NEAR EAST UNIVERSITY
INSTITUTE OF GRADUATE STUDIES
DEPARTMENT OF MEDIAL MICROBIOLOGYAND CLINICAL MICROBIOLOGY

DETERMINATION OF THE PREVALENCE AND RISK FACTORS OF COVID-19 IN JORDAN

M.Sc. THESIS

Ahmad Ali AL-MHARMAH

Nicosia
February, 2023

NEAR EAST UNIVERSITY
INSTITUTE OF GRADUATE STUDIES
DEPARTMENT OF MEDIAL MICROBIOLOGY AND CLINICAL MICROBIOLOGY

DETERMINATION OF THE PREVALENCE AND RISK FACTORS OF COVID-19 IN JORDAN

M.S.c Thesis

Ahmad Ali Qaied AL-MHARMAH

Supervisor
Assoc. Prof. Emrah RUH

Nicosia
February, 2023

Approval

We certify that we have read the thesis submitted by Ahmad Ali Qaied Al-Mharmah titled **“Determination of the Prevalence and Risk Factors of COVID-19 in Jordan”** and that in our combined opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Science.

Examining Committee	Name-Surname	Signature
Head of the Committee:	Prof. Dr. Nedim Çakır	…………
Committee Member:	Prof. Dr. Waleed Mahmoud Husein Almomani	…………
Committee Member:	Assoc. Prof. Dr. Umut Gazi	…………
Committee Member:	Assist. Prof. Dr. Mehmet İlktaç	…………
Supervisor:	Assoc. Prof. Dr. Emrah Ruh	…………

Approved by the Head of the Department

06 02
…../…../2023

Prof. Dr. Nedim Çakır

Head of Department

Approved by the Institute of Graduate Studies

…../…../2023

Prof. Dr. Kemal Hüsnü Can Başer

Head of the Institute

Declaration

I hereby declare that all information, documents, analysis and results in this thesis have been collected and presented according to the academic rules and ethical guidelines of Institute of Graduate Studies, Near East University. I also declare that as required by these rules and conduct, I have fully cited and referenced information and data that are not original to this study.

Ahmad Ali Qaied Al-MHARMAH

06/02/2023

Acknowledgements

Firstly, I would like to thank God for completing my thesis, and I thank my University, Near East University for giving me opportunities to accomplish my thesis, especially the Department of Medical Microbiology and Clinical Microbiology.

I am greatly thankful to my academic advisers who guided me in this process. I would like to thank Assoc. Prof. Dr. Emrah Ruh, I am very grateful to him for this thesis, from which I learned a lot, and thank him for his support, examination, and supervision of thesis. I also extend my great thanks and gratitude to Prof. Dr. Waleed Mahmoud Husein Almomani for his help and useful guidance. I owe a deep sense of gratitude of Assist. Prof. Dr. Özgür Tosun for her help in statistical analysis for this thesis.

I sincerely thank Diamond Medical Laboratory and its staff for providing me all information that was needed regarding my thesis project. Finally, I would like to thank every person support me, taught me and stood by me in my journey, thank you.

Ahmad Ali Qaied AL-MHARMAH

Abstract

Determination of the Prevalence and Risk Factors of COVID-19 in Jordan

Al-Mharmah, Ahmad Ali Qaied

M.Sc., Department of Medial Microbiology and Clinical Microbiology

Supervisor: Assoc. Prof. Dr. Emrah Ruh

February 2023, 71 pages

Aim: The primary aim of this study was to determine the prevalence of COVID-19 in Jordan. The secondary objective was to evaluate the risk factors associated with COVID-19 in the Jordanian population.

Methods: A cross sectional study was conducted to collect data from study participants between December 2020 and February 2021. Study population included 2500 participants. The study was conducted in Diamond Medical Laboratory, Jordan. Study procedure included filling a questionnaire that was prepared for this study and taking nasopharyngeal swabs for the molecular test. Reverse transcription-polymerase chain reaction (RT-PCR) was performed for the COVID-19 test. Statistical analysis was carried out using SPSS version 21. Level of significance was accepted as 0.05.

Results: In the study 1500 of the study participants were tested positive for COVID-19 by RT-PCR. The data of the study showed that 95.3% of the participants with COVID-19 were symptomatic, and the most frequent symptoms were loss of smell and taste (71.9%), fever (37.7%), fatigue (22%), dry cough (18.3%), difficulty breathing (65.2%), and muscle or joint pain (60.6%). The results also showed low commitment level of using protective measures. In the study, previous diagnosis with COVID-19 was found to significantly reduce the rate of current COVID-19 ($p \leq 0.001$). Lifestyle impacts showed that current COVID-19 was under the significant effect of number of people living in house ($p \leq 0.001$), and number of people in the workplace ($p = 0.003$).

Conclusion: The study showed that 95.3% of the participants with COVID-19 were symptomatic. The statistical analysis showed that factors such as the number of people living in house and the workplace significantly affected the presence of COVID-19.

