), which represents 40.5 % of all patients were in normal range and 89 (44.5 %) patients were hypermagnesia.

Table (5): Hypo and Hyper Electrolytes

Electrolytes	Percentage (N = %)	Mean±SD	Min. - Max.	Median	P value
Potassium					
Hypokalemia	60 (30 %)	2.81±0.60	1.8 - 3.6	2.8	< 0.012
Normal	82 (41 %)	4.20±0.42	3.7 - 5.1	4	< 0.020
Hyperkalemia	58 (29 %)	7.13±1.21	5.2 - 9.1	6.5	< 0.035
Sodium					
Hyponatremia	91 (45.5 %)	93.93±17.85	54 - 135	92	> 0.525
Normal	66 (33 %)	139.74±2.51	136 - 144	140	> 0.952
Hypernatremia	43 (21.5 %)	7.13±1.21	145 - 261	160	< 0.484
Calcium					
Hypocalcemia	23 (11.5 %)	6.35±2.13	1.2 - 8.4	6.8	> 0.071
Normal	139(69.5 %)	9.18±0.46	8.5 - 10.2	9.1	< 0.020
Hypercalcemia	38 (19 %)	13.8±3.21	10.3 - 20.1	12.7	> 0.113
Chloride					
Hypochloremia	69 (34.5 %)	78.20±11.19	42 - 94	79	> 0.600
Normal	109(54.5 %)	100.44±2.54	96 - 106	101	> 0.450
Hyperchlormia	22 (11 %)	120.5±28.61	108 - 201	110	> 0.521
Magnesium					
Hypomagnesaemia	30 (15 %)	0.93±0.33	0.3 - 1.6	0.9	< 0.0006
Normal	81 (40.5 %)	1.97±0.15	1.7 - 2.2	2	< 0.0007
Hypermagnesmia	89 (44.5 %)	5.79±2.36	2.3 - 10	5.9	<0.0001

SD: Standard deviation, **N:** Number, **%:** Percentage, ***:** highly significance, **<0.05:** statistically significant, **>0.05:** statistically non-significant

VI. High-Resolution Computed Tomography (HRCT):

All the HRCT of the included patient were calculated. **Acute pulmonary edema (acute GGO):** The percentage of Acute pulmonary edema (acute GGO) included in this study was (28/200 patients), which represents 14 % of the total patients. **Alveolar Proteinosis (Chronic GGO):** The percentage of Alveolar Proteinosis (Chronic GGO) included in this study was (20/200 patients), which represents 10 % of the total patients. **Chronic Bronchoalveolar (GGO):** The percentage of Chronic Bronchoalveolar (GGO) included in this study was (19/200 patients), which represents 9.5 % of the total patients. **Chronic Eosinophilic Pneumonia (GGO):** The percentage of Chronic Eosinophil Pneumonia (GGO) included in this study was (21/200 patients), which represents 10.5 % of the total patients. **Chronic Pneumonia:** The percentage of Chronic Pneumonia included in this study was (16/200 patients), which represents 8 % of the total patients. **Chronic Bronchoalveolar (GGO):** The percentage of Chronic Bronchoalveolar (GGO) included in this study was (56/200 patients), which represents 28 % of the total patients. **Normal:** The percentage of normal included in this study was (40/200 patients), which represents 20 % of the total patients.

Table (6): HRCT of COVID-19 patients.

High Resolution Computerized Tomograph	
CT examination comment	**Finding: Percentage (N = %)**
Acute pulmonary edema (Acute GGO)	28 (14 %)
Alveolar Proteinosis (Chronic GGO)	20 (10 %)
Chronic Bronchoalveolar (GGO)	19 (9.5 %)
Chronic Eosinophilic Pneumonia (GGO)	21 (10.5 %)
Chronic Pneumonia	16 (8 %)
Chronic Bronchoalveolar (GGO)	56 (28 %)
Normal	40 (20 %)

N: Number, **%:** Percentage, **GGO:** ground glass opacity.

VII. Laboratory Investigations:

Laboratory investigations of the included patients were statistically calculated and tabulated.

