Sudan University of Science and Technology
College of Graduate Studies

Assessment of Serum Sodium and Potassium Levels among Patients with COVID-19 in Khartoum State

تقيم مستويات الصوديوم والبوتاسيوم في مصل الدم لدى المرضي بفيروس كوفيد ١٩ في ولاية الخرطوم

A dissertation submitted in partial fulfilment for the requirement of M.Sc. degree in Medical Laboratory Sciences- Clinical Chemistry

By

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الآية:

قال الله تعالي: (**هُوَ الَّذِي بَعَثَ فِي الْأُمِّيِّينَ رَسُولًا مِّنْهُمْ يَتْلُو عَلَيْهِمْ آيَاتِهِ وَيُزَكِّيهِمْ وَيُعَلِّمُهُمُ الْكِتَابَ وَالْحِكْمَةَ وَإِن كَانُوا مِن قَبْلُ لَفِي ضَلَالٍ مُّبِينٍ**)

Dedication

The sake of Allah, my Creator and my Master, My great teacher and messenger, Mohammed (May Allah bless and grant him), who taught us the purpose of life.

Thank you to my academic adviser who guided me in this process and the committee who kept me on track.

I dedicate my dissertation work to my family and many friends. A special feeling of gratitude to my loving parents, whose words of encouragement and push for tenacity ring in my ears, My beloved brothers and sisters

My friends who encourage and support me,

All the people in my life who touch my heart, I dedicate this research

Acknowledgments

I am most grateful to Allah for the breath of life and blessings, I want to also express my sincere gratitude to my supervisor Dr.Nuha for her guidance, encouragement, and provided information to make this project.

The project would like to acknowledge the contribution and effort of all individuals, I want to use this opportunity to say a special thanks to the management of Jabra Isolation center. I extend appreciation to our students, colleagues and mentors in the profession who have helped shape our ideas about electrolyte disturbance among covid-19. Also, I want to thank the many individuals.

I again request and welcome our readers for improvement, Finally I give due respect and credit to all the authors whose articles and book provided information for my project work.

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Abbreviations

WHO World Health Organization

GIT: Gastro Intestinal Tract

SARS: Sever Acute Respiratory Syndrome

ACE: Angiotensin Converting Enzyme

TMPRSS: Transmembrane Protease Serine

RNA: Ribonucleic Acid

SSRNA: single strand Ribonucleic Acid

ARDS: Acute Respiratory Distress Syndrome

CT: Computed Tomography

ELISA: Enzyme-Linked Immunosorbent Assay

NAAT: Nucleic Acid Amplification Test

CDC: Center of Disease Control

RT-PCR: real time polymerase chain reaction

PPE: personal protective equipment

ENaC: Epithelial Sodium Channel

RAS: Renin–Angiotensin– System

RAAS: Renin–Angiotensin–Aldosterone System

ECF: Extracellular Fluid

CNS: Central Nervous System

RMP: Resting Membrane Potential

ISE: Ion Selective Electrode

Abstract

Background: Corona virus (Covid-19) affected more than 500 million confirmed cases and over six million deaths which have been reported globally by WHO statistical report on May 2021. Electrolyte disorders particularly potassium and sodium abnormalities have been repeatedly reported as common clinical manifestations of COVID-19.

Aim: This study aimed to assess plasma sodium and potassium among Sudanese patients with covid-19 in Khartoum state**.**

Method: A quantitative method was used to measure the levels of serum potassium and sodium in covid-19 Sudanese male and female patients during the period from March to August 2022. This is case control study was conducted in Jabra isolation Canter for Covid-19. The study included 50 patients with Covid-19 and 50 healthy people as control.

Plasma sodium and potassium were estimated using EasyLyte analyzer is a completely automated. The data was analysed by SPSS**.**

Results: result of this study showed there was significant decrease in sodium (131.7 ±7.203 **versus** 139.1 ±2.911 IU/L, P- value =0.00), while there was significant increase in potassium (3.7 ±0.657 **versus** 3.4 ±0.078 IU/L, P- value =0.00) respectively.

Also this study showed the comparison between the mean and standard deviation of sodium and potassium in case group according to its health situation. The result showed there were significant increase in mean of potassium among CCU patients compared to floor patients (p- value =0.03) and no significant difference in the mean of sodium (p-value =0.15). There was no correlation between sodium and potassium levels in case group (r=-0.08, p= 0.54). Also there were no correlation between sodium, potassium levels and age of patients **(**r= -0.17, p= 0.23) (r= -0.14, p= 0.31) respectively.

Conclusions: According to result of this study it is concluded that sodium is decreased and potassium is increased in Covid-19 patients compared with healthy patients, according to health situation there were no difference in mean concentration of sodium among Floor, CCU and ICU. But there was significant increase in mean concentration of potassium among CCU patients compare with Floor patients.

There was no correlation between sodium. Potassium level and age.

المستخلص

خلفية: أثر فيروس كورونا (كوفيد-١٩) على أكثر من ٥٠٠ مليون حالة مؤكدة وأكثر من ستة ملايين حالة وفاة تم الإبلاغ عنها عالميًا بواسطة التقرير الإحصائي لمنظمة الصحة العالمية في مايو ٢٠٢١. وقد تم الإبلاغ مرارًا وتكرارًا عن اضطرابات البوتاسيوم والصوديوم باعتبارها مظاهر سريرية شائعة لدي مرضي كوفيد-١٩.

الهدف: هدفت هذه الدراسة إلى تقييم بلازما الصوديوم والبوتاسيوم بين مرضى كوفيد-١٩ السودانيين في ولاية الخرطوم.

الطريقة: تم استخدام الطريقة الكمية لقياس مستوى البوتاسيوم والصوديوم في الدم في مرضى كوفيد-١٩ السودانيين الذكور والإناث خلال الفترة من مارس إلى أغسطس ٢٠٢٢. هذه دراسة حالة مراقبة. أجريت في مركز عزل جبرة للعزل، وشملت الدراسة مرضى الكوفيد-١٩ وأصحاء كمجموعة تحكم، وشملت ٥٠ مريضًا مصابًا بـ كوفيد-١٩ كحالة و٥٠ فردًا سليمًا كمجموعة تحكم تم تقدير الصوديوم والبوتاسيوم في البلازما باستخدام محلل EasyLyte، (تم التعبير عن التركيز من حيث ملي مول / لتر أو ملي مكافئ / لتر.) تم تحليل البيانات بواسطة برنامج التحليل الاحصائي SPSS.