Keywords: COVID-19, pandemic, symptomatic, WHO, lifestyle.

Table of Contents

CHAPTER I

CHAPTER II

CHAPTER III

CHAPTER IV

CHAPTER V

CHAPTER VI

List of Tables

List of Figures

List of Abbreviations

ACE2:	Angiotensin-Converting Enzyme 2
AI:	Artificial intelligence
CDC:	Centers for Disease Control and Prevention
cDNA:	Complementary deoxyribonucleic acid
CoV:	Coronavirus
COVID-19:	Coronavirus Disease 2019
CT:	Computed tomography
DUTP:	Deoxyuridine triphosphate
E gene:	Envelope glycoprotein gene
ELISA:	Enzyme-linked immunosorbent assay
FDA:	Food and Drug Administration
HCoV-HKU1:	Human coronavirus HKU1
HCoVs:	Human coronaviruses
IFN-α:	Interferon Alpha
IFN-β:	Interferon Beta
IgG:	Immunoglobulin G
IgM:	Immunoglobulin M
IRB:	Institutional Research Board Committee
M gene:	Membrane gene
M:	Mean
MERS-COV:	Middle East respiratory syndrome Coronavirus
mRNA:	Messenger Ribonucleic Acid
N gene:	Nucleocapsid Protein Gene
Nacl:	Sodium Chloride
NCSCM:	The National Center for Security and Crisis Management
ORF:	Open Reading Frames

PCR:	Polymerase Chain Reaction
PPE:	Personal protective equipment
RBD:	The receptor binding domain
RecA:	Recombination Protein A
RNA:	Ribonucleic acid
RNase P:	Ribonuclease P
RT-PCR:	Reverse Transcription Polymerase Chain Reaction
S gene:	Spike gene
SARS-COV:	Severe Acute Respiratory Syndrome Coronavirus
SARS-CoV-2:	Severe Acute Respiratory Syndrome CoronaVirus 2
SD:	Standard Deviation
UNG:	Uracil DNA glycosylase
UNRWA:	The United Nations Relief and Works Agency
WHO:	World Health Organization

CHAPTER I

Introduction

Since December 2019, an unknown illness referred to as pneumonia of unknown purpose took place in Wuhan. In a few days, the unknown agent of this strange pneumonia was identified as a distinct coronavirus (nCoV) by independent medical laboratories (Ashour et al., 2020). The virus that causes this disease has been termed as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Coronavirus disorder 2019 is the name given to the functional inflammatory illness (COVID-19) (He et al., 2020).

Besides the currently ongoing COVID-19, Comparable epidemic respiratory disorders, such as SARS-COV (severe acute respiratory syndrome Coronavirus) which was firstly discovered in November 2002 and MERS-COV (Middle East respiratory syndrome Coronavirus) which was firstly discovered in September 2012, have been related to respiratory infections. This virus has similarities with MERS-CoV and SARS-CoV. (Lai et al., 2020; Zhang et al., 2020). MERS and SARS viruses can be transmitted to humans from camels and civet cats, respectively (Rabi et al., 2020). SARS-CoV-2 spreads from animals to humans, and according to studies, bats or pangolins are the intermediate host (Shehata et al., 2022)

The severity of the COVID-19 pandemic has been escalating since 2019 (Lu et al.,2020). Coronaviruses (CoVs) are a collection of exceptionally diverse, enveloped, positive-sense, and single-stranded RNA viruses. The reason numerous illnesses concerning respiratory, enteric, hepatic, and neurological structures ranging in severity amongst human beings and animals (He et al., 2020). The levels of infection seen in excessive SARS and MERS range from asymptomatic or mild illnesses to severe respiratory tract infections in people. Fever, coughing, dyspnea, watery diarrhea, myalgia, extremely low lymphocyte counts, prolonged coagulation profiles, heart illness, and unexpected death are among the symptoms (Huang et al., 2020). Fortunately, there's no any fatalities and rather infrequent effects on children (Singhal et al.,2020).

SARS-CoV-2 is extremely contagious (Adhikari et al., 2020). There is a lack of understanding regarding how COVID-19 viruses move from host to host (Sohrabi et al., 2020). The vectors of COVID in humans are respiratory droplets, aerosols, and contaminated surfaces (Adhikari et al., 2020; Lai et al., 2020). In order to combat COVID-19, a number of nations all over the world have implemented a variety of preventive and control measures in their respective healthcare systems. Individual preventive measures include keeping a three-foot social space between persons, frequently washing hands, using hand sanitizers, avoiding handshakes and kisses, avoiding direct contact with sick people, particularly those who have respiratory illnesses, as well as wearing face masks (Janakat et al., 2020; Lai et al., 2020).

Jordan is a country that is located in the Eastern Mediterranean region. It has a population of approximately 10.6 million people and a total land area that covers 89,342 square kilometers (Al-Tammemi, 2020). Jordan’s neighboring countries are Saudi Arabia and Syria, in addition to Iraq and Palestine (Al-Tammemi, 2020). Since the beginning of the COVID-19 outbreak, the government of Jordan has been following the instructions that have been provided by the World Health Organization (WHO) carefully and has been providing regular updates. To lessen the possibility of COVID-19 spreading throughout Jordan, a number of preventive and control measures have been implemented at both the national and municipal levels (Muthu et al., 2021).

