Sudan University of Science and Technology

College of Graduate Studies

Assessment of Plasma Uric acid, Sodium and Potassium levels among Patients with COVID-19 Disease in Jabra Isolation Center -Khartoum state

تقييم مستويات حمض البوليك والصوديوم والبوتاسيوم في البلازما لدى المرضى المصابين بمرض كوفيد-19 في مركز جبرة للعزل بولاية الخرطوم

A dissertation submitted in partial fulfillment for requirement of M.Sc. degree in Medical Laboratory Science (Clinical Chemistry)

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الآية

قَالَ تَعَالَىٰ: ﴿ وَأَن لَّيْسَ لِلْإِنسَٰنِ إِلَّا مَا سَعَىٰ ﴿٣٩﴾ ﴾

صدق الله العظيم

سورة النجم الآية: (39)

Dedication

The entire work is dedicated to my parents for their love and caring,

My brother, my sisters, my family and my close friends

Acknowledgements

First of all, I thank God for all the beneficent and most merciful. My all and deepest thank to my family for their support, bearing, and encouragement.I am very thankful to my supervisor Dr.Abdelgadir Elmugadam for his help and guidance. I thank him for his advice and suggestions, my gratitude to all staff in Jabra isolation center, I finally, my thanks go to all the people who have supported me to complete my research.

Abstract

Background: In December 2019, a series of acute atypical respiratory disease occurred in Wuhan, China. This rapidly spread from Wuhan to other areas. It was soon discovered that a novel corona virus was responsible. The disruption of uric acid, sodium and potassium, tends to be a common occurrence in patients with COVID-19.

Aim: To assess uric acid, sodium and potassium levels among Sudanese patients with COVID-19.

Methods: This study (case-control) was conducted in Jabra isolation center at Jabra hospital for emergency and injuries- Khartoum state, during the period from February 2022 to August 2022. A total of 100 samples were collected, included 50 patients with COVID-19 as case and 50 healthy individual as control were informed about study and informed consent for participation was obtained. 3 ml of venous blood was collected in lithium heparin containers and investigated for plasma uric acid, sodium and potassium levels using Mindray BS-200 for measurement of uric acid and Easylyte for measurement of sodium and potassium. Statistical package for social science (SPSS) computer program version 26 was used for data analysis.

Results: The study results showed a significant increase in plasma uric acid (mg/dl) and potassium (mmol/l) in COVID-19 patients when compared to normal individuals without COVID-19, mean$\pm$ SD :(5.45 $\pm$1.89 versus 4.35 $\pm$ 0.79, p- value 0.00), (3.76 $\pm$ 0.65 versus 3.41 $\pm$ 0 .28, p- value 0.00) respectively, while there was significant decrease in plasma sodium (mmol/l) in COVID-19 patients when compared to normal individuals without COVID-19, mean$\pm$ SD: (131.9 $\pm$ 7.10 versus 135.0 $\pm$ 4.54, p- value 0.01).

The study revealed insignificant difference between the mean of plasma uric acid, sodium and potassium according to gender in case group, The mean $\pm$ SD of uric acid in male (5.01 $\pm$ 1.73) versus female (6.10 $\pm$ 1.96) with p value 0.052, plasma sodium in male (132.5$\pm$ 8.24) versus female (130.9$\pm$ 4.96) with p value 0.422, and plasma potassium in male (3.69$\pm$ 0.67) versus female (3.88$\pm$ 0.62) with p value 0.321.

Person correlation showed that there were no correlation between age of patients and the level of uric acid, sodium and potassium, ($r = 0.15$, p value = 0.29), ($r = 0.01$, p value = 0.93), ($r = 0.03$, p value = 0.82) respectively.

Conclusion: the study concluded that the plasma uric acid and potassium levels had increased in Sudanese patients with COVID-19.

المستخلص

الخلفية: في ديسيمبر2019، حدثت سلسلة من الحالات غير النمطية الحادة في ووهان، الصين. انتشرت هذه الحالات سريعا من ووهان إلى مناطق أخرى. سرعان ما اكتشف أن فيروس كورونا الجديد هو المسؤول. الإضطراب في حمض البوليك والصوديم والبوتاسيوم يميل إلى أن يكون شائعا لدى مرضى كوفيد-19.

الهدف: لتقييم مستويات حمض البوليك والصوديوم والبوتاسيوم بين المرضى السودانيين المصابين بكوفيد-19.

الطريقة: أجريت هذه الدراسة في مركز جبرة للعزل بمستشفى جبرة للطوارئ والإصابات بولاية الخرطوم، خلال الفترة من فبراير 2022 إلى أغسطس 2022. تم جمع 100 عينة، 50 عينة من المرضى المصابين بكوفيد-19 و 50 عينة من أشخاص أصحاء كمجموعة تحكم (مجموعة ضابطة) تم اخبارهم بغرض الدراسة واخذ موافقتهم. تم جمع 3 مل من الدم الوريدي في حاويات تحتوي على مانع التجلط ليثيوم هيبارين وتم قياس مستويات حمض البوليك والصوديوم والبوتاسيوم في البلازما بإستخدام جهاز مندري BS-200 لقياس حمض البوليك و جهاز Easylyte لقياس الصوديوم والبوتاسيوم. تم إستخدام برنامج الحزمة الإحصائية للعلوم الإجتماعية (SPSS) النسخة 26 لتحليل البيانات.

النتائج: أظهرت نتائج الدراسة أن مستوى حمض البوليك والبوتاسيوم يزداد في مجموعة مرضى الكورونا مقارنة بمجموعة الأصحاء، المتوسط± الإنحراف المعياري:(1.89± 5.45مقابل ± 4.35 0.79 ، p- value 0.00)، (0.65 ± 3.76 مقابل 28. 0 ± 3.41، p- value 0.00) على التوالي، بينما كان هناك نقصان في مستوى الصوديوم في مجموعة المرضى مقارنة بمجموعة الأصحاء، المتوسط± الإنحراف المعياري: (7.10 ± 131.9مقابل 4.54 ± 135.0 ،p- value 0.010).

أظهرت الدراسة وجود إختلاف ليس ذو أهمية بين متوسط حمض البوليك والصوديوم والبوتاسيوم حسب النوع في مجموعة المرضى، المتوسط± الإنحراف المعياري لحمض البوليك في الرجال(± 5.01 1.73) مقابل (1.96 ± 6.10) في النساء مع p value 0.052، مستوى الصوديوم في الرجال(±132.5 8.24) مقابل (4.96 ±130.9) في النساء مع p value 0.422، مستوى البوتاسيوم في الرجال (0.67 ±3.69) مقابل 0.625 ±3.88) في النساء مع p value 0.321.

تحليل أرتباط بيرسون أظهر عدم وجود علاقة بين عمر المرضى المصابين بالكورونا ومستوى حمض البوليك والصوديوم والبوتاسيوم لديهم (r = 0.15, p value = 0.29)، (r =0.01, p value = 0.93)، (r = 0.03, p value = 0.82) على التوالي.

إستنتاج: توصلت الدراسة إلى أن مستوى حمض البوليك والبوتاسيوم في البلازما يزيد عند المرضى السودانيين المصابين بمرض الكورونا.

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List of abbreviations

Abbreviations	Full term
4.AAP	4-Aminoantipyrine
ACE 2	angiotensin converting enzyme 2
AKI	Acute kidney injury
ALT	Alanine aminotransferase
ANP	Atrial natriuretic peptide
ARDS	Acute respiratory distress syndrome
AST	Aspartate transaminase
AT 2	Type-2 alveolar
ATP	Adenosine Tri-phosphate
AVP	Arginine Vaso-pressin
CAD	Coronary artery disease
CDC	Center for Disease Control and Prevention
COVID-19	Corona virus disease 2019
COVS	Coronaviruses
ECF	Extra cellular fluid
ESR	erythrocyte sedimentation rate
GCSF	Granulocyte colony stimulating factor
GI tract	Gastrointestinal tract
H2O2	Hydrogen peroxide
HPRT	Hypoxanthine phospho-ribosyl-transferase
ICF	Intra cellular fluid
ICTV	International Committee on Taxonomy of Viruses
ICU	Intensive care unit
IL	Interleukin
IP 10	Interferongamma protein-10
ISE	Ion Selective Electrode
LDH	lactate dehydrogenase
LMW	Low molecular weight
MCP-1	Monocyte chemoattractant protein-1
MERS-cov	Middle East respiratory syndrome coronavirus
MIP 1A	Macrophage inflammatory protein-1α
mRNA	Messenger ribonucleic acid
NA	nasal aspirate
n-cov	Novel coronavirus
NP	Nasopharyngeal
OP	Oropharyngeal
PRPP	Hypoxanthine phospho-ribosyl-transferase
PT	Proximal tubules
RAS	renin–angiotensin system
RNA	Ribonucleic acid
RT-PCR	Real-time polymerase chain reaction
SARS-cov	Severe acute respiratory syndrome coronavirus
TNF	Tumor necrosis factor
URTI	Upper respiratory tract infection
WHO	World Health Organization

Chapter one

Introduction, Rationale and Objective

1. Introduction, Rationale and Objectives

1.1Introduction:

In December 2019, a series of acute atypical respiratory disease occurred in Wuhan, China. This rapidly spread from Wuhan to other areas. It was soon discovered that a novel corona virus was responsible. The novel coronavirus was named as the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2, 2019-nCoV) due to its high homology (~80%) to SARS-CoV, which caused acute respiratory distress syndrome (ARDS) and high mortality during 2002–2003(Yuki *et al*., 2020; Perlman, 2020; Bulut and Kato, 2020) ,On February 11th, 2020, the World Health Organization (WHO) announced a new name for disease caused by SARS-CoV-2: CoV disease (COVID-19),and exactly a month later, on March 11th, 2020, It was declared as a pandemic (Ochani *et al*., 2021), SARS-CoV-2 is a novel member of CoVs, which are a large group of highly diverse, enveloped, positive-sense, and single-stranded RNA viruses(He *et al*., 2020).