Complete Blood Picture:

Leukocytes: The mean leukocytes of the included patients were 11.60 ± 7.59 × 109/L, ranged between 2.4 - 50.2 × 109/L with median 9.6 × 109/L, p value < 0.0007. **Hemoglobin:** The mean hemoglobin of the included patients was 10.09 ± 1.93 gm/dL, ranged between 6.2 - 14.9 gm/dL with median 10 gm/dL, p value < 0.0134. **Platelets:** The mean platelets count of the included patients were 190.31 ± 106.84 ul/L, ranged between 17 - 490 ul/L with median 170 ul/L, p value > 0.434.

Kidney Function:

Urea: The mean urea of the included patients was 159.28±81.57 mg/dL, ranged between 40 - 424 mg/dL with median 145 mg/dL, p value > 0.2892. **Creatinine:** The mean creatinine of the included patients was 4.83 ± 2.80 mg/dL, ranged between 1.2 - 3.5 gm/dL with median 4.5 gm/dL, p value < 0.0003*.

Liver Function:

SGPT: The mean SGPT of the included patients were 60.08± 130.64 unit/L, ranged between 0.5 - 700 unit/L with median 16 unit/L, p value > 0.207. **SGOT:** The mean SGOT of the included patients were 28.04± 36.64 unit/L, ranged between 0.9 - 432 unit/L with median 21 unit/L, p value < 0.0163. **Total Bilirubin:** The mean total bilirubin of the included patients was 3.93 ± 1.97 umol/L, ranged between 0.1 - 10.1 umol/ L with median 4.1 umol/L, p value < 0.0003*. **Direct Bilirubin:** The mean direct bilirubin of the included patients was 6.37 ± 5.28 umol/L, ranged between 0.1 - 40.1 umol/ L with median 4.7 umol/L, p value < 0.0001*.

Table (7): Laboratory Investigation of our COVID-19 patients.

Laboratory Investigation	Mean±SD	Min. - Max.	Median	P value
Complete Blood Picture				
Leukocytes (4.5 to 11.0 × 109/L)	11.60±7.59	2.4 - 50.2	9.6	< 0.0007*
Hemoglobin (11.6 to 16.6 gm/dL)	10.09±1.93	6.2 - 14.9	10	< 0.0134
Platelets 150, 000 to 450, 000 ul/L	190.31±106.84	17 – 490	170	> 0.434
Kidney Function				
Urea (6 to 24 mg/dL)	159.28±81.57	40 – 424	145	> 0.2892
Creatinine (0.59 to 1.35 mg/dL)	4.83±2.80	1.2 - 13.5	4.5	< 0.0003*
Liver Function				
SGPT (7 to 56 unit/L)	60.08±130.64	0.5 - 700	16	> 0.207
SGOT (8 to 45 unit/L)	28.04±36.64	0.9 - 432	21	< 0.0163
Total Bilirubin (1.71 to 20.5 umol/L)	3.93±1.97	0.1 - 10.1	4.1	< 0.0003*
Direct Bilirubin (< 5 umol/L)	6.37±5.28	0.1 - 40.1	4.7	< 0.0001*

SD: Standard deviation, **N:** Number, **%:** Percentage, ***:** highly significant,
<0.05: statistically significant**, >0.05:** statistically non-significant

DISCUSSION

COVID–19 has affected millions of people worldwide. Many chronic medical diseases were reported as risk factors for increased mortality and severity of COVID–19, such as diabetes, hypertension, chronic obstructive pulmonary disease, malignancies, and CKD. [11]

According to ***World Health Organization (WHO)*** [12], In Egypt, from 3 January 2020 to 9: 26 pm CET, 17 January 2023, there had been 515, 580 confirmed cases of COVID-19 with 24, 805 deaths, reported to WHO. As of 2 January 2023, 101, 068, 826 vaccine doses had been administered.