The National Center for Security and Crisis Management (NCSCM) in Jordan is the organization working to combat the pandemic. This crisis task force is made up of specialists who come from a diverse assortment of departments, fields, and organizations. The members of this task force are constantly looking for recommendations that are supported by evidence, and then they put those recommendations into action (Muthu et al., 2021). In relation to the recent outbreak of the disease, the relevant authorities regularly update and disseminate any new information. In order to identify positive cases, as well as carry out random virus testing and surveillance, specialized teams were dedicated to epidemiological surveillance travel. It is the responsibility of the Centers for Disease Control and Prevention (CDC) to ensure that all of their efforts are properly coordinated (Al-Shaikh et al., 2021).

The government published daily updates on the number of fatalities, confirmed cases, and recovered individuals. In order to keep up with the most recent developments in digital health, the Ministry of Health and the Ministry of Digital Economy and Entrepreneurship have worked together to develop a website in Arabic language for COVID-19 (Al-Tammemi, 2020). Jordan is a very popular country to visit due to its status as a well-known tourist destination and is one of the reasons that led to the continuous increase in the number of cases of corona infections (Al-Shaikh et al., 2021). The government began to implement strict rules and regulations concerning travel, education, religious and social gatherings, and employment in a variety of industries (Muthu et al., 2021). First, travelers arriving in the Jordan from countries with high COVID-19 transmission rates had their temperatures measured, and if a positive test for fever was obtained, the traveler was placed in quarantine (Muthu et al., 2021).

The service delivery locations have been carefully selected in order to provide for the needs of the entire populace, including governmental and non-governmental organizations. The Ministry of Health, Royal Medical Services, UNRWA, university hospitals, Ministry of Youth-sponsored sports facilities, as well as a variety of other public and private organizations offer vaccination clinics. Jordan started its COVID-19 immunization program on January 13, 2021, and enrolment opened on December 24, 2020. More than 300,000 people registered via the online system within the first month of registration. (Ala'a Al-Shaikh et al.,2021). Given the dearth of available treatment options and the virus's quick spread, vaccination would be a war against SARS-CoV-2 pandemic. Recent emergency approval from the US Food and Drug Administration (FDA) was given to American company Pfizer/BioNTech December 11, 2020 and Chinese company Sinopharm December 18, 2020 (Meo et al., 2021). 4.14 billion vaccination doses had been given in over all the world until the beginning of August 2021, and 1.14 billion people (14.6 percent of the population) were considered fully immunized (Alqassieh et al., 2021). The major objective of a vaccination program is to decrease serious illness as hospitalization and death, scheduled two-dose of vaccine's showed extremely high efficacy with respect to this end aim (Heath et al., 2021).

Aim of the Study

This study aims to explore the prevalence rates with increasing numbers of COVID-19 cases, it became crucial to study the prevalence and risk factors of the disease. Therefore, the most important goal of this research was to assess the prevalence of COVID-19 patients in Jordan during a certain period. The secondary objective of the study was to evaluate the risk factors associated with COVID-19 in the Jordanian population.

CHAPTER II

Literature Review

2.1. Origin of Coronaviruses

The family *Coronaviridae* contains all of the coronaviruses (subfamily *Coronavirinae*). The spikes of the Coronavirus are shaped like crowns, which is how the virus got its name (Rabi et al., 2020). Humans, birds, and mammals are all susceptible to the respiratory, neurologic, gastrointestinal, and hepatic illnesses that are caused by CoVs (Weiss and Leibowitz, 2011). Seven different human coronaviruses (HCoVs) are capable of infecting people, causing infections ranging from mild to severe and possibly even fatalities (Dhama et al., 2020).

The effects of the Corona epidemic on the global economy have exceeded those related to health due to closures, partial or complete loss of income, and negative effects on global markets (Nicola et al., 2020). In addition, the genetic makeup of the virus has undergone certain mutations, which are referred to as mutant variations. This has led to an increase in the problems that are associated with the possibility of pandemic waves. Because of this, there is an increased risk of failing to contain the epidemic. There have been reports of differences in Alpha, Beta, and Delta variants in a number of countries and regions across the world. These differences have been spotted in a variety of places. In December of 2020, investigators in the United Kingdom made the momentous discovery that the Alpha variant was the first of its kind to be found. This revelation accompanied a new era in the study of genetic diversity. Following this, the Beta variant was discovered in South Africa, and the Delta variant was discovered in Brazil (Dhama et al., 2020).