As recently determined, COVID-19 transmission has been identified to originate from bats but may have been transmitted to humans through other intermediate animals potentially sourced from the local seafood market in Wuhan city, Hubei province, China. Transmission via Aerosols although multiple reports have mentioned that a carrier must be present for SARS-CoV-2 to transmit, there are additional forms of viral transmission that have been observed throughout this pandemic (Sharma *et al.,* 2021).

In the human body, the virus causes COVID-19, a disease characterized by shortness of breath, fever, and pneumonia, which can be fatal in vulnerable individuals (Atzrodt *et al*., 2020), Some people with SARS-CoV-2 infection remain asymptomatic, whilst the infection can cause mild to moderate COVID-19 and COVID-19 pneumonia in others. This can lead to some people requiring intensive care support and, in some cases, to death, especially in older adults (Struyf *et al*., 2022), Initial diagnosis includes collecting the testing sample from the upper respiratory tract. Collection of the sample from nasopharyngeal region for swab-based SARS-COV-2 testing is highly recommended. However, alternatively oropharyngeal specimen, Nasal mid-turbinate swab, anterior nares specimen can also be exploited for the diagnosis purpose. CDC also recommends sampling from the lower respiratory tract for patients complaining of cough and sputum. (MA *et al*., 2020).

COVID-19 is characterized by extra-pulmonary manifestations involving the gastrointestinal tract, the neurological and cardiovascular systems, and the kidneys(Gupta *et al*., 2020), Corona virus disease 2019 (COVID-19) is commonly associated with kidney damage,

patients with COVID- 19 present specific manifestations of proximal tubule dysfunction, as attested by low-molecular-weight proteinuria (70-80%), neutral aminoaciduria (46%), and defective handling of uric acid (46%) or phosphate (19%)(Werion *et al*., 2020),patients with severe coronavirus disease 2019 (COVID-19) and severe acute respiratory syndrome (SARS) can show marked hypouricemia(Chen *et al*., 2021;Hu *et al*., 2021).

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 (Pourfridoni *et al*., 2021),plasma sodium imbalance is a common characteristic feature and associated with severe illness, poor clinical outcome(s) and increased in-hospital mortality in COVID-19 patients.(Hu *et al*., 2020),SARS-CoV-2 binds angiotensin I converting enzyme 2 (ACE2) of renin–angiotensin system (RAS) and causes prevalent hypokalemia (Chen *et al*., 2020), Patients with COVID-19 experience multiple clinical conditions that may cause electrolyte imbalances. Hypokalemia is a concerning electrolyte disorder closely associated with severe complications (Alfano *et al*., 2021; Sarvazad, 2020).

1.2 Rationale:

The recently emerged novel coronavirus, "severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)", caused a highly contagious disease called coronavirus disease 2019 (COVID-19). The virus was first reported from Wuhan city in China in December, 2019, which in less than three months spread throughout the globe and was declared a global pandemic by the World Health Organization (WHO) on 11th of March, 2020. So far, the ongoing pandemic severely damaged the world's most developed countries and is becoming a major threat for low- and middle-income countries (Lone and Ahmad, 2020).The severity of coronavirus disease 2019 (COVID-19) is highly variable between individuals, ranging from asymptomatic infection to critical disease with acute respiratory distress syndrome requiring mechanical ventilation. Such variability stresses the need for novel biomarkers associated with disease outcome. As SARS-CoV-2 infection causes a kidney proximal tubule dysfunction with urinary loss of uric acid, hypothesized that low serum levels of uric acid (hypouricemia) may be associated with severity and outcome of COVID-19(Dufour *et al*., 2021).Animal studies found that COVID-19 uses angiotensin converting enzyme 2 (ACE2)

as a cellular entry receptor ACE2, one of the key enzymes in the renin–angiotensin system (RAS), plays a significant role in regulating fluid and electrolyte balance. Thus, hypokalemia has been described in COVID-19 patients in China (De Carvalho *et al*., 2021). This study assesses the level of serum uric acid, sodium and potassium among COVID -19 patients which can be used as predictors of severity of disease.

1.3 Objectives:

1.3.1 General Objective

To assess plasma uric acid, Sodium and Potassium levels among patients with COVID-19 disease in Jabra isolation center.

1.3.2 Specific Objective

1. To measure plasma uric acid concentration and electrolytes level {Na+,K+} among individuals with COVID-19 (Cases) and without COVID-19 (Controls).
2. To compare between UA, N+ and K+ among individuals with COVID-19 (Cases) and without COVID-19 (Controls).
3. 4. To correlate UA, N+ and K+ with age in COVID-19 paitents.

Chapter two

Literature review

2. Literature review

2.1 History of COVID-19:

Coronaviruses (CoVs) were first isolated from humans in 1962. The CoVs were thought to cause only mild respiratory and gastrointestinal infections in human and animals. The outbreaks of Severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) in 2002–2003 In Guangdong province, China and the Middle East respiratory syndrome coronavirus (MERS-CoV) in the Middle Eastern countries, particularly Saudi Arabia in 2012, changed the prevailing concept on coronavirus infections. Both the viruses originated in bats and their Chain of transmission established between animal to human and human to human. A similar outbreak of pneumonia like respiratory infections, reported from the Wuhan city, Hubei province, China in late December 2019 made a new addition to the list of human CoVs. (Rastogi *et al.,* 2020). The International Committee on Taxonomy of Viruses (ICTV) nominated it as SARS-CoV2 considering it as akin to severe acute respiratory syndrome coronaviruses (SARS-CoVs) species and the disease as COVID-19. As the virus continues to spread around the globe, many countries have imposed lockdown to prevent transmission by social distancing. (Poonam and Gill, 2021)

2.2Taxonomy and classification of coronaviruses:

Coronaviruses are a group of human and animal ribonucleic acid (RNA) viruses arising from the family Coronaviridae, and the subfamily Coronavirinae. Members of the Coronavirinae subfamily are categorized into four genera: α-coronaviruses, β-coronaviruses, γcoronaviruses and δ-coronaviruses. The first two are exclusively found in mammals, while the subsequent two are primarily associated with birds. Human coronaviruses (HCoV) 229E and NL63, alongside many animal viruses, are within the α-coronavirus genus. (Abdul-Fattah *et* al., 2021). In contrast, SARS- CoV, Middle East respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV-2 are classified to β coronaviruses. (Yuki *et al.,* 2020).

2.3 Structure of coronaviruses:

Coronaviruses are enveloped, icosahedral symmetric particles, approximately 80–220 nm in Diameter containing a non-segmented, single-strand, positive-sense RNA genome (Helmy *et al*., 2020). The most notable characteristic of CoV is the club-shaped spike projections protruding from its surface giving it a crown like appearance under the electron microscope; CoV has the largest identified RNA genomes, containing approximately 30 kilo base (kb) genomes. This is packed inside a helical capsid formed by the nucleocapsid (N) protein (Ochani *et al*., 2021; Singhal, 2020).

2.4 Transmission:

The newly identified SARS-CoV-2 has been suspected to extend to humans from bats through pangolins even though conclusive evidence in support of this is yet to be found.

After successful infection of a human host, further horizontal transmission of the SARS-CoV-2 occurs chiefly through human-to-human contact, either directly through respiratory droplets or indirectly by touching contaminated surfaces (Ochani *et al*., 2021). These droplets then can be collected at the mucous membranes of the eyes, nose or mouth of the adjacent person (Al-Qahtani, 2020). Asymptomatic carriers (during the incubation period of the virus) and patients after recovery from the acute form of the disease are also considered a potential source of virus transmission to healthy persons. Interestingly, human coronaviruses are able to survive on steel, metal, wood, aluminum, paper, glass, plastic, ceramic, disposable gowns, and surgical gloves for 2–9 days. High temperature (≥30 ◦C) can reduce the persistence period, while low temperature (4 ◦C) increases the persistence time up to 28 days. Transmission of the virus vertically from mother to fetus or via breast milk has not been confirmed yet (Helmy *et al*., 2020).