النتائج: أظهرت نتيجة هذه الدراسة وجود انخفاض معنوي في الصوديوم (١٣١,٧ ± ٧,٢٠٣ مقابل ١٣٩,١ ± ٢,٩١١ وحدة دولية / لتر، القيمة =٠,٠)، بينما كانت هناك زيادة معنوية في البوتاسيوم (٣,٧١٨ ± ٠,٦٥٧ مقابل ٣,٤,١٤ ± ٠,٠٧٨ وحدة دولية / القيمة =٠,٠) على التوالي ٠

واظهرت هذه النتيجة وجود ارتباط سلبي بين الصوديوم والبوتاسيوم مع العمر

(r= ٠,٠٥٦ p. value=٠,٧٠٠) ، (r=٠,٠٥٤ p. value = ٠,٧٠٨)

الاستنتاجات: وفقًا لنتائج هذه الدراسة، استنتج أن مستوي الصوديوم ينخفض ويزداد مستوي البوتاسيوم لدي مرضي كوفيد-١٩.

Chapter One

Introduction – Rational – Objective

1.1 Introduction

Covid-19 is infectious disease caused by corona virus affected millions of lives worldwide, affected more than 500 million confirmed cases and over six million deaths which have been reported globally by WHO weekly statistical report. (Ertuglu *et al.*, 2020; WHO., 2022).

A serious medical condition increase incidence of death, social community, secological increase incidence of chronic depression, and economic effect of the life quality this problem found all over the world and Sudan, its fatal unless controlled and treated properly (Mohammad *et al.,* 2020).

Coronaviruses (CoVs) are a positive-sense single-stranded RNA viruses that cause diseases in humans and animals. The human coronaviruses (HCoVs) were first identified as causes of acute upper respiratory infection (URI) in 1962. Over the past few years, HCoVs have more often been found to be associated with severe upper and lower respiratory tract infection. They have been identified as a main cause of pneumonia in older adults and immunocompromised patient. (Khaled *et al*.,2020).

Impaired renal function leads to electrolyte disturbances, GI disorders can also lead to electrolyte imbalances Controlling electrolyte balance involves several processes in which the kidneys and GI tract play an essential role, As a result, damage to them usually disrupts fluids and electrolyte balance, Studies on COVID-19 confirm electrolyte disturbances in patients, including sodium and potassium. (Mohammad *et al*,2021).

Accordingly, this study high light the electrolyte disturbance in patients with covid-19, One of the most common electrolyte disorders is hyponatremia.

1.2 Rationale

In COVID-19, the kidneys and GI tract are at risk, and a variety of complications have been reported, electrolyte disturbances are complications of the kidney and GI injuries in COVID-19 patients, Which can lead to many problems and even death, clinicians should have special supervision over electrolyte balance in COVID-19 patients, especially in patients under intensive care and it can raise mortality rate Hyponatremia, hypernatremia, hypokalemia, and changes in fluid body volume are the most common fluid and electrolyte disorders in SARS-CoV-2 infection that should be given special attention, Since electrolyte disturbances can be seen in COVID-19, body electrolyte concentrations can be used to measure disease status and disease progression. (Giuseppe *et al*., 2020).

This study may be providing base line data by measuring sodium and potassium concentration to avoid electrolyte disturbance in covid-19 patients that may help in avoiding complication of covid-19.

1.3 Objectives

General objective:

-To assess serum sodium and potassium levels in Covid-19 Patients in Khartoum State.

Specific Objectives:

-To measure and compare mean concentration of sodium and potassium in study groups.

- To measure and compare mean concentration of sodium and potassium level according to its health situation in case groups.

- To correlate between sodium and potassium levels with study variables (age) among case group.

- To correlate between sodium and potassium levels among case group.

Chapter Two

Literature Review

2.1. background of Covid-19:

The severe acute respiratory syndrome (SARS) coronavirus-2 is a novel coronavirus belonging to the family Coronaviridae and is now known to be responsible for the outbreak of a series of recent acute atypical respiratory infections originating in Wuhan, China. The disease caused by this virus, termed coronavirus disease 19 or simply COVID-19, has rapidly spread throughout the world at an alarming pace and has been declared a pandemic by the WHO on 2020 (Annant.,2020).

A series of acute atypical respiratory infections ravaged the Wuhan city of Hubei province of China in December 2019. The pathogen responsible for these atypical infections was soon discovered to be a novel coronavirus belonging to the family Coronaviridae and was named as the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). It was seen to be highly homologous to the SARS coronavirus (SARS-CoV), which was responsible for the respiratory pandemic during the 2002–2003 period. (Jeong-Hoon *et al*.,2020).

Previous studies have shown that in COVID-19, in addition to the respiratory system, the nervous system, cardiovascular system, gastrointestinal (GI) tract, and urogenital system are also affected by the disease and its complications. 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 (Mohammad *et al*.,2021).

2.1.1 Disease Transmission:

The transmission characteristics of SARS-CoV-2 are very similar to those of SARS-CoV and pandemic influenza.; The first evidence of potential person-to-person transmission was reported, They investigated the transmission of the virus in a group of family members who had recently visited Wuhan. They had no history of contact with animals, visits to markets, or eating game meat, but stayed in the same hotel throughout their travel. With no direct zoonotic involvement, this was the first indication that the virus could be spread by human contact. These initial findings were subsequently confirmed with increasing evidence demonstrating sustained human-to-human transmission SARS-CoV-2 uses the same receptor, ACE2, as SARS-CoV, and mainly spreads through the respiratory tract. As a respiratory infectious disease, the virus is transmitted primarily by droplets, respiratory secretions, and direct contact. However, viral particles have been isolated from fecal swabs and blood, implying several alternative routes for transmission It is worth noting that the ACE2 protein is also expressed by enterocytes in the small intestine Previous Chinese reports have shown no evidence of vertical transmission of the virus by blood products or the fecal-oral route. (Sayeeda *et al*.,2021).

However, some recent studies from the United Kingdom (UK) and other countries have confirmed a low rate of vertical transmission due to COVID-19 SARS-CoV-2 targets the respiratory system, and transmission occurs via contact droplets and fomites from an infected person who may be symptomatic or asymptomatic, During the incubation period, the virus triggers a slow response in the lungs. SARS-CoV-2 mainly invades alveolar epithelial cells, resulting in respiratory symptoms. (Sayeeda *et al.*, 2021).

The S-glycoprotein on the surface of SARS-CoV-2 binds to ACE2, The receptor and the enzyme on the surface of type 2 alveolar cells induce a conformational change in S-glycoprotein initiating proteolytic digestion by host cell proteases (TMPRSS2 and furin), ultimately leading to internalization of the virion; This implies that SARS-CoV-2 has a pathogenesis similar to that of SARS-CoV, Coronaviruses generally enter via endocytosis or direct fusion of the viral envelope with the host membrane. Once internalized by the host cell, the viral particle is uncoated, and its genome enters the cell cytoplasm. Coronaviruses have an RNA genome from which they can directly produce their proteins and new genomes in the cytoplasm by attaching to the host ribosomes. The host ribosomes translate viral RNA into RNA polymerase proteins. This RNA polymerase then reads the positive strand again to generate single-stranded, negative-sense RNA (ssRNA-) strands. (Sayeeda *et al*.,2021).