CoVs are a group of viruses that are able to infect humans as well as animals and are known to be a potential cause of gastrointestinal and respiratory conditions (Masters et al., 2006). In the past, it was thought that human infection was connected to infections of the upper respiratory tract that were moderately severe and caused by HCoV. The discovery of SARS-CoV in the year 2003 marked a significant turning point in our understanding of historical events (Stadler et al., 2003). Researchers established that there was a link between HCoVs and diseases that affect the respiratory system. Human coronavirus HKU1 (HCoV-HKU1) is a type of coronavirus in humans and animals that is responsible for persistent lung disease (Woo et al., 2005). MERS-CoV was linked to pneumonia as well as the occasional failure of the kidneys, while HCoV was linked to infections in the upper and lower respiratory tracts of children and adults worldwide (van der Hoek et al., 2004; Zaki et al., 2012).

Both the SARS-CoV and the MERS-CoV caused global outbreaks of coronaviruses in the years 2002–2003 and 2011, respectively. These outbreaks put the entire world at risk of a pandemic in both of these instances. An outbreak of SARS-CoV in 2002 and an outbreak of MERS-CoV in 2012 were both caused by newly discovered coronaviruses of the genus Beta-coronavirus that have a zoonotic origin (de Wit et al., 2016; Cui et al., 2019). In addition, research indicated that SARS-CoV and MERS-CoV would be capable of infecting humans in addition to camels, bats, cows, and civets, which could lead to acute respiratory illnesses in humans that have the potential to be fatal (Hilgenfeld et al., 2013).

2.2. SARS-CoV (2003) and MERS-CoV

Concern on a global scale was raised in response to the discovery that the MERS-CoV first appeared on the Arabian Peninsula. This virus is responsible for the SARS. This is due to the fact that MERS-CoV is the virus responsible for an acute respiratory disease that is almost always fatal. There is a high degree of similarity between the symptoms of this disease and those of SARS (De Groot et al., 2013; Hajjar et al., 2013). Estimates provided by the WHO indicate that death was reported in 43% of individuals who were infected with the MERS-CoV (De Groot et al., 2013). This ratio, which varies depending on a person's age as well as the gender is significantly higher than the ratio for SARS, which was 15% (Penttinen et al., 2013). The origin of Corona virus is almost certainly animal (Hijawi et al., 2013). Several case clusters, which included patients in health care facilities as well as members of the same family, demonstrated minimal human-to-human transmission of MERS-CoV; however, the extent of each of these cases was extremely limited. The MERS coronavirus is contagious when it comes into contact with skin or droplets. MERS-CoV has the potential to become airborne and spread throughout the hospital during invasive procedures involving the respiratory system. Early diagnosis and the robust implementation of infection prevention and control programs are essential for preventing the spread of an epidemic (Hajjar et al, 2013). Since there is currently neither a vaccine that can prevent the disease nor an antiviral treatment that is effective, it is necessary for alternative treatments to be discovered (Hajjar et al, 2013).

Even though human coronaviruses weren't found until the 1960s, it's highly likely that they've been circulating for a much longer period than that. Around 120 years ago, HCoV-OC43 began to spread from cattle to humans and is now considered an endemic virus (Vijgen et al., 2005). SARS caused an outbreak of pneumonia that occurred all over the world in 2003 and resulted in 800 deaths across 30 countries (Van der Hoek, 2007).

A severe respiratory illness and kidney failure were contributing factors in the death of a Saudi Arabian businessman in the month of June in 2012. He was a local of Saudi Arabia during his life. Following this, the virus was reported in hospitals as isolated cases, relatively small clusters, and caused widespread outbreaks all at the same time. There were confirmed cases of the disease in a number of countries, including Jordan, Saudi Arabia, Qatar, the United Kingdom, Germany, the United Arab Emirates, Tunisia, France, and Italy. Every event either took place in the Middle East or was connected to the region (Van der Hoek, 2007).

For the newly discovered coronavirus, MERS-CoV was named by the International Committee on Taxonomy of Viruses' Coronavirus Study Group in May 2013. The progression of the outbreak was used as a basis for determining this classification (De Groot et al., 2013). Both the Reverse transcription polymerase chain reaction (RT-PCR) testing and the virus isolation from respiratory secretions both came back positive for the presence of MERS-CoV (Benoit et al., 2013). On the other hand, MERS is a beta coronavirus that belongs to lineage C. This is in contrast to SARS-CoV, which is also a beta coronavirus belongs to lineage B. MERS-CoV is also distinct from human beta coronaviruses OC43 and HKU1, both of which belong to lineage b (Penttinen et al., 2013; Zaki et al., 2013). This virus is genetically related to bat coronaviruses that were discovered in both Africa and Eurasia (Augustina et al., 2011). VM314, the virus that is most closely related to MERS-CoV, is only 1.8% different from it, whereas HKU5 is 5.5%–5.9% different from it (Augustina et al., 2011). In their study, MERS-CoV sequences were collected from 21 Saudi cases and 9 genomes that had been previously published. It was discovered, as a result of two separate investigations, that dromedary camels in Egypt, the Canary Islands, and Oman might have been affected in the past. There were no reports of infections in humans found (Perera et al., 2013).