2.5 SARS-CoV-2 entry process:

Coronaviruses consist of four structural proteins; Spike (S), membrane (M), envelop (E) and nucleocapsid (N) (Yuki *et al.*, 2020), To enter host cells, coronaviruses first bind to a cell surface receptor for viral (attachment) (Shang *et al*., 2020), The coronavirus spike (S) protein attaches to angiotensin converting enzyme 2 (ACE2) receptors that is found on the surface of many human cells, including those in the lungs allowing virus entry. The coronavirus S protein is subjected to proteolytic cleavages by host proteases (i.e. trypsin and furin), in two sites located at the boundary between the S1 and S2 subunits (S1/S2 site). In a later stage happens the cleavage of the S2 domain (S20 site) in order to release the fusion peptide. This event will trigger the activation of the membrane fusion mechanism. (Boopathi *et al.*, 2020), Once viral contents are released inside the host cells, viral RNA enters the nucleus for replication. Viral mRNA is used to make viral proteins (biosynthesis). Then, new viral particles are made (maturation) and released. (Yuki *et al.*, 2020).

2.6 Epidemiological characteristics:

The outbreak of COVID-19 originated from Wuhan City, Hubei province, in China. Fifty five Percent of the infected cases before 1 January 2020 were linked to the Huanan Seafood Wholesale Market. However, the first human-to-human case of SARS-CoV-2 infection reported on 1 December 2019 did not have any exposure to this market (Helmy *et al*., 2020).

The COVID- 19 pandemic is considered the one among the biggest pandemics to humans. As the pandemic is still ongoing, the number of countries involved confirmed cases and mortality rates are changing every day. As the virus enters different countries at different time points, these countries are at different stages of the outbreak. With this complicity, true epidemiology is only possible at the end of this pandemic (Lone and Ahmad, 2020).

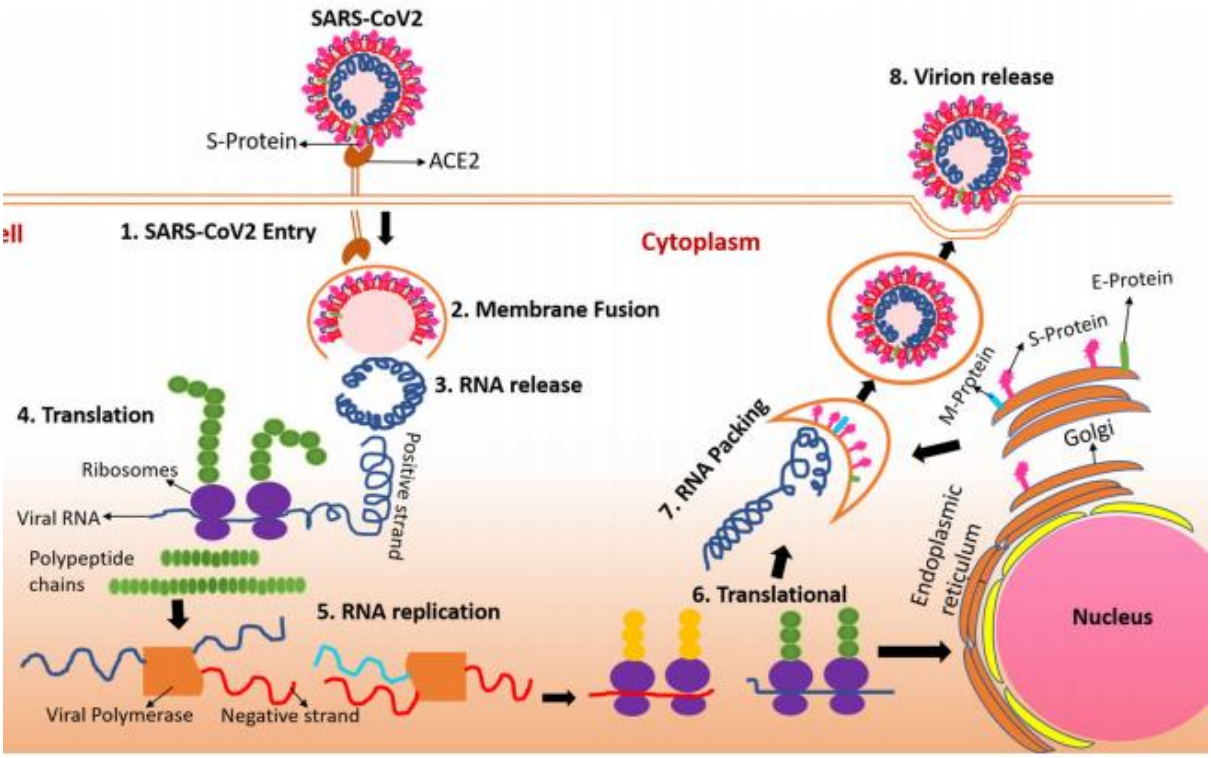

Figure 2.1 The schematic diagram of the mechanism of COVID-19 entry and viral replication and viral RNA packing in the human cell. (Boopathi *et al.*, 2020)**.**

2.7 Diagnosis:

The diagnosis of CoV infection early in the course of the illness is essential to minimize the risk of large-scale outbreaks in hospitals and local communities. The Center for Disease Control and Prevention (CDC) and WHO recommends respiratory specimens for SARS-CoV-2 nucleic acid amplification tests. Screening of asymptomatic patients is conducted using upper respiratory specimens such as nasopharyngeal (NP) swabs, oropharyngeal (OP), nasopharyngeal wash/aspirate or nasal aspirate(NA), throat swab while symptomatic patients or those with productive cough are screened via lower respiratory specimens such as sputum, a lower respiratory tract aspirate and bronchoalveolar lavage. (Ochani *et al.*, 2021). The serological reports of COVID-19 patients show a sharp increase in their C reactive proteins, lactate dehydrogenase (LDH), erythrocyte sedimentation rate (ESR), creatinine kinase,

alanine aminotransferase (ALT), aspartate transaminase (AST), D-dimer and low serum albumin indicating sepsis which may lead to multi-organ failurelduring the later stages of infection. The higher levels of pro-inflammatory cytokines like, IL2, IL7, IL10, granulocyte-colony stimulating factor (GCSF), interferongamma protein-10 (IP10), monocyte chemoattractant protein-1 (MCP1), macrophage inflammatory protein-1α (MIP1A), and TNFα may contribute to "cytokine storm" similar to SARS-CoV1 and MERS . The CT-scans and X-Ray reports of COVID-19 patients revealed the opacities and bilateral diffuse alveolar damage followed by cellular exudates, pleurisy, pericarditis, lung consolidation and pulmonary edema. The nasopharyngeal swab/oropharyngeal swab (upper respiratory tract), sputum, lavage or aspirate (lower respiratory tract) is used for diagnosis. In addition, blood, stool and urine sample are also used for need based diagnosis. The diagnosis is carried by RT-qPCR or by high throughput sequencing of viral genome. (Rastogi *et al.,* 2020).

2.8 clinical manifestations:

The symptom of patients infected with SARS-CoV-2 ranges from minimal symptoms to severe respiratory failure with multiple organ failure. (Yuki *et al.,* 2020; Perlman *et al*., 2020; Bulut and Kato, 2020).

Table (2.1) clinical symptoms associated with COVID-19:

Clinical type	Symptoms
Mild type	Nonpneumonia or mild pneumonia
Sever type	Dyspnea, respiratory frequency>30/min, blood oxygen saturation <93%, partial pressure of arterial oxygen to fraction of inspired oxygen ratio<300, and/or lung infiltrates >50% within 24/48h
Critical type	Respiratory failure, septic shock, and/or multiple organ dysfunction or failure

(He *et al*., 2020).

2.9 Effect of COVID-19 on the organs:

The respiratory system is the most commonly affected. However, the virus can affect any organ in the body. In critically ill patients, multiple organs are often affected. The virus binds to angiotensin converting enzyme 2 (ACE2) receptors present in vascular endothelial cells, lungs, heart, brain, kidneys, intestine, liver, pharynx, and other tissue. It can directly injure these organs. In addition, systemic disorders caused by the virus lead to organ malfunction (Jain, 2020).

2.9.1 Pulmonary effects:

Obviously, respiratory system is the first to bear the brunt of SARS-CoV-2, which as a danger signaling is sent to immune system. As a receptor of S surface protein on SARS-CoV-2, angiotensin converting enzyme II (ACE2) is mainly expressed in type-2 alveolar (AT2) cells (83% in average) and other certain cells such as epithelial cells, which exists widely in various tissues and organs including oral mucosa , airway , lung , colon , kidney and prostate. Depending on the context, lungs are directly under the strongest attack to cause lung inflammation and functional injury. (Shen *et al*., 2022), Pulmonary manifestations in COVID-19 may be mild, moderate, and severe. Mild cases such as upper respiratory tract infection (URTI), cough, or sore throat can progress to moderate and severe degrees. The moderate type of pulmonary presentation of COVID-19 could be pneumonia and fever. The COVID-19 pneumonia type has been reported in some cases as silent pneumonia with fever or silent pneumonia in a sick patient. We found cases of silent hypoxia as a result of silent COVID-19 pneumonia. The severe manifestation of COVID-19 is ARDS. (Elrobaa and New, 2021).