2.1.2 Incubation period of disease:

The incubation period on average is 1–14 days, however, generally is 3–7 days. SARS-CoV-2 may be present in the throat or the nose a few days before symptom onset. Interestingly, completely asymptomatic subjects may have viral loads similar to those of symptomatic patients. This implies that asymptomatic individuals may be possible sources of infection. (Sayeeda *et al*.,2021).

2.1.3. Sign and symptoms of disease:

After the incubation period, patients present with similar symptoms, including fever, cough, and malaise. A small percentage of patients also manifest gastrointestinal symptoms, such as diarrhea and vomiting. The elderly and those with underlying disorders rapidly develop acute respiratory distress syndrome (ARDS), septic shock, metabolic acidosis, and coagulation dysfunction, which may ultimately lead to multiple organ failure and even death (Sayeeda *et al*.,2021).

2.1.4 pathophysiology of disease:

Pathophysiological mechanisms of virus-induced multi organ dysfunction have been identified as follows: (1) direct cytotoxicity of virus, (2) altered regulation of RAS by depletion and downregulation of ACE2, (3) endothelial cell injury, apoptosis, and thromboinflammation (4) dysregulation of immune response such as over-release of pro inflammatory cytokines that cause cytokine storm (Jeong-Hoon *et al.*, 2020).

2.1.5 Diagnosis of COVID-19:

the accurate diagnosis of COVID-19 is challenging. The routine clinical diagnosis of COVID-19 is primarily based on epidemiological history, clinical manifestations, and confirmed by a variety of laboratory detection methods, including computed tomography (CT) scan, nucleic acid amplification test (NAAT), and serological techniques. (Pai *et al.*,2021).

the detection of the viral genomic regions has been almost solely dependent on the RT-PCR method, or molecular tests in general. (Yuce *et al*., 2020). Rapid antibody (serology) tests are certainly needed for vast immune screening, but they do not confirm the presence of the virus, Serology tests are also important as they can help assess follow up on the progression of the disease The serologic test is an enzyme-linked immunosorbent assay (ELISA)-based test that detects SARS-CoV-2 antibodies (IgG and IgM) in serum or plasma, The ELISA used by the CDC utilizes purified SARS-CoV-2 S protein (no live virus) as an antigen, The problem with serologic tests is that the cross-reactivity to antibodies generated by other coronaviruses cannot be completely ruled out , Comparative information on the use of different diagnostic techniques for COVID-19.(Sayeeda *et al* .,2021).

2.1.7 Public health and preventive measures of COVID-19: Public health and preventive approaches are the current strategies to curb the transmission of COVID-19 and focus on testing, case tracing, isolation, social distancing, and personal hygiene, Important COVID-19 prevention and control measures in the community include hand hygiene, personal protective equipment (PPE), crowd avoidance, social distancing, isolation, school measures closures, workplace measures closures, quarantine, and travel restrictions. (Sayeeda *et al*., 2021).

2.2.1 Sodium metabolism:

Na+ is most abundant cation in the extracellular fluid, representing 90% of all extracellular cations and largely determines the osmolality of the plasma, Na+ concentration in ECF is the much larger than inside the cell.

The plasma Na+ concentration depends greatly on the intake and excretion of water and, to a somewhat lesser degree, on the renal regulation of Na+. (Bishop *et al* 2018).

Sodium is an essential nutrient involved in the maintenance of normal cellular homeostasis and in the regulation of fluid and electrolyte balance and blood pressure (BP). Its role is crucial for maintaining ECF volume because of its important osmotic action and is equally important for the excitability of muscle and nerve cells and for the transport of nutrients and substrates through plasma membranes. (Strazzullo *et al.,* 2014)

Three processes are of primary importance: (1) the intake of water in response to thirst, as stimulated or suppressed by plasma osmolality; (2) the excretion of water, largely affected by AVP release in response to changes in either blood volume or osmolality; and the blood volume status, which affects Na+ excretion through aldosterone, angiotensin II, and ANP. The kidneys have the ability to conserve or excrete large amounts of Na+, depending on the Na+ content of the ECF and the blood volume. Normally, 60% to 75% of filtered Na+ is reabsorbed in the proximal tubule; electro neutrality is maintained by either Cl− reabsorption or hydrogen ion (H+) secretion. Some Na+ is also reabsorbed in the loop and distal tubule and (controlled by aldosterone) exchanged for K+ in the connecting segment and cortical collecting tubule. (Bishop *et al*.,2018)

Hyponatremia:

Hyponatremia is a common condition affecting hospitalized and ambulatory patients as well. The clinical spectrum of hyponatremia can range from asymptomatic laboratory findings to severely symptomatic conditions such as acute epileptic seizures. Etiologies of hyponatremia include excessive intake of solute-free fluids, side-effects of medication, diseases associated with hypervolemic states such as congestive heart failure, and the syndrome of inappropriate antidiuretic hormone secretion. (Kylies *et al.*, 2020).

is defined as a serum/plasma level less than 135 mmol/L, and levels below 130 mmol/L are clinically significant.4 Hyponatremia is one of the most common electrolyte disorders in hospitalized and nonhospitalized patients and can be assessed either by the cause of the decrease or with the osmolality level. Decreased levels may be caused by increased Na+ loss, increased water retention, or water imbalance. (Bishop *et al*.,2018)

Increased Na+ loss in the urine can occur with decreased aldosterone production, certain diuretics (thiazides), ketonuria. (Na+ lost with ketones), or a salt-losing nephropathy (with some renal tubular disorders). K+ deficiency also causes Na+ loss because of the inverse relationship of the two ions in the renal tubules; when serum K+ levels are low, the renal tubules will conserve K+ and excrete Na+ in exchange for the loss of the monovalent cation. Each disorder results in an increased urine Na+ level (≥20 mmol/d), which exceeds the amount of water loss,

Pseudohyponatremia, as mentioned earlier, may also be seen with in vitro hemolysis, considered the most common cause for a false decrease. When red blood cells (RBCs) lyse, Na+, K+, and water are released, and since Na+ concentration is lower in RBCs, this results in a false decrease. Hyponatremia with a high osmolality is associated with hyperglycemia. The elevated levels of glucose increase the serum osmolality and cause a shift of water from the cells to the blood, resulting in a dilution of Na+.

Symptoms depend on the serum level. Between 125 and 130 mmol/L, symptoms are primarily gastrointestinal (GI). More severe neuropsychiatric symptoms are seen below 125 mmol/L, including nausea and vomiting, muscular weakness, headache, lethargy, and ataxia. More severe symptoms also include seizures, coma, and respiratory depression. A level below 120 mmol/L for 48 hours or less (acute hyponatremia) is considered a medical emergency Serum and urine electrolytes are monitored as treatment to return Na+ levels to normal occurs. (Giuseppe *et al.,* 2020).