SARS-CoV-2 infection and transmissibility levels are much more than MERS-CoV and SARS-CoV. In spite of the fact that COVID-19 is linked to relatively low death rates, the virus is still dangerous to people's health (Reynolds et al., 2021). For this reason, acquiring an understanding of the etiology of SARS-CoV-2, the immunological evasion, and the progression of the disease is an absolute necessity (Reynolds et al., 2021).

2.3. SARS-CoV-2 Structure

A beta coronavirus, or SARS-CoV-2, is a coronavirus that is a member of the *Coronaviridae* family (Wu et al., 2020). Ribonucleic acid (RNA) virus that is coated, resembles a sphere, and has good judgment The genome is thought to be thirty thousand bytes in size and contains eleven genes that together code for twenty different proteins that can carry out their designated functions (Wu et al., 2020). A 5' untranslated region, 5' replicas polysaccharide protein gene open reading frames (ORF), membrane glycoprotein gene (M), envelope glycoprotein gene (E), spike glycoprotein gene (S), and nucleocapsid protein gene (N) (Figure 1), are all parts of SARS-CoV-2 . A 3' untranslated region in the virus' DNA that cannot be translated is also present (Zhou et al., 2020; Thye et al., 2021). Significant sequence conservation exists between the SARS-associated coronavirus 2 nonstructural protein 13 (CoV-2 Nsp13) and the coronavirus 2 nucleocapsid protein (CoV-2 N). Both of their amino acid sequences demonstrate this. Treatments for SARS-CoV-2 will be more effective if the CoV-2 Nsp13 and CoV-2 N viruses are well understood (Gurung, 2020; Gussow et al., 2020; Mirza and Froeyen et al., 2020).

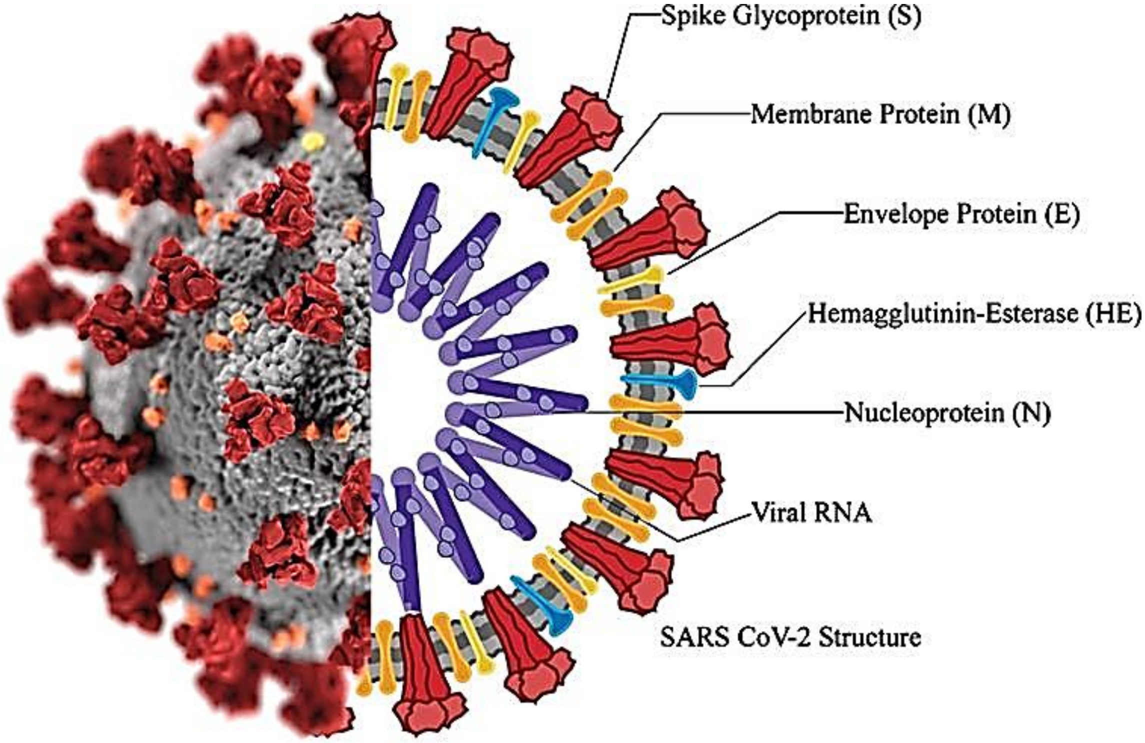

Figure 1. SARS-CoV-2 structural diagram (Mittal et al., 2020).