2.9.2 Cardiac effects:

ACE1 as a target receptor for SARS-CoV-2 is significantly expressed in the heart. This transmembrane aminopeptidase involved in the development of hypertension and heart function performs an extremely critical role in the cardiovascular system. Therefore, the possibility of cardiovascular injury or myocarditis should also be considered as a COVID-19 manifestation. (Behzad et *al.,* 2020).In COVID-19, cardiac complications can precede and can occur in the absence of pulmonary and other complications. Ischemic cardiac injury can occur in patients with established coronary artery disease (CAD), those with latent CAD, and those without CAD. (Jain, 2020)

2.9.3 Liver effect:

The pathogenesis of liver injury caused by SARS-CoV-2 is still unclear. Several possible mechanisms are taken under consideration: direct cytopathic effect of the virus through the ACE2 receptor, immune-mediated hepatitis as a result of uncontrolled inflammatory response following COVID-19 infection, leading to cytokine storm syndrome, anoxia as a cause of hypoxic hepatitis due to pneumonia and respiratory failure and drug-induced liver injury secondary to medications used for the treatment, among others, as well as Antipyretic drugs or antiviral agents. (Łykowska-Szuber *et al*., 2021).

2.9.4 Gastrointestinal effect:

The well-established signs and symptoms of COVID-19 patients are fever and respiratory symptoms. However, gastrointestinal symptoms such as diarrhea, vomiting and abdominal pain seem to frequently also be part of the manifestations of the disease. There has been escalating evidence of SARS-CoV-2 RNA being detected in stool specimens, and anal, or rectal swabs, of COVID-19 patients despite the clearance of SARS-CoV-2 in the respiratory cells/upper respiratory tract. Besides that, the angiotensin converting enzyme-2 (ACE-2) receptor is highly expressed in gastrointestinal epithelial cells, particularly the ileum, duodenum, jejunum, caecum and colon. (Thye *et al*., 2021), GI disorders in COVID-19 patients can lead to fluid and electrolyte disturbance (Pourfridoni *et al*., 2021).

2.9.5 Renal effect:

The most important renal manifestation of COVID-19 is AKI, acute kidney injury (AKI) has been reported in up to 25% of critically ill patients with SARS-CoV-2 infection, in particular in those with serious infections, and has been associated with substantial morbidity and mortality, AKI develops more frequently in patients with the most severe diseases (especially ARDS, requiring invasive mechanical ventilation), including elderly patients or those with hypertension or diabetes (Shen *et al*., 2022),Viral overload and co morbidity may play a role in determining the severity of AKI in COVID-19. In high viral overload, the ACE2 receptor has a direct effect from SARS-CoV-2, leading to AKI, and a cytokine storm that results from high infection may lead to AKI (Elrobaa and New, 2021), SARS-CoV-2 infection causes an early and specific dysfunction of the kidney PT characterized by LMW proteinuria, defective tubular handling of uric acid . These transport defects are associated with structural and molecular alterations of PT cells, and detection of particles resembling coronaviruses. The presence of hypouricemia and inappropriate uricosuria is associated with disease severity and outcome (Werion et al., 2020), Binding of SARS-CoV-2 to ACE2 decreases the counter-act of ACE2 on the RAS, which affects electrolyte balance and increases blood pressure (Hu *et al*., 2020).

Due to effect of SARS-COV-2 on gastrointestinal tract and kidney followed by defect in handling of uric acid excretion and disturbance in electrolyte balance we should be measure the level of uric acid, sodium and potassium.

2.10 Uric acid:

Uric acid is the product of catabolism of the purine nucleic acids. Although it is filtered by the glomerulus and secreted by the distal tubules into the urine, most uric acid is reabsorbed

in the proximal tubules and reused. Uric acid is relatively insoluble in plasma and, at high concentrations, can be deposited in the joints and tissue, causing painful inflammation (Bishop *et al*., 2010).

Rena handling of uric acid is complex and involves our sequential steps: (1) glomerular filtration of virtually all the uric acid in capillary plasma entering the glomerulus; (2) reabsorption in the proximal convoluted tubule of about 98% to 100% of filtered uric acid; (3) subsequent secretion of uric acid into the lumen in the distal portion of the proximal tubule; and (4) further reabsorption in the distal tubule. Total urinary excretion of uric acid is 6% to 12% of the amount filtered.

2.10.1 Clinical applications:

2.10.1.1 Hyperuricemia:

Hyperuricemia is most commonly defined by serum uric acid concentrations greater than 7.0 mg/dL (0.42 mmol /L) in men or greater than 6.0 mg/dL (0.36 mmol /L) in women (Burtis and Bruns, 2015).

This elevated level is the result of increased production, decreased excretion of uric acid, or a Combination of both processes.

2.10.1.1.1 Causes of Hyperuricemia:

1. Urate Overproduction:

- Purine rich diet, error of purine metabolism: hypoxanthine phospho-ribosyl-transferase (HPRT) deficiency, Phospho-ribosyl-pyro-phosphate (PRPP) synthetase over activity, cell breakdown or turnover: lymphoproliferative diseases, myeloproliferative disease, polycythemia vera, Paget disease, psoriasis, tumor lysis, hemolysis, rhabdomyolysis, exercise and tissue hypoxia.

2. Decreased Uric acid Excretion:

- Acute or chronic kidney disease, increased renal reabsorption, reduced secretion, hyperparathyroidism, bartter syndrome and Down syndrome (George and Minter, 2021).

2.10.1.2 Hypouricemia:

Is defined as a condition whereby serum urate concentrations are less than 2.0 mg/dL (0.12 mmol /L). It is much less common than hyperuricemia. It may be secondary to any of a number of underlying conditions. Examples include (1) severe hepatocellular disease with reduced purine synthesis or xanthine oxidase activity and (2) defective renal tubular reabsorption of uric acid. Defective reabsorption may be congenital, as in generalized fanconi

syndrome, oracquired. The reabsorption defect may be acquired acutely as a result of injection of radiopaque contrast media or chronically because of exposure to toxic agents (Burtis and Bruns, 2015).

2.10.2 Effects of COVID-19 on the uric acid:

Proximal tubule dysfunction develops in a subset of patients with COVID-19 and is characterized by LMW proteinuria, hypophosphatemia, and hypouricemia due to inappropriate urinary loss of phosphate and uric acid, and neutral aminoaciduria. The PT dysfunction is independent from preexisting kidney disease, glomerular proteinuria, viral load, or toxic medications (Werion *et al*., 2020).

2.11 Sodium:

Na+ is the most abundant cation in the ECF, representing 90% of all extracellular cations, and largely determines the osmolality of the plasma. A normal plasma osmolality is approximately 295 mmol/L, with 270 mmol/L being the result of Na+ and associated anions. Na+ concentration in the ECF is much larger than inside the cells. Because a small amount of Na+ can diffuse through the cell membrane, the two sides would eventually reach equilibrium. To prevent equilibrium from occurring, active transport systems, such as ATPase ion pumps, are present in all cells.

The plasma Na+ concentration depends greatly on the intake and excretion of water and, to a somewhat lesser degree, the renal regulation of Na+. 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 (3) the blood volume status, which affects Na+ excretion through aldosterone, angiotensin II, and ANP (atrial natriuretic peptide) (Bishop *et al*., 2010).

2.11.1 Clinical applications:

2.11.1.1 Hpernatremia:

Hpernatremia is defined as a serum/plasma level more than145 mmol/L. occurs in patients with inadequate access to water or impaired thirst mechanism usually in infants or elderly adults.

2.11.1.1.1 Causes of Hypernatremia:

1. Pure Water deficit:

- Inadequate intake, insensible losses (skin, Respiratory tract (mechanical ventilation)) and renal Loss (Diabetes insipidus).

2. Water and Sodium deficit:

-Extrarenal loss (skin as in burns, Gastrointestinal Tract) and renal Loss (Loop Diuretics, Osmotic diuresis, renal disease, Post obstructive diuresis).

3. Sodium Gain:

-Hyperaldosteronism, Cushing's syndrome, ingestion of salt or baking soda and hypertonic feeding (Agrawal *et al*., 2008).

2.11.1.2 Hyponatremia:

Hyponatremia is defined as a serum/plasma level less than 135 mmol/L. Hyponatremia is one of the most common electrolyte disorders in hospitalized and nonhospitalized patients.Levels below 130 mmol/L are clinically significant. Hyponatremia can be assessed by the cause for the decrease or with the osmolality level.

2.11.1.2.1 Causes of Hyponatremia:

1. Increased sodium loss:

-Hypoadrenalism, potassium deficiency, diuretic use, ketonuria, salt-losing nephropathy, prolonged vomiting or diarrhea and severe burns.

2. Increased water retention:

- Renal failure, nephrotic syndrome, hepatic cirrhosis and congestive heart failure.

3. Water imbalance:

- Excess water intake, pseudohyponatremia (Bishop *et al*., 2010).

2.11.2 Effects of COVID-19 on the sodium:

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).

2.12 Potassium:

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 kidneys are important in the regulation of K+ balance. Initially, the proximal tubules reabsorb nearly all the K+. Then, under the influence of aldosterone, additional K+ is

secreted into the urine in exchange for Na+ in both the distal tubules and the collecting ducts. Thus, the distal nephron is the principal determinant of urinary K+ excretion. Most individuals consume far more K+ than needed; the excess is excreted in the urine but may accumulate to toxic levels if renal failure occurs. K+ uptake from the ECF into the cells is important in normalizing an acute rise in plasma K+ concentration due to an increased K+ intake. Excess plasma K+ rapidly enters the cells to normalize plasma K+. As the cellular K+ gradually returns to the plasma, it is removed by urinary excretion. Note that chronic loss of cellular K+ may result in cellular depletion before there is an appreciable change in the plasma K+ concentration because excess K+ is normally excreted in the urine (Bishop *et al*., 2010).