Treatment of hyponatremia is directed at correction of the condition that caused either water loss or Na+ loss in excess of water loss. In addition, the onset of hyponatremia— acute or chronic (less than or more than 48 hours)—and the severity of hyponatremia are considered in treatment. Conventional treatment hyponatremia involves fluid restriction and providing hypertonic saline and/or other pharmacologic agents that may take several days to reach the desired effect and may have deleterious side effects. Correcting severe hyponatremia too rapidly can cause cerebral myelinolysis and too slowly can cause cerebral edema. Appropriate management of fluid administration is critical. Fluid administration and monitoring are required during treatment of the underlying cause of the hyponatremia (Bishop *et al*., 2018.)

Hypernatremia:

(increased serum Na+ concentration) results from excess loss of water relative to Na+ loss, decreased water intake, or increased Na+ intake or retention. Hypernatremia is less commonly seen in hospitalized patients than is hyponatremia, Symptoms most commonly involve the CNS as a result of the hyperosmolar state. These symptoms include altered mental status, lethargy, irritability, restlessness, seizures, muscle, hyper reflexes, fever, nausea or vomiting, difficult respiration, and increased thirst. Serum Na+ of more than 160 mmol/L is associated with a mortality rate of 60% to 75%. (Bishop *et al*.,2018).

Treatment of hypernatremia is directed at correction of the underlying condition that caused the water depletion or Na+ retention. The speed of correction depends on the rate with which the condition developed. Hypernatremia must be corrected gradually because too rapid a correction of serious hypernatremia (≥160 mmol/L) can induce cerebral edema and death; the maximal rate should be 0.5 mmol/L/h (Chen *et al*., 2020).

Potassium metabolism:

Potassium (K+) is the major intracellular cation in the body, with a concentration 20 times greater inside the cells than outside. Many cellular functions require that the body maintain a low ECF concentration of K+ ions. As a result, only 2% of the body's total K+ circulates in the plasma. Functions of K+ in the body include regulation of neuromuscular excitability, contraction of the heart, ICF volume, and H+ concentration

The K+ concentration has a major effect on the contraction of skeletal and cardiac muscles (Bishop *et al*.,2018).

Total body potassium content and proper distribution of potassium across the cell membrane is of critical importance for normal cellular function. Potassium homeostasis is maintained by several different methods. In the kidney, total body potassium content is achieved by alterations in renal excretion of potassium in response to variations in intake (Palmer *et al.*,2016).

Hypokalemia:

Hypokalemia is low level of potassium concentration, can occur with GI or urinary loss of K+ or with increased cellular uptake of K+, Hypokalemia was defined as a serum potassium level < 3.5 mEq/l. The normal level of serum potassium ranges from 3.5 to 5.3 mEq/L. The diagnosis of hypokalemia was performed on a single value of serum potassium < 3.5 meq/L at any time during hospitalization. We excluded all serum values of potassium measured on plasma and by blood gas analyzer. Severity was classified as mild when the serum potassium level was 3–3.4 mmol/L, moderate when the serum potassium level was 2.5–3 mmol/L, and severe when the serum potassium level was less than 2.5 mmol/L. (Mohammad *et al*.,2021).

Symptoms (e.g., weakness, fatigue, and constipation) often become apparent as plasma K+ decreases below 3 mmol/L. Hypokalemia can lead to muscle weakness or paralysis, which can interfere with breathing. The dangers of hypokalemia concern all patients, but especially those with cardiovascular disorders because of an increased risk of arrhythmia, which may cause sudden death in certain patients. Mild hypokalemia (3.0 to 3.4 mmol/L) is usually asymptomatic. (Maryam *et al*.,2021).

Treatment typically includes oral KCl replacement of K+ over several days. In some instances, intravenous (IV) replacement may be indicated. In some cases, chronic mild hypokalemia may be corrected simply by `including food in the diet with high K+ content, such as dried fruits, nuts bran cereals, bananas, and orange juice. Plasma electrolytes are monitored as treatment to return K+ levels to normal occurs. (Bishop *et al*., 2018)

Hyperkalemia:

results either from the shift of potassium out of cells or from abnormal renal potassium excretion. Cell shift leads to transient increases in the plasma potassium concentration, whereas decreased renal excretion of potassium leads to sustained hyperkalemia. Impairments in renal potassium excretion can be the result of reduced sodium delivery to the distal nephron, decreased mineralocorticoid level or activity, or abnormalities in the cortical collecting duct. (Palmer *et al*., 2017).

Hyperkalemia is a potentially life-threatening metabolic problem caused by inability of the kidneys to excrete potassium, impairment of the mechanisms that move potassium from the circulation into the cells, or a combination of these factors. Acute episodes of hyperkalemia commonly are triggered by the introduction of a medication affecting potassium homeostasis; illness or dehydration also can be triggers. In patients with diabetic nephropathy, hyperkalemia may be caused by the syndrome of hyporeninemic hypoaldosteronism. (Hollander-Rodriguez *et al*., 2006).

K+ may be quickly removed from the body by use of diuretics (loop), if renal function is adequate, or sodium polystyrene sulfonate (Kayexalate) enemas, which bind to K+ secreted in the colon. Hemodialysis can be used if other measures fail. Patients treated with these agents must be monitored carefully to prevent hypokalemia as K+ moves back into cells or is removed from the body. (Bishop *et al*.,2018).

Mechanism of sodium and potassium disorder in covid-19:

Electrolyte are involved in many essential processes in your body, They conducting nervous impulses, contracting muscles, keeping you hydrated and regulating your body pH levels (Giuseppe *et al*., 2020).

In early COVID-19 studies, some evidence has been provided that electrolyte disorders may also be present upon patients' presentation, including sodium, potassium, abnormalities (Guan *et a*l., 2020; Huang *et al.*, 2020).

In COVID-19, the kidneys and GI tract are at risk, and a variety of complications have been reported that are very common, Fluid and electrolyte disturbances are complications of the kidney and GI injuries in COVID-19 patients. Because fluid and 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, and changes in fluid body volume are the most common fluid and 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 fluid and electrolyte disturbances can be seen in COVID-19, body fluid volume and electrolyte concentrations can be used to measure disease status and disease progression. (Mohammed *et al*.,2021)

The other hypothesis describe the incidence of hyperkalemia based on the key role of furin, it is necessary for cleaving both SARS-CoV-2 spike protein and ENaC subunits. While the furin is hijacked by the virus, the decreased activity of ENaC would be expected, which causes retention of potassium ions and hyperkalemia. (Maryam *et al*.,2021).

Abnormal serum sodium levels are particularly common in hospitalized patients with COVID-19, with observational studies reporting 20% to 30% prevalence of hyponatremia (<136 mmol/L) and 4% to 7% hypernatremia (>145 mmol/L)5 on admission. Hyponatremia and hypernatremia are important prognostic markers and have been associated with higher risk of sepsis, respiratory failure, length of hospital stay, and all-cause mortality in patients with COVID-19. (Timothy et al.,2022).