There are 596 unique amino acids that make up the CoV-2 Nsp13 protein, and all of them can be found in the ORF1ab polyprotein between positions 5,325 and 5,925. These amino acids make up the protein (Gurung, 2020). CoV-2 Nsp13 possesses five domains and has a structure that is comparable to that of SARS-CoV Nsp13 and MERS-CoV Nsp13. Additionally, it has a shape that is comparable to that of SARS-CoV Nsp13(Mirza and Froeyen, 2020). The pyramid-shaped CoV-2 Nsp13 protein comprises a Recombination Protein A (RecA)-like helicase subdomain (1A) that forms the triangular base, an N-terminal zinc-binding domain, a helical "stalk" domain, a beta-barrel 1B domain, and a helical "stalk" domain that forms the triangular base. In addition to this, the Nsp13 molecule contains a helical domain that is referred to as the "stalk" (Mirza and Froeyen, 2020; Newman et al., 2021). Nsp13 proteins are present in both SARS-CoV and MERS-CoV, and the structures of these proteins are extremely similar (Mirza and Froeyen, 2020; Newman et al., 2021). CoV-2 Nsp13 is a helicase that is responsible for unwinding single RNA in addition to its role as a 5'-triphosphatase that caps viral messenger ribonucleic acid (mRNA). This is because it also caps viral mRNA (Min et al., 2021). The ability of CoV-2 Nsp13 to inhibit the signaling of type I interferon demonstrates the adaptability of the virus during viral infection (Lei et al., 2020; Xia et al., 2020). During infection, SARS-CoV-2 suppresses the activation of the immune system, which suggests that CoV-2 Nsp13 prevents the activation of interferon alpha (IFN-α) and Interferon-β (IFN-β) and functions as an immune regulator (Vazquez et al., 2021).

There are 413 different amino acids that make up the CoV-2 N protein, and it is this protein's function to bind to the genomic RNA that is contained within nucleocapsids (Kang et al., 2020). It has an impact not only on the reproduction of viruses but also on the signaling between cells (Carlson et al., 2020). There is a protein in all coronaviruses that is referred to as CoV-2 N (McBride et al., 2014). Coronavirus 2N, also referred to as CoV-2 N, is highly immunogenic and is the root cause of an intense immune response (Aboagye et al., 2018; Smits et al., 2021). Because it can stimulate an immune response that is capable of protecting humans from infections caused by coronaviruses, CoV-2 N was suggested as a possible candidate for use in a vaccine (Yang et al., 2009; Shi et al., 2015). It was demonstrated that CoV-2 N possesses three of these putative genetic determinants. This study was carried out by combining machine learning strategies with more traditional research methods, one of which was the application of genome comparison technology. It is possible that CoV-2 N will become an important target in the fight against COVID-19 (Gussow et al., 2020).

Researchers were under the impression, at one point in time, that the N protein was a viral RNA-binding protein. Due to the fact that it is capable of binding to RNA, it is able to interfere with the function of host mRNAs and, as a result, the host itself (Nabeel-Shah et al., 2022). This protein may be responsible for certain cellular activities since it binds to DNA in a manner that is not particularly specific (Tang et al., 2005; Zhao et al., 2021).

2.4. History of COVID-19.

Even though the coronavirus has been linked to human illness as far back as the 1960s, the discovery that it is also linked to epidemics is a relatively new one. The outbreak of COVID-19, which is the third major coronavirus epidemic in the past 20 years, is having a negative impact on the economies of all countries in the world. The Nidovirales family, which also includes the *Coronaviridae* contains SARS-CoV-2 (King et al., 2011). Both the Coronavirinae and the Torovirinae are collectively known as the Virinae family. These two subfamilies are distinct from each other. Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus are coronavirus genera. In the past, researchers were able to distinguish between the various lineages of betacoronavirus, which were given the letters A, B, C, and D respectively. Within the betacoronavirus family, there are several different subgenera. Embecovirus (lineage A), Sarbecovirus (lineage B), Mercovirus (lineage C), and Nobecovirus are some examples of the subgenera that fall under this category (lineage D). The virus that causes SARS is known as betacoronavirus/sarbecovirus 2, also known simply as SARS-CoV-2. Coronaviruses are spherical, encapsulated, and pleiomorphic viruses. Their size can range anywhere from 80 to 120 nanometers, and they can be either positive or negative. The surface of the virus is covered in protrusions that resemble clubs and are shaped like spikes (Fehr and Perlman, 2015). The name of the virus comes from the distinctive appearance of the coronavirus, which is characterized by spikes. According to the findings of the researcher, all viruses can be eradicated by heating at 56^{o}C for 30 minutes. In order to prevent the replication of coronaviruses, disinfectants with active ingredients chlorine, peracetic acid, and ethanol in a concentration of 75% are necessary (Yang and Wang, 2020).

2.5. Epidemiology of COVID-19

SARS-CoV-2 and the coronaviruses that have been discovered in bats and pangolins, in addition to SARS, share a connection with one another (Li et al., 2021; Temmam et al., 2021). It wasn't until December of 2019 that the first confirmed case was discovered, and it was in Wuhan, which is located in Hubei Province in China. Customers or visitors to the Huanan Seafood Wholesale Market were those who were found to be infected in the earliest cases that were reported (Xinhua News, 2020). There is a possibility that human-to-human transmission started much earlier (Shereen et al., 2020). It is very likely that the virus is zoonotic and that it was transmitted from bats or a species that is related to bats (Paden et al., 2018).