2.12.1 Clinical applications:

2.12.1.1 Hperkalemia:

Hyperkalemia is defined as a serum or plasma potassium level above the upper limits of normal, usually greater than 5.0 mEq/L to 5.5 mEq/L. While mild hyperkalemia is usually asymptomatic, high levels of potassium may cause life-threatening cardiac arrhythmias, muscle weakness, or paralysis.

Pseudohyperkalemia is quite common and represents a false elevation in measured potassium due to specimen collection, handling, or other causes.

2.12.1.1.1 Causes of Hyperkalemia:

1. Increased Potassium Intake:

- Increased potassium intake from food is a very uncommon cause of hypokalemia in adult patients with normal renal function but can be an important cause in those with kidney disease.

2. Intracellular Potassium Shifts:

- Cellular injury can release large quantities of intracellular potassium into the extracellular space. This can be due to rhabdomyolysis from a crush injury, excessive exercise, or other hemolytic processes. Metabolic acidosis may cause intracellular potassium to shift into the extracellular space without red cell injury.

3. Impaired Potassium Excretion:

- Acute or chronic kidney disease is a common cause of hyperkalemia. Hyperkalemia is usually not seen until the glomerular filtration rate falls below 30 ml/min. This is commonly due to primary renal dysfunction but may be due to acute volume depletion from dehydration or bleeding or decreased circulating blood volume due to congestive heart failure or cirrhosis.

Tubular dysfunction due to aldosterone deficiency or insensitivity can also cause hyperkalemia (Simon *et al*., 2021).

2.12.1.2 Hypokalemia:

Hypokalemia is an electrolyte characterized by low serum potassium concentrations (normal range: 3.5–5.0mEq/L). Severe and life-threatening hypokalemia is defined when potassium levels are <2.5mEq/L.

2.12.1.2.1 Causes of Hypokalemia:

1. decreased intake of potassium

2. Gastrointestinal tract losses:

- Chronic diarrhea, including chronic laxative abuse and bowel diversion, clay (bentonite) ingestion, which binds potassium and greatly decreases absorption and villous adenoma of the colon, which causes massive potassium secretion (rarely).

3. Intracellular shift:

- Glycogenesis during total parenteral nutrition or enteral hyperalimentation (stimulating Insulin release), insulin administration, stimulation of the sympathetic nervous system, particularly with beta 2-agonists (albuterol, terbutaline), thyrotoxicosis (occasionally) due to excessive beta-sympathetic stimulation (hypokalemic thyrotoxic periodic paralysis) and familial periodic paralysis.

4. Renal potassium losses:

- Adrenal steroid excess (Cushing's syndrome), primary hyperaldosteronism, glucocorticoid-remediable congenital adrenal hyperplasia, renal tubular acidosis, fanconi syndrome and hypomagnesemia.

5. Drugs:

- Thiazides, loop diuretics, osmotic diuretics and Laxatives (Kardalas *et al*., 2018).

2.12.2 Effects of COVID-19 on the potassium:

The etiology of potassium abnormalities in COVID-19 patients is multifactorial. In the case of hypokalemia, urinary potassium loss is most likely cause of lowered serum potassium levels, which could be linked to ACE2 utilization by SARS-CoV-2 and the resultant hyperaldosteronism state, or viral-induced tubular injury. As common gastrointestinal symptoms of COVID-19, such as a loss of appetite, diarrhea, or vomiting could also trigger hypokalemia (Noori *et al*., 2021).

2.13 Previous studies:

- Study done by Hu and et al in Zhuhai city, Guangdong province to detect the Association of serum uric acid levels with COVID-19 severity that founds levels in patients with COVID-19 were 2.59% lower, UA/Cr ratios 6.06% lower at admission compared with healthy controls (Hu *et al*., 2021).

- Study done by Dufour and et al to determine the relationship between Serum uric acid, disease severity and outcomes in COVID-19 they found that acute and severe hypouricemia is highly prevalent among patients with COVID-19 requiring hospitalization and is independently associated with disease severity and with progression toward respiratory failure requiring mechanical ventilation. These data suggest that serum uric acid could be used as a reliable biomarker to identify patients at risk of life-threatening COVID-19(Dufour *et al*., 2021).

- Hu and et al in 2020 they found that Sodium balance disorder, particularly hyponatremia, is a common condition among hospitalized patients with COVID-19 in Hubei, China, and it is associated with a higher risk of severe illness and increased in-hospital mortality (Hu *et al*., 2020).

- Study (case –control) done by De Carvalho and et al in Franceto describe electrolyte disturbance and explore risk factors for COVID-19 infection in patients visiting the Emergency department they found that hyponatremia and hypokalemia were independently associated with COVID-19 in adults visiting the Emergency department . Hyponatremia and hypokalemia were more frequent among patients who were infected with COVID-19 than among the controls who were matched for age and sex and after multivariable adjustment. Hyponatremia was also associated with COVID-19 and the most severe presentation of the disease (De Carvalho *et al*., 2021).

- Study achieved by Pourfridoni and et al for investigating the fluid and electrolyte disturbances in COVID-19 patients and the complications that may occur following these disorders in patients found that Hyponatremia, hypernatremia, hypokalemia, hypocalcemia, hypochloremia, 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 (Pourfridoni *et al*., 2021).

- Study done by Alfano and et al at the University Hospital of Modena to estimate prevalence, risk factors and outcome of hypokalemia in a confirmed COVID-19 found that Hypokalemia was a frequent electrolyte disorder in hospitalized patients with COVID-19(Alfano *et al*., 2021).

Chapter three

Materials and methods

3. Materials and Methods

3.1. Study design:

This is a Case control Study.

3.2. Study area:

The study was conducted In Jabra Isolation center at Jabra hospital for emergency and injuries Khartoum state.

3.3. Study duration:

The study was carried out during the period from February 2022 to August 2022

3.4. Study population:

Sudanese patients clinically diagnosed with covid-19 will be selected for this study as case group and compared with healthy subjects as control group.

3.5. Inclusion criteria:

Patients diagnosed with covid-19 by real-time polymerase chain reaction (RT-PCR) assay from naso-pharyngeal swab specimens or by CT scan and meet diagnostic criteria set out by World Health Organization for COVID-19 at jabra isolation center were including in the study as Cases and healthy individual serve as controls.

3.6. Exclusion criteria:

Among cases and controls, any individual with preexisting history of renal disease, chronic renal failure.

3.7. Ethical consideration:

The ethical clearance was approved by the Ethical and Scientific Committee of Medical Laboratory Science College, Sudan University of Science and Technology, permission to carry out the study was taken from jabra isolation center at jabra hospital for emergency and injuries, and verbal consent were taken from patients with COVID-19.

3.8. Sample size:

This study included 50 patients with COVID-19 as case and 50 healthy individual as control (age and gender were matched).

3.9. Data collection method:

Personal data were obtained by reviewing medical questionnaire.

3.10. Collection of sample:

Three ml from venous blood will collected by standard procedure from Sudanese patients with covid-19, into heparinized blood containers and centrifuged at 3000 rpm for 3 min and then the plasma is removed in plain container and stored at 4-8 0C until time of analysis.

3.11. Methods:

3.11.1 Measurement of Uric acid:

Serum uric acid was estimated using Uricase-Peroxidase (Uricase-POD) method using Mindary BS-200. (Appendix II)

3.11.1.1 Principle:

By using ascorbic oxidase to eliminate the interference of ascorbic acid, the uric acid is catalyzed to produce H2O2, which oxidize the 4-AAP to yield a colored dye of quinoneimine. The absorbency decrease is directly proportional to the concentration of uric acid.

3.11.1.2 Reagents:

Reagent 1(R1): phosphate buffer, peroxidase, ascorbate oxidase, toos

Reagent 2(R2): phosphate buffer, peroxidase, 4-Aminoantipyrine, uricase

3.11.1.3 Procedure:

	Blank	sample
Reagent 1	1200 ul	1200 ul
Dist. Water	25 ul	-
Sample	-	25ul

Mix, incubate for 5min at 37c, and read the blank absorbance, then add:

Reagent 2	300 ul	300 ul

Mix thoroughly at 37 c, and read the absorbance again 4-5 min. later

3.11.2 Measurement of sodium and potassium:

Sodium and potassium were estimated using ion selective electrode (ISE) method using Easylyte. (Appendix III)

3.11.2.1 Principle:

An ion selective electrode also known as specific ion electrode (SIE) is atransducer or sensors that convert the activity of a specific ion dissolved in a solution into an electrical potential which can be measured by a voltmeter or pH meter. The voltage is theoretically dependent on the logarithm of the ionic activity, according to the Nernst equation, the sensing part of the

electrode is usually made as an ion- specific membrane, along with a reference electrode (Burtis and Bruns, 2015).