Electrolytes are essential for basic life functioning, such as maintaining electrical neutrality in cells, generating and conducting action potentials in the nerves and muscles. Sodium, potassium, calcium, chloride, phosphate and magnesium are the significant electrolytes, which their imbalance in the form of either high or low levels leading to disturbance in normal bodily functions and can lead to even life-threatening complications. [13]

Recent studies have reported high prevalence of electrolyte imbalances in COVID-19 patients and associated these imbalances with more severe infection. Previous study reported that dysnatremia was associated with a higher risk for mechanical ventilation and mortality. [14]

Several hypotheses exist that explain this prevalence, such as the involvement of cell entry receptor angiotensin-converting enzyme 2 (ACE2), a key enzyme in the renin-angiotensin system (RAAS). As serum electrolytes tests are readily available in laboratories, they are useful as prognostic markers in COVID-19 to help risk stratify patients. [15]

While previous meta-analyses have reported associations of hypocalcemia and hyponatremia with COVID-19 severity, recent published studies have also suggested associations of other electrolyte imbalances such as dysnatremia, dyskalemia, dysmagnesemia and dyschloremia with COVID-19 severity. [11]

Therefore, our study was aim for the determination of electrolytes imbalance among confirmed COVID-19 patients with PCR in isolation department at Aswan University Hospital.

In this cross-sectional study, 200 adult patients with proved COVID-19 admitted in isolation department at Aswan University Hospital, which is a selected hospital for the treatment of COVID19 patients by the government, from October 2021 till April 2022. Among these patients, 200 COVID-19 adults with CKD were homogenized with regard to age, gender, and underlying electrolytes. All COVID-19 patients were confirmed by the reverse transcription-polymerase chain reaction for SARS- CoV2 RNA with nasopharyngeal specimens. The present work was conducted under the approval of the Ethics Committee of the Aswan University Hospital. Based on the cross-sectional design of this study, written informed consent forms were obtained from all patients.

In our study, 52% of our patients (104/200 patients) were males and 48% (96/200 patients) were females.

Their ages ranged between 18 years old as minimum age and 78 years old as maximum age with median as 46 years old.

More than one third of the patients (35.5%) (71/200 patients) were smokers and 64.5% of our patients were non-smokers (129/200 patients).

According to previous systematic review; *Cpere* [11] Reported in a study included 500 COVID-19 patients which confirmed with PCR assay, the age was ranged between 20 to 85 years old, the percentage of male were higher than that of females, in addition to smoking habit among male were higher than that of female. Therefore, there study observed that no correlation between smokers and non-smokers, however number of males were higher In line with our findings.

In addition to previous cross-sectional study, *Wang et al.* [13] observed that included the age of COVID-19 patients were varied between 15 to 85 patients.

Although another study Nehme et al. [14] observed that the age of their included patients were 19 to 75 patients.

Moreover, Wang et al. [13] in a study included 1000 COVID-19 patients the age was varied between 20 to 85 patients, number of smokers males were higher than non-smokers males although non-smokers females were higher than smokers females.

In our study, 51.5% of our patients had abdominal pain which included (103/200 patients), 51% of our patients had ageusia(loss of taste) which included (102/200 patients), 39.5% of our patients had cough which included (79/200 patients), 47.5% of our patients had diarrhea which included (95/200 patients), 54.5% of our patients had dyspnea which included (109/200 patients) 52.5% of our patients had fever which included (105/200 patients), 54.5% of our patients had nausea which included (109/200 patients), 41.5% of our patients had vomiting which included (83/200 patients) and 48% of our patients had weakness which included (96/200 patients)

In addition to, previous study done by ***Chen et al.*** [4] reported that the impact of other symptoms at admission on COVID–19 was common and varied among patients mainly included diarrhea, vomiting and fever in addition to cough.

However, ***Alfano et al.*** [2] showed that symptoms of COVID-19 with CKD were associated with increased fever, cough, vomiting and weakness.

As per a previous study by ***Machiraju et al.*** [15]**;** demonstrated that symptoms at admission represent were varied among patients, however all the patients were suffering fever, weakness and nausea. There were significant differences regarding symptoms. In line with our results there was significant differences were observed regarding symptoms.