Hyponatremia occurs in about 30% of patients with pneumonia and it has been previously reported in 30–60% of SARS CoV-1 patients, In SARS CoV-1 patients hyponatremia was associated with a worse outcome (ICU transfer, death). As per SARS CoV-2 patients, early observations reported that hyponatremia was associated with progression to a more severe disease (Berni *et al*., 2021).

SARS-CoV-2 cell entry through angiotensin-converting enzyme 2 (ACE2) may enhance the activity of renin–angiotensin–aldosterone system (RAAS) classical axis and further leading to over production of aldosterone. Aldosterone is capable of enhancing the activity of ENaC and resulting in potassium loss from epithelial cells. However, type II transmembrane serine protease (TMPRSS2) is able to inhibit the ENaC, but it is utilized in the case of SARS-CoV-2 cell entry, therefore the ENaC remains activated. (Maryam *et al*.,2021).

Potassium and sodium have an inverse relationship; As sodium goes up, potassium level decrease, and vice versa, Previous study has assessed the that no association between sodium and potassium with age; just affected by intake in covid-19. (Alberto *et al*., 2020)

Chapter Three

Materials and methods

3.1. Materials:

3.1.1. Study approach:

A quantitative method was used to measure the level of serum potassium and sodium in covid-19 Sudanese male and female patients during the period from march to August 2022.

3.1.2. Study design:

This is case control study.

3.1.3. Study area:

The study was conducted in Jabra isolation center for Covid-19.

3.1.4. Study population:

The study included fifty patients with Covid-19 and fifty healthy people as control.

3.1.5. Sample size:

This study included All patients affected with Covid-19 in study period from March to August. (age and gender were matched).

3.1.6. Inclusion criteria:

Patients diagnosed with covid-19 by real-time polymerase chain reaction (RT-PCR) assay from naso-pharyngeal swab specimens and meet diagnostic criteria set out by World Health Organization for COVID-19 and voluntarily accepted to participate in this study will be included.

3.1.7. Exclusion criteria:

Patients with chronic Renal and liver dehydrated disease or any other disease, alcoholism and medication that increase sodium and potassium level were excluded.

3.1.8. Ethical consideration:

Formal speech was taken from Postgraduate of Sudan University of Science and Technology to Ministry of health that given me another formal speech to Jabra Isolation Center Before the specimen was collected, to knew that this specimen was collected for research purpose.

3.1.9. Data collection:

Data were collected using structural interviewing questionnaire, which was designed to collect and maintain all valuable information concerning each case examined**.** Questionnaire (Appendix 1).

3.2. Methods:

3.2.1 Sample collection and processing:

About 3ml of venous blood were collected by safe aseptic procedure. Serum may be used for the assay of sodium and potassium; the volume of sample is recommended that at least 2.5ml of whole blood is collected. In serum sample; blood should be allowed to colt at room temperature. After retraction of the clot, the sample should be centrifuged, and the serum separated. Serum sample should be stored frozen below -20C. Sample should be thawed and mixed before assay.

3.2.2. Estimation of sodium and potassium:

EasyLyte analyzer is a completely automated, microprocessor controlled electrolyte system that uses ISE (Ion selective electrolyte measurement was used**.**

3.2.2.1. Principle and procedure (Appendix 11):

3.3. Quality control:

The precision and accuracy of all methods used in this study were checked by commercially prepared control sample before it is application for the measurement of the test and control samples.

3.4. Statistical analysis:

Data obtained from this study was analyzed using statistical package for the social science (SPSS version 23). Independent t test was used for comparison of mean, One-way Anova used for determined whether they are any statistically significant differences between the mean and the and pearson's correlation was used for correlation**.**

Probability < 0.05 was considered significant.

Chapter Four

4-Results

The results of biochemical determine serum of Sodium and Potassium in Covid-19 patients (case) and control group are given in tables and figures:

Figure (4.1): shows age distribution among case group, most of case age between 64-75 years.

Figure (4.2): Regarding the health situation of the cases, most of them were admitted to the floor (28), (18) in ICU and (4) in CCU.

Table (4.1): represents the comparison between the mean and standard deviation of sodium and potassium in case versus control group. The result showed there were significant decrease in sodium (131.7 ±7.203 versus (139.1 ±2.911 IU/L, P- value =0.00), while there was significant increase in potassium (3.718 ±0.657 versus 3.4.14 ±0.078 IU/L, P- value =0.00) respectively.

Table (4.2): represents the comparison between the mean and standard deviation of sodium and potassium in case group according to its health situation. The result showed there were significant increase in mean of potassium among CCU patients (4.3 ± 0.52 IU/L, p- value =0.03) compared to floor patients (3.5 ± 0.72 IU/L, p-value =0.15).

Figure (4.3): Correlation between Sodium and Potassium level in case group (r=-0.08, p= 0.54) (significantly There was `no correlation).

Figure (4.4): correlation between age and sodium levels in case group **(**r= -0.17, p= 0.23) (significantly There was no correlation).

Figure (4.5): correlation between age and potassium levels in case group (r= -0.14, p= 0.31) (significantly There was no correlation).

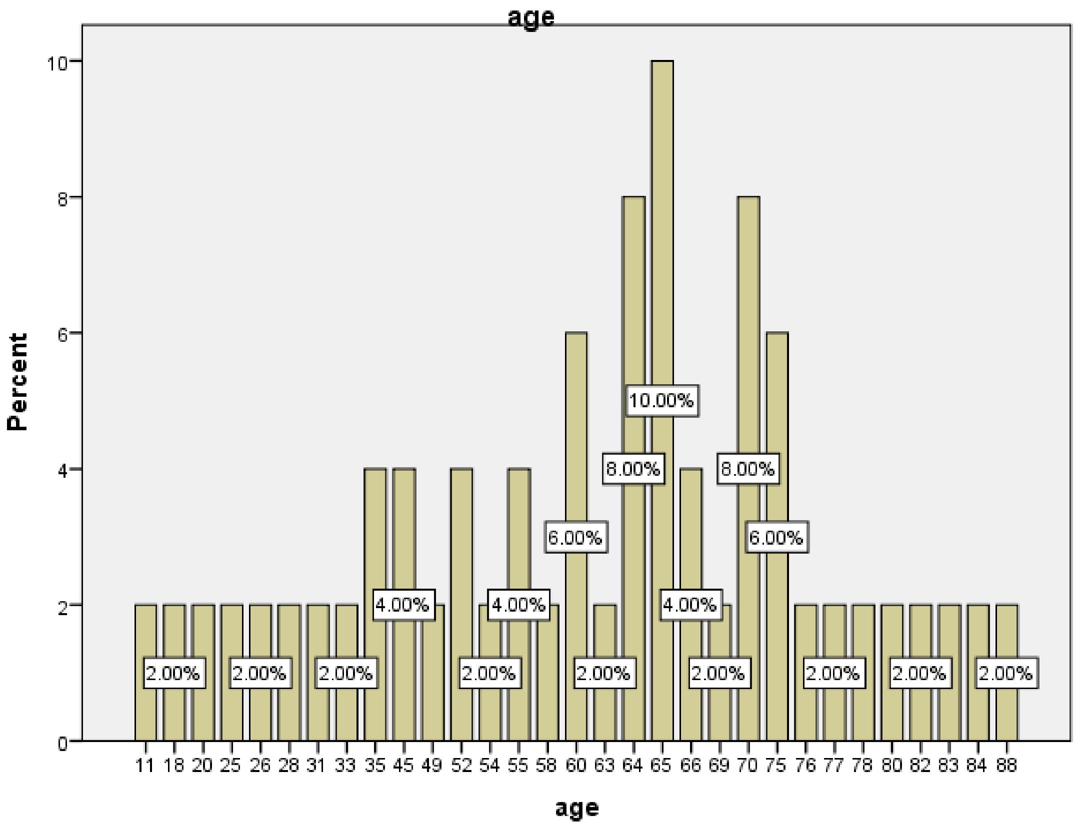

Figure (4.1): shows age distribution among Covid-19 case group.