On December 31, 2019, the first confirmed case of the disease was found (Riou et al., 2020). In the beginning, a number of countries did not test individuals who exhibited only mild symptoms because they thought it was unnecessary (Ng et al., 2020). Being overweight, having diabetes, struggling with mental illness, and having multiple illnesses are all factors that increase the likelihood of developing a serious illness (Hales et al., 2020; Pal and Bhadada, 2020).

In a meta-analysis in China that was carried out in the year 2020, it was discovered that there was a comparatively small number of patients younger than 20 years old (Ou et al., 2020) (figure 2). People under the age of 30 had a lower risk of becoming infected with the disease, developing symptoms, or getting tested for it. A study that was carried out in China came to the conclusion that there is no difference in the likelihood of infection between children and adults of any age (Bi et al., 2020).

The fundamental reproduction number, R0, is a factor that can influence the degree to which a newly discovered pathogen can be contained (Fraser et al., 2004; Anderson and May, 2010). The case data from Wuhan were used in the first epidemiological studies to estimate the geographical spread of the virus. These studies were conducted in China. The generation interval was parameterized utilizing data from earlier coronavirus epidemics SARS-CoV and MERS-CoV in addition to data from early SARS-CoV-2 transmission pairs. Before the shutdown of Wuhan, it was anticipated that R0 would fall somewhere in the range of 2 to 4, but it ended up being closer to 3. The disparities that were discovered between these estimations are primarily attributable to the method that was utilized for the purpose of parameterizing the generation interval (Park et al., 2020).

The response to this inquiry is determined by the percentage of diseases that present either no symptoms at all or very few symptoms (and their transmission potential). In order for the infection to take place, it must first be passed on from asymptomatic carriers to susceptible hosts. In the beginning, it was unknown how common infections had few or no obvious symptoms. The results of mass screening and surveillance of passengers on cruise ships and airplanes where outbreaks occurred in the months of February and March of 2020 indicated that 18 to 31% of those individuals had asymptomatic infection (Mizumoto et al., 2020; Nishiura et al., 2020). According to the preliminary data, it was discovered that the disease had a relatively low prevalence, particularly among younger age groups. Experiments with contact tracing showed an increased infectivity around the onset of symptoms, with frequent transmission from presymptomatic and moderately symptomatic individuals (He et al., 2020; Johansson et al., 2021), and less frequently transmission from completely asymptomatic individuals (He et al., 2020; He et al., 2021; Johansson et al., 2021; Qiu et al., 2021), In contrast to SARS-CoV-1 and MERS-CoV, SARS-CoV-2 is a coronavirus that has the potential to start a pandemic that affects the entire world (Koelle et al., 2022).

2.6. COVID-19 Transmission

Aerosols, which are airborne particles, are responsible for the transmission of the coronavirus from animals to humans as well as between humans (Van Doremalen et al., 2020). Camels, pigs, turkeys, mice, dogs, bats, and cats are just some of the animals that can act as the viral reservoirs. Bats are known to be responsible for transmitting the virus to humans (Anthony et al., 2017). Around the year 1960, it was widely believed that infections with the coronavirus in humans were the root cause of colds. In later years, scientists made the discovery that the coronavirus is the infectious agent that causes respiratory illness. Before the SARS-CoV epidemic in 2002, a wide variety of coronavirus subtypes were responsible for causing mild respiratory infections (Fehr and Perlman, 2015). These viruses are represented by the following strains: HCoV-229E, HCoV-NL63, HCoV-OC43, and HCoV-HKU1 (Fehr and Perlman, 2015).

Both the SARS-CoV and the MERS-CoV are members of the family *Coronaviridae* and have large RNA genomes that are interpreted in a constructive manner. Both of these coronaviruses have the potential to cause severe respiratory disease (De Wit et al., 2016). The majority of coronaviruses, the most well-known of which are SARS-CoV and MERS-CoV, are thought to have originated from bats (Drexler et al., 2016). The primary mode of transmission for SARS-CoV and MERS-CoV is through nosocomial infection; 43.5%–100% of MERS cases linked to individual outbreaks were associated with hospitals. The clinical manifestations of SARS and MERS are similar to one another. It's possible that the same pathophysiological mechanisms can explain how MERS and SARS work (Petrosillo et al., 2020).