In our study, the mean respiratory rate and temperature of the included patients was highly statistically significant difference. The mean blood pressure and pulse of the included patients was statistically non-significant difference.

In addition to, previous study by ***Liu et al.*** [16] observed that blood pressure, heart rate was decreased after the admission period at hospital, temperature was increased after the admission period at the hospital. However, random blood sugar and blood oxygen level were non-significant. In line with our findings.

According to recent study for COVID-19, patients with COVID-19 have a greater impact on clinical data outcomes. However, patients with COVID-19 and low clinical variations improved and completely resolved after hospitalized period. [17] In comparison with our results.

In our study, the mean complete blood count included, leukocytes of the included patients were highly statistically significant difference. The mean hemoglobin of the included patients was statistically significant difference. The mean platelets count of the included patients was statistically non - significant difference.

In our study, Kidney functions including, the mean urea of the included patients were statistically non-significant difference. The mean creatinine of the included patients was highly statistically significant difference.

In our study, Liver function including, the mean SGPT of the included patients were statistically non-significant difference. The mean SGOT of the included patients were statistically significant difference. The mean total and direct bilirubin of the included patients were highly statistically significant difference.

In our study, the percentage of Acute pulmonary edema (acute GGO) was included (28/200 patients), which represents 14 % of the total patients. The percentage of Alveolar Proteinosis (Chronic GGO) was included (20/200 patients), which represents 10 % of the total patients. The percentage of Chronic Bronchoalveolar (GGO**)** was included (19/200 patients), which represents 9.5 % of the total patients. The percentage of Chronic Eosinophil Pneumonia (GGO) was included (21/200 patients), which represents 10.5 % of the total patients. The percentage of Chronic Pneumonia was included (16/200 patients), which represents 8 % of the total patients. The percentage of Chronic Bronchoalveolar (GGO**)** was included (56/200 patients), which represents 28 % of the total patients. In addition, the percentage of normal was included (40/200 patients), which represents 20 % of the total patients.

According to previous study by ***Sharma et al.*** [18]**;** in all admitted patients indicated higher rate in bilateral, right lung only in addition, left lung only GGO in the first day of admission however it decreases at the last day of admission. In line with our findings.

In addition, another study by ***Krolicka et al.*** [19] observed that chest radiographic findings showed pulmonary involvement, bilateral patches and pneumonic patches, with no significant differences among patients.

In our study, the mean potassium, calcium and magnesium of the included patients were was statistically significant difference. The mean sodium and chloride of the included patients was statistically non-significant difference.

In our study, the mean hypokalemia, normal range and hyperkalemia of the included patients were statistically significant difference. The percentage of potassium included in this study; (60/200 patients), which represents 30 % of all patients were hypokalemia, (82/200patients), which represents 41% of all patient were in the normal range and (58/200 patients), which represents 29 % of all patients were hyperkalemia.

In our study, the mean hyponatremia and normal range of the included patients was statistically non-significant difference, while, the mean hypernatremia of the included patients was statistically significant difference. The percentage of sodium included in this study; (91/200 patients), which representing 45.5 % of all patients were hyponatremia, (66/200 patients), which represents 33 % of all patients were in the normal range and (43/200 patients), which represents 21.5 % of all patients were hypernatremia.

In our study, the mean hypocalcemia and normal range of the included patients was statistically significant difference, while, the mean hypercalcemia of the included patients was statistically non-significant difference. The percentage of calcium included in this study; (23/200 patients), which representing 11.5 % of all patients were hypocalcemia, (139/200 patients) which represents 69.5 % of all patients were in the normal range and (38/200 patients), which represents 19% of all patients were hypercalcemia

In our study, the mean hypochloremia, normal range and hyperchloremia of the included patients were statistically non- significant difference. The percentage of chloride included in this study; (69/200 patients), which representing 34.5 % of all patients in hypochloremia, (109/200 patients), which represents 54.5 % of all patients in normal range and (22/200 patients), which represents 11 % of all patients were hyperchloremia.