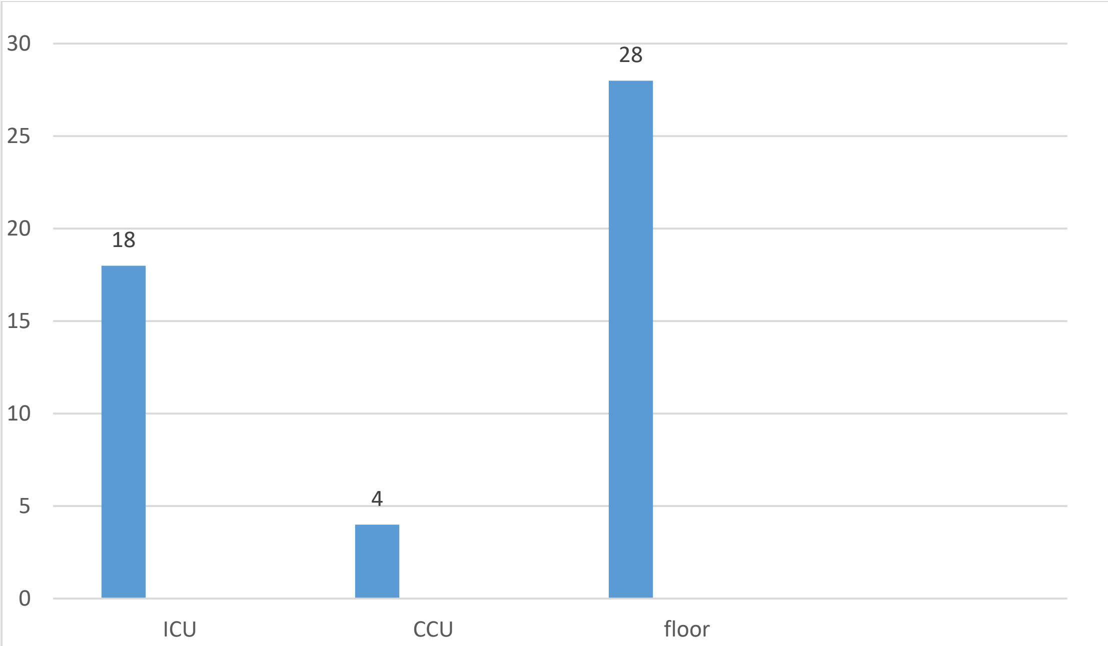

Figure (4.2) The health situation of the cases

Table (4.1): The comparison of mean and standard deviation of sodium and potassium in study groups

Variable	Case Mean ±SD	Control Mean ±SD	P. value
Na	131.7 ±7.203	139.1 ±2.911	0.00
K	3.718 ±0.657	3.414 ±0.078	0.00

Independent sample t-test used for comparison.

P-value < 0.05 is considered significant.

Table (4.2) The comparison between the mean and standard deviation of sodium and potassium in case group according to its health situation:

Variables	ICU	CCU	Floor	P value		
				ICU& Floor	CCU &Floor	ICU & CCU
Na	132 ± 7.1	130.8 ± 2.6	130.9 ± 8.8	0.65	0.79	0.74
K	3.8 ± 0.67	4.3 ± 0.52	3.5 ± 0.72	0.15	0.03	0.15

One-Way ANOVA used for comparison.

P-value < 0.05 is considered significant.

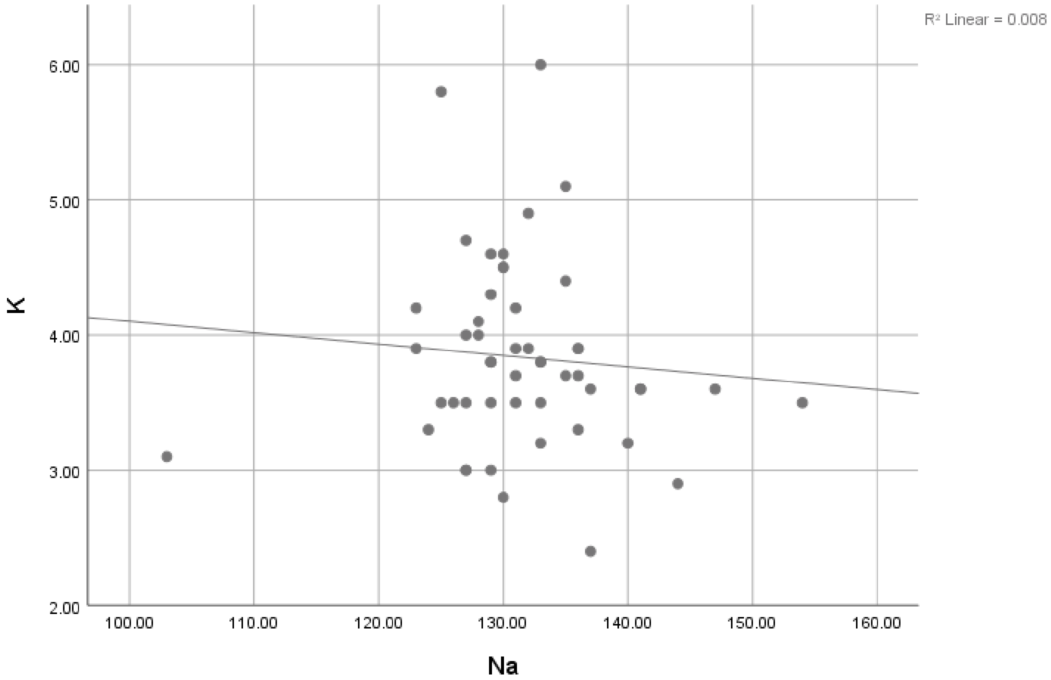

Figure (4.3): Correlation between Sodium and Potassium level in case group (r=-0.08, p= 0.54).

Pearson's correlation was used.