3.12 Data analysis:

Data were analyzed to obtain means, standard deviation and correlation of the sampling using statistical package for social science (SPSS) version 26 computer programs using independent t test and person correlation were applied for correlation between variables and result was expressed as Mean$\pm$ SD and significant difference as p value $\leq$0.05).

Chapter four

Results

4. Results

In this study the results of changes in the serum uric acid, sodium and potassium level were represented in Tables and Figures.

The populations in this study were divided into 50 normal individuals without COVID-19(Controls) and 50 patients with COVID-19(Cases), among Cases there were 30 males and 20 females, while in the controls there were 25 males and 25 females, fifty nine years old was the mean of age among cases and 48 years was the mean of age among controls, as described at Table (4.1).

Figure(4.1): showed distribution of chronic disease among cases and controls, it showed that most of cases (24) have no history of chronic disease, 9 of them have Diabetes mellitus (DM), 11 of them have Hypertension (HTN) and 6 of them have both Hypertension and Diabetes (DM/HTN) while among controls 39 have no history of chronic disease, 6 of them have diabetes mellitus (DM),4 of them have Hypertension (HTN) and 1 of them have both Hypertension and Diabetes (DM/HTN).

Table (4.2): represents the comparison between the mean and standard deviation of uric acid, sodium and potassium in cases versus controls group, the result showed there were significant increase in uric acid (5.45 $\pm$1.89 versus 4.35 $\pm$ 0.79, p- value 0.00), and potassium (3.76 $\pm$ 0.65 versus 3.41 $\pm$ 0 .28, p- value 0.00), while there was significant decrease in sodium (131.9 $\pm$ 7.10 versus 135.0 $\pm$ 4.54, p- value 0.01).

Table (4.3): show the comparison between the mean level of uric acid, sodium and potassium in case group according to gender, The mean $\pm$ SD of uric acid in male (5.01 $\pm$ 1.73) versus female (6.10 $\pm$ 1.96) with p value 0.052, plasma sodium in male (132.57$\pm$ 8.24) versus female (130.90$\pm$ 4.96) with p value 0.422, and plasma potassium in male (3.69$\pm$ 0.67) versus female (3.88$\pm$ 0.62) with p value 0.321 and there were insignificant difference between the mean of serum uric acid, sodium and potassium according to gender.

Figure (4.2): correlation between age and level of uric acid in case group, a scatter plot shows there was no correlation between age and level of uric acid ($r = 0.15$, p value = 0.294).

Figure (4.3): correlation between age and sodium level in case group, a scatter plot shows there was no correlation between age and level of sodium ($r = 0.01$, p value = 0.936).

Figure (4.4): correlation between age and potassium level in case group, a scatter plot shows there was no correlation between age and level of potassium ($r = 0.03$, p value = 0.821).

Table (4.1): Demographics table of study group, sex and mean of age:

Study group	Sex	No. of population	Mean of age± STD
Case (50)	Male	30	59± 14.8
	Female	20	
Control(50)	Male	25	48± 12
	Female	25	

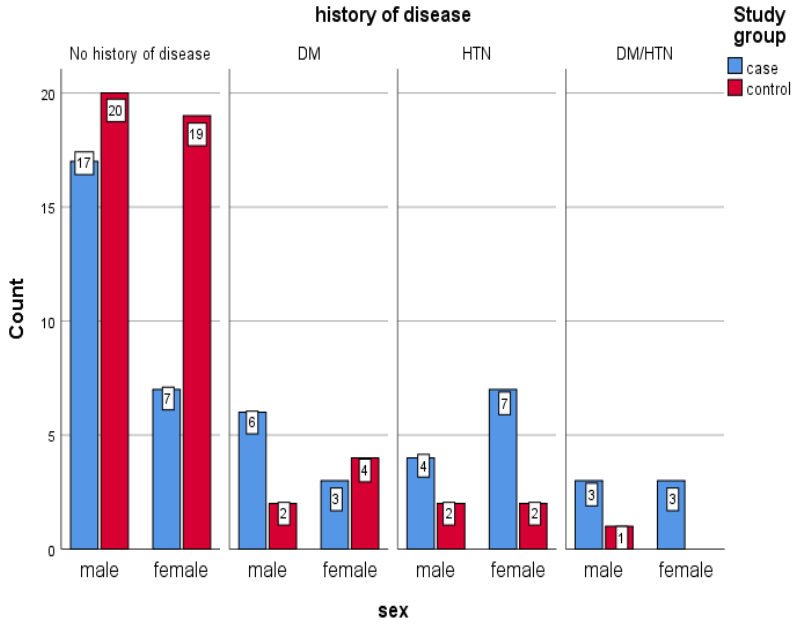

Figure (4.1): Presence of Chronic Disease among Population.

Table (4.2): comparison of plasma uric acid, sodium and potassium level in COVID-19 patients (cases) and healthy individual (controls):

	Study group	Mean± STD	P value
Uric acid (mg/dl)	Case	5.45± 1.89	0.00
	Control	4.35± 0.79	
Sodium (mmol/l)	Case	131.9± 7.10	0.01
	Control	135.0± 4.35	
Potassium (mmol/l)	Case	3.76±0.65	0.00
	Control	3.41± 0.28	

-Independent T-test was used for comparison p value ≤ 0.05 was considered significant.

Table (4.3): comparison of uric acid, sodium and potassium level in case group according to gender:

	Sex	Mean± STD	P value
Uric acid (mg/dl)	Male	5.01± 1.73	0.052
	Female	6.10± 1.96	
Sodium (mmol/l)	Male	132.5± 8.24	0.422
	Female	130.9± 4.96	
Potassium (mmol/l)	Male	3.69± 0.67	0.321
	Female	3.88± 0.62	

- Independent T-test was used for comparison p value ≤ 0.05 was considered significant.

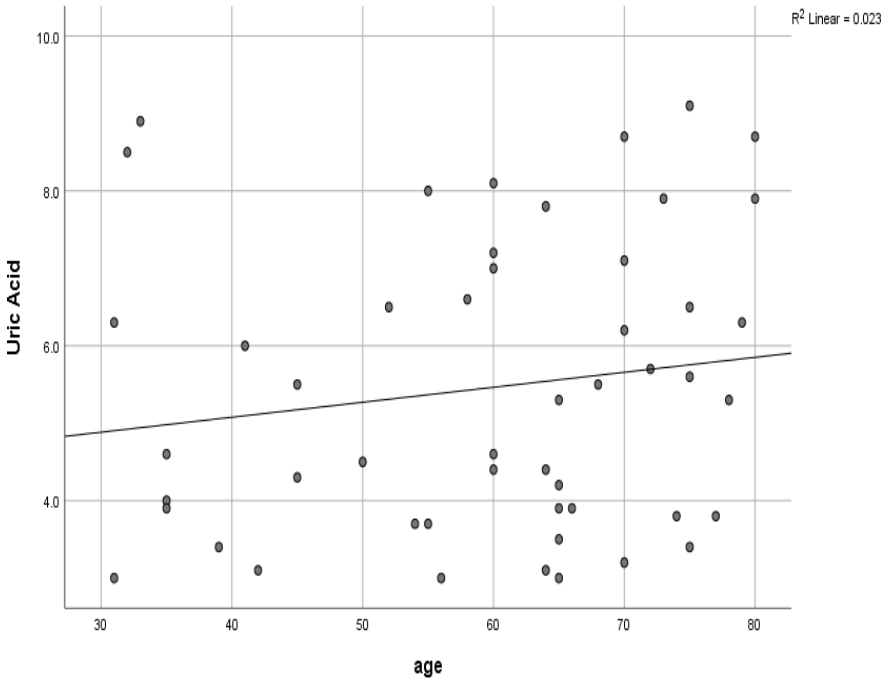

Figure (4.2): correlation between uric acid level and age of COVID-19 patients (r= 0.15, p value= 0.29).

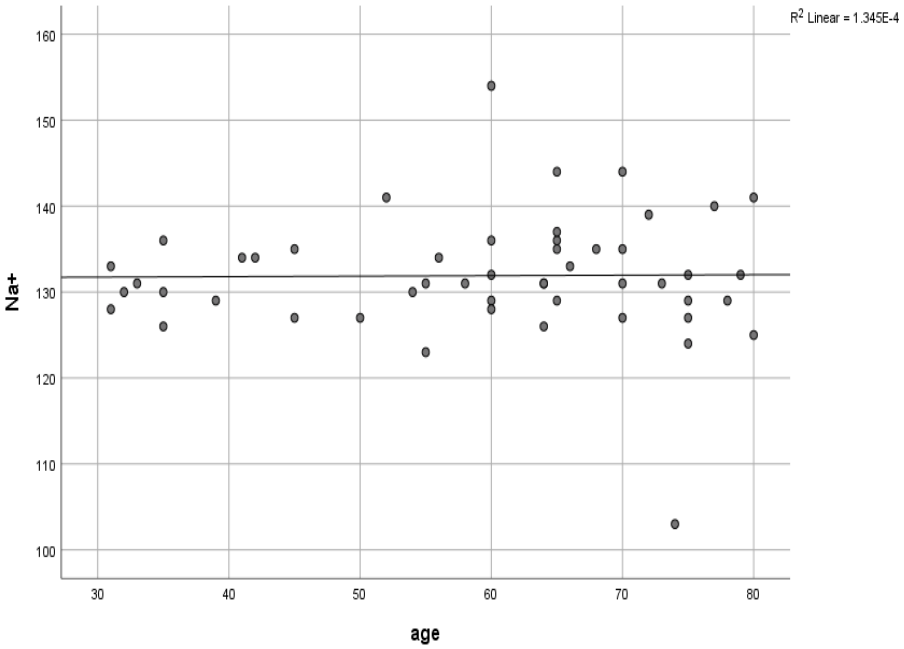

Figure (4.3): correlation between sodium level and age of COVID-19 patients(r=0.01, p value= 0.93).