In our study, the mean hypomagnesia, normal range and hypermagnesemia of the included patients were highly statistically significant difference. The percentage of magnesium included in this study; (30/200 patients), which represents 15 % of all patients were hypomagnesia, (81/200 patients), which represents 40.5 % of all patients were in normal range and 89 (44.5 %) patients were hypermagnesia.

As per previous study, *Martha et al.* [20] showed low rates of hyponatremia in patients with severe COVID-19. Sodium plays an important role in ACE2 expression and electrolyte imbalance in COVID-19. In addition, the level of sodium decreases in the more severe disease.

As mentioned previously, *di Filippo et al.* [21] reported that the underlying mechanism for the hyponatremia in COVID-19 is supposed to be related to low intake due to anorexia, excretion of sodium from skin through sweating, loss of sodium from the gastrointestinal system due to vomiting or diarrhea, increased excretion of sodium from kidney due to the use of diuretic drugs or decreased excretion of water from kidney due to the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). This syndrome occurs because of increased release of inflammatory cytokines.

As per previous study *Raesi et al.* [22]**,** mentioned that, Hypokalemia in the setting of COVID19 can increase the risk of ARDS, arrhythmia, and acute heart injury. Hypokalemia in the setting of SARS-CoV2 infection may result from over activation of the renin–angiotensin–aldosterone system (RAAS), low intake, and gastrointestinal or kidney loss.

According to previous hypothesis *Tan et al.* [23]**,** proved that tubular damage may be related to the direct cytotoxic effect of SARS-CoV-2, as the virus is associated with diffuse tubular damage.

There is high heterogeneity in different studies in terms of the prevalence and severity of the potassium disturbances. Therefore, the role of potassium disturbances in the COVID-19 and its complication is unclear, so further studies are needed.

According to previous study of *Radujkovic et al.* [24]**,** the low serum level of Magnesium and sodium has been shown in patients who are admitted to ICU in a study from Iran.

Furthermore; *DiNicolantonio and O'Keefe* [25], Special attention has been paid to Magnesium in COVID-19, as there seems to be a bi-directional relationship between hypomagnesaemia and COVID-19 prognosis; COVID-19 impairs Magnesium homeostasis and Magnesium deficiency increases the sensitivity of endothelial cells to oxidative stress and the resulting Endothelial dysfunction causes decreased fibrinolysis, which increases the risk of coagulation.

In a previous study *Trapani et al.* [26], mentioned that Hypocalcemia occurs in patients with COVID-19 by several mechanisms, such as anorexia and malnutrition during acute illness, change in blood levels of unsaturated fatty acids due to the inflammatory process, hypomagnesemia, and vitamin D deficiency.

Among previous studies, *Sarvazad et al.* [8], on COVID- 19 patients due to viral infections researchers have been able to find RNA virus and antigenic substances in parathyroid cells. The ACE 2 receptor has also been detected in these cells. In the acute critically ill patients with COVID-19, as in other acute systemic diseases, parathyroid function decreases with increasing inflammatory response and cytokine levels, and hypocalcemia intensifies.

According to previous study, *Guerrero-Romero et al.* [27], on COVID-19, confirm electrolyte disturbances in patients, including sodium, potassium, chlorine, and calcium imbalances. One of the most common electrolyte disorders is hyponatremia during and after infection with COVID-19, which occurs with a heightened risk of mortality in hospitalized patients.

In a previous case-control study, *Cooper et al.* [28], showed that hyponatremia, hypokalemia, and hypochloremia, which are electrolyte disturbances, were more common in COVID-19 patients than in controls.

Although previous study, *Noori et al.* [29], mentioned that Hypokalemia, a complication of COVID-19, can exacerbate acute respiratory distress syndrome (ARDS) and increase the risk of heart injuries in patients.

Moreover, *Trecarichi et al. 30,* determined that Hypernatremia is very common in patients with acute COVID-19. Patients with hypernatremia have been in intensive care for a more extended period and have a higher risk of death. Hypocalcemia is also one of the electrolyte disorders in patients with COVID-19, which can be dangerous if not controlled and can even increase the mortality rate.