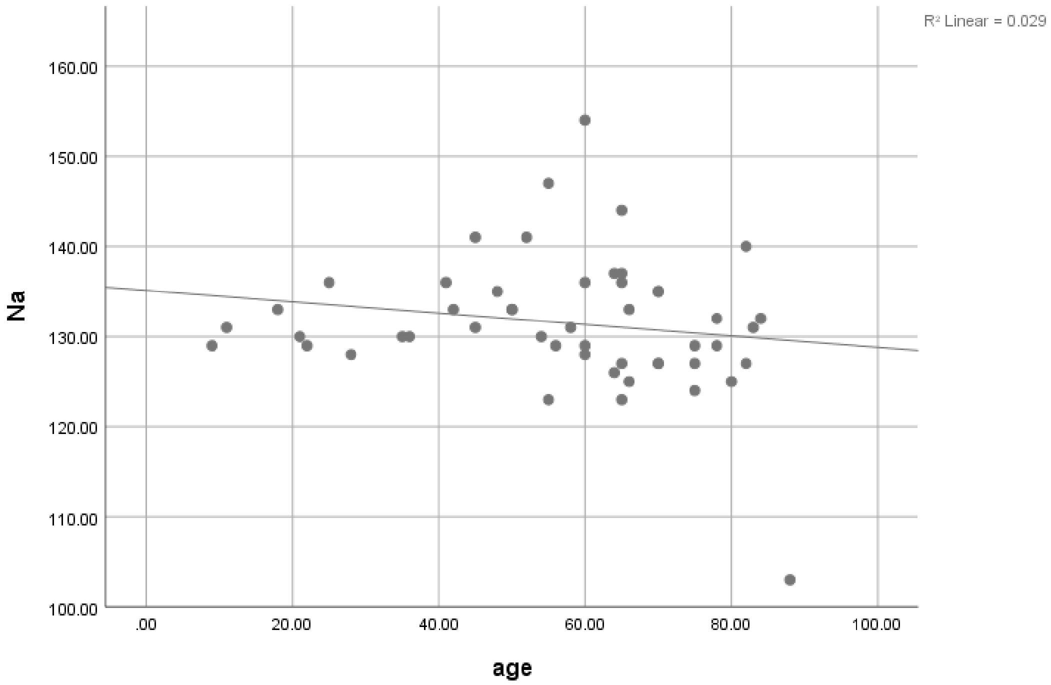

Figure (4.4): Correlation between age and sodium in case group (r= -0.17, p= 0.23).

Pearson's correlation was used.

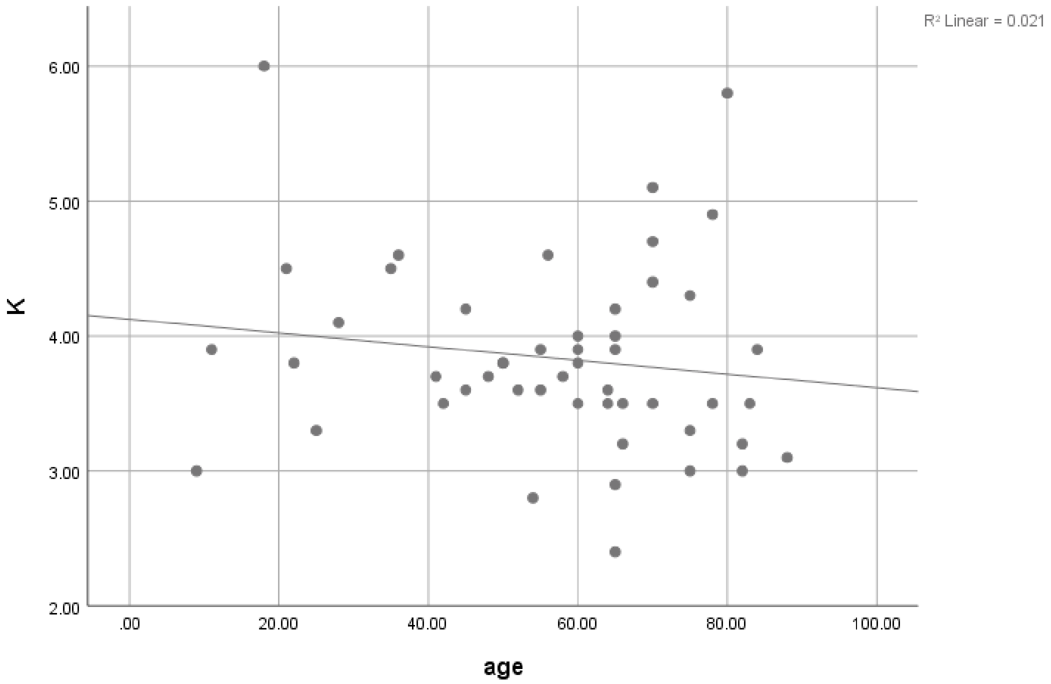

Figure (4.5): correlation between age and potassium levels in case group (r= -0.14, p= 0.31).

Pearson's correlation was used.

Chapter Five

Discussion – Conclusions - Recommendations

5.1 Discussion:

Covid-19 is a serious medical condition and increase incidence of death and many complication effects on the life quality**.**

The finding of this study showed significant decrease in sodium level in patients with covid-19. (p- value=0.00), This finding agreed with study carried by (Mohammad *et al*,2021), (Berni *et al*., 2021) and (Maryam *et al*.,2021); which found there were significant decrease in Na level in Covid-19 patient, Electrolyte imbalances are caused by alteration of RAS, gastrointestinal loss and renal tubular dysfunction by the invasion of SARS-CoV-2, The spike protein of SARS-CoV-2 binds to ACE2 and causes depletion and downregulation of ACE2.

also this result showed, increase in mean of potassium in case group compare with control group (p-value= 0.00), This finding agreed with study carried by (Maryam *et al*.,2021), which found there incidence of hyperkalemia based on the key role of furin, that it is necessary for cleaving both SARS-CoV-2 spike protein and epithelial sodium channels subunits. While the furin is hijacked by the virus, the decreased activity of Epithelial sodium channel would be expected, which causes retention of potassium ions and hyperkalemia.

Also this study showed there were significantly increase The mean of potassium levels among CCU patients compared to flower patients.

(P-value =0.03)

Also the finding of this study showed, statistically significant there were no correlation between sodium and potassium level). but there was negative correlation according to r value. ($r= -0.08$, $p= 0.54$). This study agreed with study carried by (Alberto *et al*., 2020) which found there inverse relationship between Sodium and Potassium; As sodium goes up, potassium level decrease, and vice versa.

Also showed no correlation between age and concentration of sodium and potassium, this study agreed with study carried by (Alberto *et al*., 2020) which found there no association between sodium and potassium with age.

5.2. Conclusions:

According to results of this study:

Sodium is decreased, and potassium increased in Covid-19 patients compared with healthy patients.

According to health situation there were no difference in mean concentration of sodium among Floor, CCU and ICU. But there was significant increase in mean concentration of potassium among CCU patients compare with Floor patients.