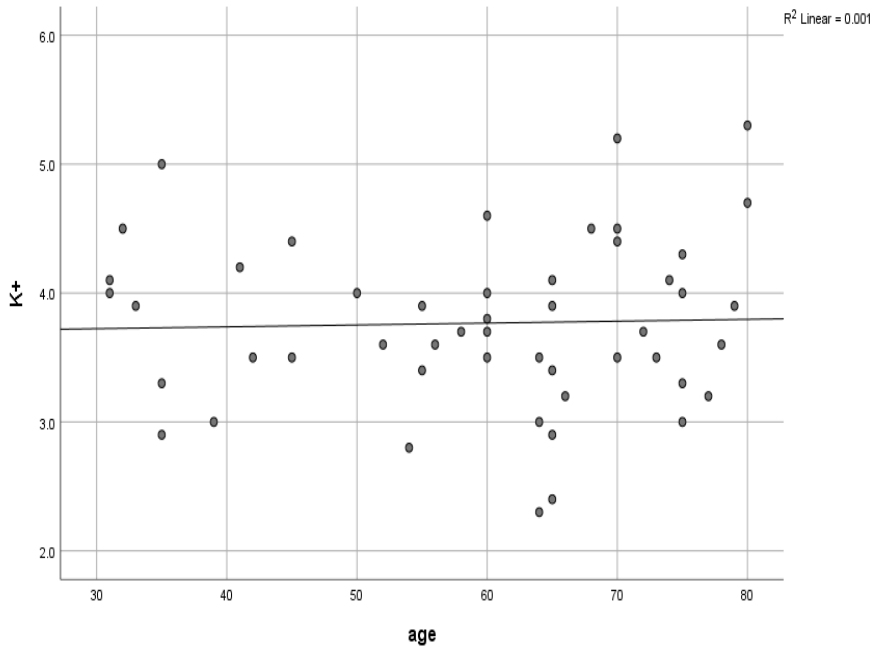

Figure (4.4): correlation between potassium level and age of COVID-19 patients (r= 0.03, p value= 0.82).

Chapter five

Discussion, Conclusion and Recommendations

5. Discussion, Conclusion and Recommendations

5.1 Discussion:

This study conducted to assess the levels of plasma uric acid, sodium and potassium in COVID-19 patients.

The result obtained from this study indicated that, there were significant increasing of uric acid and potassium in the blood of COVID-19 patients when compared with control. Uric acid (p- value 0.00), potassium (p- value 0.00),The result was in agreement with find done by Chauhan and et al which showed that in patients admitted to the hospital for COVID-19; higher serum UA levels were independently associated with AKI, MAKE, and in-hospital mortality in a dose-dependent manner(Chauhan *et al*., 2021). The result agrees with another result which compared the laboratory findings of 59 Covid-19 and 83 non-Covid-19 control group in Japan; found that the potassium level in the Covid-19 group was significantly higher than in the control group [4.10 (4.04–4.02) vs. 3.93 (3.89–3.97); $p< 0.05$](Nakanishi et al., 2020).

The result of uric acid and potassium disagreed with result carried by (Hu *et al*., 2021) which found that UA levels in patients with COVID-19 were 2.59% lower, UA/Cr ratios 6.06% lower at admission compared with healthy controls also disagreed with Study (case –control) done by De Carvalho and et alwhich found that hyponatremia and hypokalemia were independently associated with COVID-19 in adults visiting the Emergency department (De Carvalho *et al*., 2021).

In this study the comparison of level of sodium between case and control showed that, there was significant decrease in the level of sodium in COVID-19 patients compared with control (p- value 0.01),this result was in agreement with previous study carried by (Hu *et al*., 2020) which found that Sodium balance disorder, particularly hyponatremia, is a common condition among hospitalized patients with COVID-19 in Hubei, China, and it is associated with a higher risk of severe illness and increased in-hospital mortality.

In this study sex has insignificant effect in level of uric acid, sodium and potassium and there were insignificant difference between the mean of serum uric acid, sodium and potassium according to gender.

Also study showed there is no correlation between age and level of uric acid, sodium and potassium in case group (r = 0.15, p value = 0.29), (r =0.01, p value = 0.93), (r = 0.03, p value = 0.82) respectively.

5.2 Conclusion:

From the results and findings in this study, it is concluded that, plasma uric acid and potassium levels were increased in COVID-19 patients compared with control group, while sodium was decreased in COVID-19 patients compared with control group.

5.3 Recommendations:

1. Uric acid, sodium and potassium should be regularly monitored in the blood of COVID-19 patients.
2. To obtain reliable results it is recommended to increase sample size in further study.

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Appendices

Appendix I

Questioner:

Sudan University of Science and Technology

Collage of Medical laboratory science

Assessment of plasma uric acid, Sodium and Potassium levels among patients with COVID-19 disease in Jabra isolation center -Khartoum state

Participant code: ……

Age: ……. /Years old

Sex: …….

Hypertension:

Yes ☐

No ☐

Diabetes Mellitus:

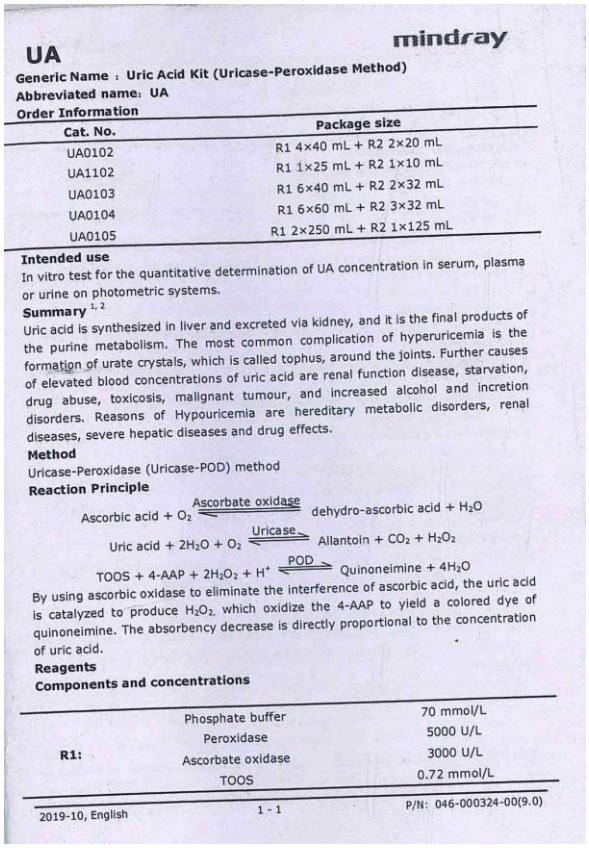
Yes ☐

No ☐

Medication use: ……

Other diseases: ……..

Appendix II



UA

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Generic Name ：Uric Acid Kit (Uricase-Peroxidase Method)
Abbreviated name：UA
Order Information

Cat. No.	Package size
UA0102	R1 4×40 mL + R2 2×20 mL
UA1102	R1 1×25 mL + R2 1×10 mL
UA0103	R1 6×40 mL + R2 2×32 mL
UA0104	R1 6×60 mL + R2 3×32 mL
UA0105	R1 2×250 mL + R2 1×125 mL

Intended use
In vitro test for the quantitative determination of UA concentration in serum, plasma or urine on photometric systems.

Summary [1, 2]
Uric acid is synthesized in liver and excreted via kidney, and it is the final products of the purine metabolism. The most common complication of hyperuricemia is the formation of urate crystals, which is called tophus, around the joints. Further causes of elevated blood concentrations of uric acid are renal function disease, starvation, drug abuse, toxicosis, malignant tumour, and increased alcohol and incretion disorders. Reasons of Hypouricemia are hereditary metabolic disorders, renal diseases, severe hepatic diseases and drug effects.