CONCLUSION

Electrolyte disturbances are complications in COVID-19 patients. Because electrolyte disturbances can lead to many problems and even death, clinicians should have special supervision over fluid and electrolyte balance in COVID-19 patients, especially in patients under intensive care because the risk of fluid and electrolyte disturbance is higher in them and it can raise mortality rate.

Hyponatremia, hypernatremia, hypokalemia, hypocalcemia, hypochloremia are the most common electrolyte disorders in SARS-CoV-2 infection that should be given special attention. If these disorders are observed, definitive and immediate treatment should be started. Since electrolyte disturbances can be seen in COVID-19, electrolyte concentrations can be used to measure disease status and disease progression.

Conflict of interest statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

REFERENCES

1. **Gibson, C. M., Mehran, R., Bode, C., Halperin, J., Verheugt, F. W., Wildgoose, P., & Fox, K. A. (2016).** Prevention of bleeding in patients with atrial fibrillation undergoing PCI. *New England Journal of Medicine*, *375*(25), 2423-2434.
2. **Alfano, G., Ferrari, A., Fontana, F., Perrone, R., Mori, G., Ascione, E., & Guaraldi, G. (2021).** Hypokalemia in patients with COVID-19. *Clinical and experimental nephrology*, *25*, 401-409.
3. **Holly, M., & Sayer, J. A. (2020).** Electrolyte Disturbances in SARS-CoV-2 Infection. *F1000Research*, *9*.
4. **Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F., Han, Y., & Zhang, L. (2020).** Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The lancet*, *395*(10223), 507-513.
5. **Wu, C., Chen, X., Cai, Y., Zhou, X., Xu, S., Huang, H., & Song, Y. (2020).** Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA internal medicine*, *180*(7), 934-943.
6. **Lau, K. K., Yu, W. C., Chu, C. M., Lau, S. T., Sheng, B., & Yuen, K. Y. (2004).** Possible central nervous system infection by SARS coronavirus. *Emerging infectious diseases*, *10*(2), 342.
7. **Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., & Cao, B. (2020).** Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The lancet*, *395*(10223), 497506.
8. **Sarvazad, H., Cahngaripour, S. H., Roozbahani, N. E., & Izadi, B. (2020).** 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 and new infections*, *38*, 100807.
9. **Lippi, G., South, A. M., & Henry, B. M. (2020).** Electrolyte imbalances in patients with severe coronavirus disease 2019 (COVID-19). *Annals of clinical biochemistry*, *57*(3), 262-265.
10. **Wan, S., Xiang, Y. I., Fang, W., Zheng, Y., Li, B., Hu, Y., & Yang, R. (2020).** Clinical features and treatment of COVID-19 patients in northeast Chongqing. *Journal of medical virology*, *92*(7), 797-806.
11. **Team, E. (2020).** The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020. *China CDC weekly*, *2*(8), 113.
12. **World Health Organization (WHO) (2022).** WHO COVID-19 Dashboard, *Available on https://covid19.who.int/ lasr assessed on August 2022.*
13. **Wang, W., Xu, Y., Gao, R., Lu, R., Han, K., Wu, G., & Tan, W. (2020).** Detection of SARSCoV-2 in different types of clinical specimens. *Jama*, *323*(18), 1843-1844.
14. **Nehme, A., Zouein, F. A., Deris Zayeri, Z., & Zibara, K. (2019).** An update on the tissue renin angiotensin system and its role in physiology and pathology. *Journal of cardiovascular development and disease*, *6*(2), 14.
15. **Machiraju, P. K., Alex, N. M., Safinaaz, & Vadamalai, V. (2021).** Hyponatremia in coronavirus disease-19 patients: a retrospective analysis. *Canadian Journal of Kidney Health and Disease*, *8*, 20543581211067069.

16. **Liu, J., Han, P., Wu, J., Gong, J., & Tian, D. (2020).** Prevalence and predictive value of hypocalcemia in severe COVID-19 patients. *Journal of infection and public health*, *13*(9), 1224-1228.