There was no correlation between Sodium and Potassium level in case group according to p-value of test. And no correlation between sodium and potassium with age.

5.3 Recommendations:

From the findings of this study it is recommended that:

- sodium and potassium should be done as screening tests to prevent the complications of covid-19. And monitor potassium level especially in CCU.
- Further studies should be conducted to investigate the other electrolyte levels to assess the impact of these parameters upon covid-19.
- Further studies recommended with large sample size.

References

Alberto L, Ellen A, Rosario O (2020). longitudinal association between sodium and potassium, the *journal of Gerontology*;75(12):2379-2386.

Annant P. (2021) clinical presentation and treatment, current understanding of its pathophysiology, *postgrad medical journal*; 97:312-320.

Berni, A., Malandrino D, Corona, G (2021). Serum sodium alterations in SARS CoV-2 (COVID-19) infection: impact on patient outcome. European Journal of Endocrinology, 185(1):137-144.

Bishop, Michael L., Edward p., Larry E., schoeff, (2018). clinical chemistry Bishop principles, technique, and correlation Philadelphia Wolters kluwer, (8) edition. *Jones & Bartlett Learning* .305-309.

Chen Y, Filiztekin E, Özkaya KG.(2021). COVID-19 diagnosis *,A review of current methods. Biosens Bioelectron*; 172(10):112-117.

Ertuglu L., Kanbay A., Afsar B., Elsurer Afsar, R., & Kanbay, M. (2020). Covid-19 and acute kidney injury. *Tuberculosis and Thorax*; 68(4): 65-70.

Giuseppe L, South AM., Henry BM., (2020). Electrolyte imbalance in patients with severe Covid-19 disease. *Annals of clinical Biochemistry***.** **;**57(3): 262-265.

Guan W, Ni Z-Y, Hu Y, Lian g W-H, Ou C-Q, He J-X. (2020). Clinical characteristics of Coronavirus Disease 2019 in China. *New England Journal of Medicinne*;28(382):1708-1720.

Hollander-Rodriguez JC, Calvert JF. (2006) Hyperkalemia, *Am Fam physician.*73(2):90-283.

Jeong-Hoon L, Jung HY, Choi JY, park SH, Kim CD, Kim YL, Cho JH. (2020) Hypertension and electrolyte disorder in patients with covid-19. *Electrolyte Blood pressure*; 18(2): 23-30.

Kylies D, Wenzel U, (2020) Hyponatremia Diagnosis and therapy. *Deutsche medizinische Wochenschrift*. 145(21):1573-1579.

Khaled H, Chioma N, Fanila, Rajendran G, (2020) Resolution of coronavirus disease 2019 (COVID-19*), Expert Review of Anti-infective Therapy,* 18(12): 1201-1211

Maryam N, Chahhoud K., Nejadghaderi SA., Sullman MJM. (2021). How SARS might affect potassium balance via impairing epithelial sodium channels; 48(9):6655-6661.

Mohammad P, Abbasnia SM, Shafaei F, Heidari R.(2021) .Fluid and electrolyte disturbance in covid-19 and their complication *.student research committee*; 32(7):23-43

Palmer BF, Clegg DJ, (2016). Physiology and pathophysiology of potassium hemostasis. *Advances in physiology education;* 40(4):480-490.

Pai M, Kumar BK, Deekshit VK, Karunasagar I, Karunasagar (2021). Detection technologies and recent developments in the diagnosis of COVID-19 infection. *Applied Microbiology Biotechnology* ; 105(2):441-455.

Strazzullo P, Leclercq C, (2014). Sodium. *Advances in Nutrition*,5(2):188-190.

Sayeeda R., Montero MTV., Rowe K., Kirton R., KuniK F., (2021). Epidemiology, pathogenesis, clinical presentation, diagnosis and clinical review of current evidence. *Expert Review treatment of covid-19* ;14(5):601-621.

Timothy E Yen, Andy Kim, Maura E. Benson, Saee R, Ann E. Woolley, and Finnian R. Mc Causland1, (2021). Serum Sodium, Patient Symptoms, and Clinical Outcomes in Hospitalized Patients with COVID-19. *Journal of Primary Care & Community Health*; 13: 1-7.

World Health Organization. (2022). Covid-19 weekly epidemiological update, edition 90.

Yuce C, Luo R., Wang K., Zhang M., Wang Z., Dong L., Yao Y., Ge, S. and Xu, G., (2020). Kidney disease is associated with in-hospital death of patient with Covid-19. *kidney international*; 97(5):829-838.

Appendices

Appendix 1

Questionnaires:

Sudan University of Science and Technology

Master Degree
Estimation of sodium and potassium in Covid-19 Patients

Name:
…………………………………………………………………
Gender ☐ Male ☐ Female
Age: ………..years
TEL: ………………………………………………………
Family history diseases of covid-19:
……………………………….
Duration of Diseases: ………………………………on week
Medications Use: …………………………………………….
Sign and symptom: …………………………………………….
Sample: serum / heparinized plasma
Parameters:
Na…………………………… Mmol/L
K…………………………Mmol/L

Number ( )

Appendix 11

Principle and procedure:

PROCEDURE NOTES:
Sodium and chloride are reported to the nearest whole number in mmol/L. Potassium is reported to the nearest tenth in mmol/L.

AMR (Analytical Measurement Range):
Sodium: 80 - 180 mmol/L
Potassium: 1.5 - 10 mmol/L
Chloride: 60 - 140 mmol/L

CALCULATIONS:
The COBAS c501 System automatically calculates the electrolyte concentration of each sample. When electrolytes (LYTES) are ordered, the LIS calculates the anion gap.

Anion Gap = Sodium – (Chloride + CO_2)

INTERPRETATION:
Expected Values:
Sodium 135 - 146 mmol/L

Potassium (plasma)
Adult: 3.4 - 5.0 mmol/L
Infant (Day 0 - 30): 3.7 - 5.9 mmol/L
Child (1mo. - 2 yrs): 4.1 - 5.3 mmol/L
Plasma potassium levels are reported to be approximately 0.3 mmol/L lower than serum levels.

Chloride 96 - 108 mmol/L

REPORTING CRITICAL RESULTS:
Please refer to Lab-0130 *Critical Call Values, Lab Reporting Protcol.*

LIMITATIONS:
Elevated White Cell Count: False elevation in potassium can be seen in heparin plasma samples from patients with elevated white cell counts. Compare plasma potassium results with serum potassium values. If serum potassium results are lower, the elevated plasma potassium value is false and probably due to heparin-mediated cell membrane leakage in the setting of an elevated white cell count. Notify the physician and then monitor serum potassium in these patients until the white cell count is reduced and plasma values are equal to or lower than serum values.
Hemolysis:
Sodium and chloride: No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 1.0 g/dL).


ANALYZE BLOOD?
Yes
No
EasyLyte PLUS
Na/K/Cl
MEDICA