Method
Uricase-Peroxidase (Uricase-POD) method

Reaction Principle

$$\text{Ascorbic acid} + O_2 \xrightleftharpoons{\text{Ascorbate oxidase}} \text{dehydro-ascorbic acid} + H_2O$$

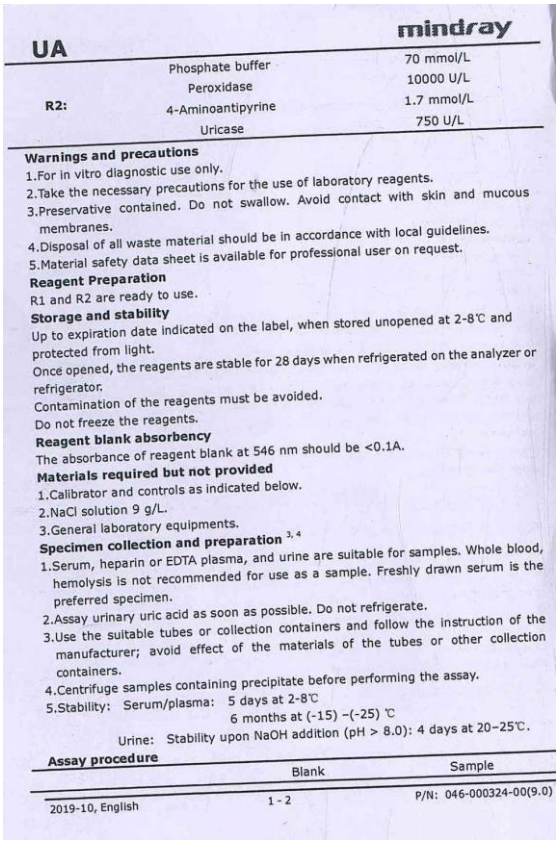
$$\text{Uric acid} + 2H_2O + O_2 \xrightleftharpoons{\text{Uricase}} \text{Allantoin} + CO_2 + H_2O_2$$

$$\text{TOOS} + \text{4-AAP} + 2H_2O_2 + H^+ \xrightleftharpoons{\text{POD}} \text{Quinoneimine} + 4H_2O$$

By using ascorbic oxidase to eliminate the interference of ascorbic acid, the uric acid is catalyzed to produce H_2O_2, which oxidize the 4-AAP to yield a colored dye of quinoneimine. The absorbency decrease is directly proportional to the concentration of uric acid.

Reagents
Components and concentrations

R1:	Phosphate buffer	70 mmol/L
	Peroxidase	5000 U/L
	Ascorbate oxidase	3000 U/L
	TOOS	0.72 mmol/L



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R2:	Phosphate buffer	70 mmol/L
	Peroxidase	10000 U/L
	4-Aminoantipyrine	1.7 mmol/L
	Uricase	750 U/L

Warnings and precautions
1.For in vitro diagnostic use only.
2.Take the necessary precautions for the use of laboratory reagents.
3.Preservative contained. Do not swallow. Avoid contact with skin and mucous membranes.
4.Disposal of all waste material should be in accordance with local guidelines.
5.Material safety data sheet is available for professional user on request.

Reagent Preparation
R1 and R2 are ready to use.

Storage and stability
Up to expiration date indicated on the label, when stored unopened at 2-8℃ and protected from light.
Once opened, the reagents are stable for 28 days when refrigerated on the analyzer or refrigerator.
Contamination of the reagents must be avoided.
Do not freeze the reagents.

Reagent blank absorbency
The absorbance of reagent blank at 546 nm should be <0.1A.

Materials required but not provided
1.Calibrator and controls as indicated below.
2.NaCl solution 9 g/L.
3.General laboratory equipments.

Specimen collection and preparation [3, 4]
1.Serum, heparin or EDTA plasma, and urine are suitable for samples. Whole blood, hemolysis is not recommended for use as a sample. Freshly drawn serum is the preferred specimen.
2.Assay urinary uric acid as soon as possible. Do not refrigerate.
3.Use the suitable tubes or collection containers and follow the instruction of the manufacturer; avoid effect of the materials of the tubes or other collection containers.
4.Centrifuge samples containing precipitate before performing the assay.
5.Stability: Serum/plasma: 5 days at 2-8℃
6 months at (-15) -(-25) ℃
Urine: Stability upon NaOH addition (pH > 8.0): 4 days at 20–25℃.

Assay procedure

	Blank	Sample
Reagent 1	1200 µL	1200 µL
Dist. water	25 µL	—
Sample	—	25 µL
Mix, incubate for 5 min. at 37 ℃, and read the blank absorbance, then add:		
Reagent 2	300 µL	300 µL
Mix thoroughly at 37 ℃, and read the absorbance again 4-5 min. later.		

ΔA = [ΔA sample]- [ΔA blank]

Application sheets for BS series analyzers are available in this document. Refer to the appropriate operator manual for the analyzer-specific assay instructions.

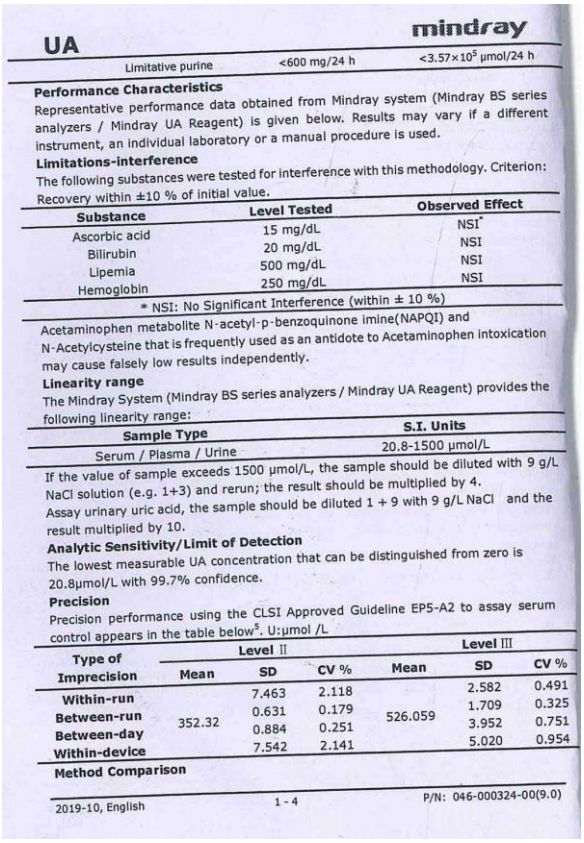
Calibration
1.It is recommended to use the Human multi-calibrator from Mindray and 9 g/L NaCl for two-point calibration. Traceability of the multi-calibrator can refer to the calibrator instructions for use of Mindray Company.
2.Calibration frequency:
After reagent lot changed.
As required following quality control procedures.

Quality control
At least two levels of control material should be analyzed with each batch of samples. In addition, these controls should be run with each new calibration, with each new reagent cartridge, and after specific maintenance or troubleshooting procedures as detailed in the appropriate system manual.
We recommend using the Human Assayed Control made by Mindray to verify the performance of the measurement procedure; other suitable control material can be used in addition.
Each laboratory should establish its own internal quality control scheme and procedures for corrective action if controls do not recover within the acceptable tolerances.

Calculation
The analyzer calculates the UA concentration of each sample automatically after calibration.
Conversion factor: mg/dL x 59.5= µmol/L
Or: C sample =(ΔA sample/ΔA calibration)×C calibration

Reference Intervals [1]
Each laboratory should establish its own reference intervals based upon its patient population. The reference intervals measured at 37℃ listed below were taken from literature:

Sample Type		Conventional Units	S.I. Units
Serum / Plasma	Men	3.6-8.2 mg/dL	214-488 µmol/L
	Women	2.3-6.1 mg/dL	137-363 µmol/L
Urine	Normal diet	<800 mg/24 h	<4.76×10^5 µmol/ 24 h



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Limitative purine	<600 mg/24 h	<3.57×10^5 µmol/24 h

Performance Characteristics
Representative performance data obtained from Mindray system (Mindray BS series analyzers / Mindray UA Reagent) is given below. Results may vary if a different instrument, an individual laboratory or a manual procedure is used.

Limitations-interference
The following substances were tested for interference with this methodology. Criterion: Recovery within ±10 % of initial value.

Substance	Level Tested	Observed Effect
Ascorbic acid	15 mg/dL	NSI*
Bilirubin	20 mg/dL	NSI
Lipemia	500 mg/dL	NSI
Hemoglobin	250 mg/dL	NSI

* NSI: No Significant Interference (within ± 10 %)

Acetaminophen metabolite N-acetyl-p-benzoquinone imine(NAPQI) and N-Acetylcysteine that is frequently used as an antidote to Acetaminophen intoxication may cause falsely low results independently.

Linearity range
The Mindray System (Mindray BS series analyzers / Mindray UA Reagent) provides the following linearity range:

Sample Type	S.I. Units
Serum / Plasma / Urine	20.8-1500 µmol/L

If the value of sample exceeds 1500 µmol/L, the sample should be diluted with 9 g/L NaCl solution (e.g. 1+3) and rerun; the result should be multiplied by 4.
Assay urinary uric acid, the sample should be diluted 1 + 9 with 9 g/L NaCl and the result multiplied by 10.

Analytic Sensitivity/Limit of Detection
The lowest measurable UA concentration that can be distinguished from zero is 20.8µmol/L with 99.7% confidence.

Precision
Precision performance using the CLSI Approved Guideline EP5-A2 to assay serum control appears in the table below[5]. U:µmol /L

Type of Imprecision	Level II Mean	SD	CV %	Level III Mean	SD	CV %
Within-run	352.32	7.463	2.118	526.059	2.582	0.491
Between-run		0.631	0.179		1.709	0.325
Between-day		0.884	0.251		3.952	0.751
Within-device		7.542	2.141		5.020	0.954

Method Comparison

Appendix III