17. **Alemzadeh, E., Alemzadeh, E., Ziaee, M., Abedi, A., & Salehiniya, H. (2021).** The effect of low serum calcium level on the severity and mortality of Covid patients: A systematic review and meta-analysis. *Immunity, inflammation and disease*, *9*(4), 1219-1228.

18. **Sharma, R., Heidari, A., Johnson, R. H., Advani, S., & Petersen, G. (2022).** Serum magnesium levels in hospitalized patients with SARS-CoV-2. *Journal of Investigative Medicine*, *70*(2), 409-414.

19. **Królicka, A. L., Kruczkowska, A., Krajewska, M., & Kusztal, M. A. (2020).** Hyponatremia in infectious diseases—A literature review. *International Journal of Environmental Research and Public Health*, *17*(15), 5320.

20. **Martha, J. W., Wibowo, A., & Pranata, R. (2021).** Hypocalcemia is associated with severe COVID-19: A systematic review and meta-analysis. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, *15*(1), 337-342.

21. **di Filippo, L., Allora, A., Locatelli, M., Rovere Querini, P., Frara, S., Banfi, G., & Giustina, A. (2021).** Hypocalcemia in COVID-19 is associated with low vitamin D levels and impaired compensatory PTH response. *Endocrine*, *74*, 219-225.

22. **Raesi, A., Dezaki, E. S., Moosapour, H., Saeidifard, F., Habibi, Z., Rahmani, F., & Taheri, E. (2021).** Hypocalcemia in Covid-19: a prognostic marker for severe disease. *Iranian Journal of Pathology*, *16*(2), 144.

23. **Tan, C. W., Ho, L. P., Kalimuddin, S., Cherng, B. P. Z., Teh, Y. E., Thien, S. Y., & Ng, H. J. (2020).** A cohort study to evaluate the effect of combination Vitamin D, Magnesium and Vitamin B12 (DMB) on progression to severe outcome in older COVID-19 patients. *MedRxiv*, 2020-06.

24. **Radujkovic, A., Hippchen, T., Tiwari-Heckler, S., Dreher, S., Boxberger, M., & Merle, U. (2020).** Vitamin D deficiency and outcome of COVID-19 patients. *Nutrients*, *12*(9), 2757.

25. **DiNicolantonio, J. J., & O'Keefe, J. H. (2021).** Magnesium and vitamin D deficiency as a potential cause of immune dysfunction, cytokine storm and disseminated intravascular coagulation in COVID-19 patients. *Missouri medicine*, *118*(1), 68.

26. **Trapani, V., Rosanoff, A., Baniasadi, S., Barbagallo, M., Castiglioni, S., Guerrero-Romero, F., & Maier, J. A. (2022).** The relevance of magnesium homeostasis in COVID-19. *European journal of nutrition*, 1-12.

27. **Guerrero-Romero, F., Mercado, M., Rodriguez-Moran, M., Ramírez-Renteria, C., Martínez-Aguilar, G., Marrero-Rodríguez, D., & Sanchez-García, M. L. (2022).** Magnesium-to-calcium ratio and mortality from COVID-19. *Nutrients*, *14*(9), 1686.

28. **Cooper, I. D., Crofts, C. A., DiNicolantonio, J. J., Malhotra, A., Elliott, B., Kyriakidou, Y., & Brookler, K. H. (2020).** Relationships between hyperinsulinaemia, magnesium, vitamin D, thrombosis and COVID-19: rationale for clinical management. *Open Heart*, *7*(2), e001356.

29. **Noori, M., Nejadghaderi, S. A., Sullman, M. J., Carson-Chahhoud, K., Kolahi, A. A., & Safiri, S. (2022).** Epidemiology, prognosis and management of potassium disorders in Covid19. *Reviews in medical virology*, *32*(1), e2262.

30. **Trecarichi, E. M., Mazzitelli, M., Serapide, F., Pelle, M. C., Tassone, B., & Arrighi, E. (2020).** Clinical characteristics and predictors of mortality associated with COVID-19 in elderly patients from a long-term care facility. *Scientific reports*, *10*(1), 20834.