In China, the city of Foshan reported the first case of an atypical form of pneumonia connected to SARS-CoV in November of 2002 (Zhong et al., 2003). After this, the disease rapidly spread throughout the world, prompting the WHO to classify it as a "global health threat"(Xu et al., 2004). More than 300 cases of the disease were documented after it was found in China, and the vast majority of those affected were people who worked in healthcare. Tourists who were already infected with the virus were the ones responsible for spreading it to Hong Kong, Vietnam, and Canada (Guan et al., 2004). The WHO along with a network of research facilities began their investigation into the potential causes of SARS in March of 2003. During their investigation of SARS cases from the same year. The hypothesis that the virus is unique was shown to be correct by genetic testing, which also demonstrated that It is just weakly correlated towards other coronaviruses, with 50 to 60% of the nucleotide sequences similar.. The SARS epidemic caused difficulties in public health as well as in the economy, particularly in China (Huang et al., 2004). In the beginning, many people believed that the epidemic would rapidly spread throughout the entire world and trigger a global economic downturn. Isolation of infected, identification of contacts, and separation of infected people all contributed to the successful containment of the virus (Anderson et al., 2004). The SARS epidemic, which began in December 2002 and lasted until July 2003, resulted in the infection of 8096 people and the death of 774 people across 27 countries (Petrosillo et al., 2020). A few additional SARS cases were attributed to zoonotic transmission at the tail end of 2003. These cases most likely involved civet cats (*Paguma larvata)*. Since then, there have been no reported cases of the SARS virus in humans anywhere in the world (Wang et al., 2005). The SARS epidemic had a significant influence on people's health despite the fact that mortality and morbidity rates were lower than average. An unusual causative virus, rapid nosocomial transmission, and the susceptibility of hospitals and healthcare workers all contributed to a significant rise in the level of concerns regarding the outbreak (Chang et al.., 2004).

A case of pneumonia and renal fever was reported in Saudi Arabia in June of 2012, ten years after the SARS-CoV was discovered for the first time. The patient's sputum contained the recently discovered coronavirus MERS-CoV, which was found in the sputum (Zaki et al., 2012). In April of 2012, the city of Zarqa in Jordan was the epicenter of an outbreak of a respiratory infection, which took place prior to the identification of the first MERS patient in Saudi Arabia (Hijawi et al., 2013). Eleven people were diagnosed with the illness, eight of whom worked in healthcare facilities; unfortunately, one of these individuals was fatally affected. The epidemiological and laboratory investigations that were conducted at the time of the outbreak produced results that were inconclusive, which meant that the cause of the disease could not be determined. Following the discovery of the novel coronavirus infection in the Arabian Peninsula, respiratory and serum samples from two people who had passed away were retested. The results confirmed the presence of MERS-CoV in both of these individuals. As infected individuals moved from one location to another, the disease quickly disseminated across the globe. The vast majority of MERS infections that were brought into the country were acquired in medical facilities (De Wit et al., 2016).

In May of 2015, South Korea was able to confirm the presence of its first MERS patient who originated from the Middle East. A total of 186 cases, including 36 fatalities and 138 recoveries, were confirmed to have been caused by the virus (Ki, 2015). Because of the movement of patients between hospitals, the MERS outbreak that took place in Korea involved transmission not only within the hospitals but also from one hospital to another. Hospital-acquired MERS was found in a total of 16 patients, making it the area outside of the Middle East with the greatest number of cases. According to the WHO, there have been 2,494 laboratory-confirmed cases of MERS disease as of November 2019, with 858 fatalities reported across 27 countries (Petrosillo et al., 2020). In addition to fever, the patients also possibly experienced shortness of breath and a dry cough. Among the cases of pneumonia that were widely reported, there were some tests that came back with negative results. There were indications of problems with the digestive tract, such as diarrhea (Petrosillo et al., 2020).

Some of the laboratory-confirmed cases of MERS-CoV infection were asymptomatic, which means that no clinical symptoms were present despite a positive test result. This is one of the ways in which the virus can spread from person to person. Most cases that exhibited no symptoms were identified as a result of contact tracing (Whitelaw et al., 2020). There have been multiple studies that point to dromedary camels as a possible reservoir host for the MERS-CoV virus and a source of the MERS infection in humans. There is still a lack of understanding regarding the specific role that dromedaries play in the transmission of viruses (Reeves et al., 2015).

2.7. Receptor Coronavirus

The structural basis for the identification of CoV-2, the SARS-receptor. A new type of SARS-CoV-2 that has recently emerged and is rapidly spreading in humans is what causes COVID-19. The receptor recognition mechanism of the virus, which controls infectivity, pathogenicity, and host range, must be understood in order to combat the pandemic. The ACE2 receptor is shared by SARS-CoV-2 and SARS-CoV in humans. Here, it was established that the receptor binding domain (RBD) of the SARS-CoV-2 spike protein has a crystal structure with aid from the enzyme angiotensin-converting enzyme 2 (ACE2).In comparison to the SARS-CoV RBD, the SARS-CoV-2 RBD has a more compact ACE2-binding ridge, and different residue changes strengthen two virus-binding hotspots at the RBD-ACE2 interface. These structural traits raise the SARS-CoV-2 RBD's propensity for ACE2-binding. Also found that the human ACE2 receptor is used by the bat coronavirus RaTG13, which is closely related to the SARS-CoV-2 virus. There is a chance that SARS-CoV-2 could be transmitted from animal to human due to differences in ACE2 recognition between SARS CoV-2, SARS-CoV, and bat coronavirus RaTG13(Shang et al., 2020), (Figure 2).

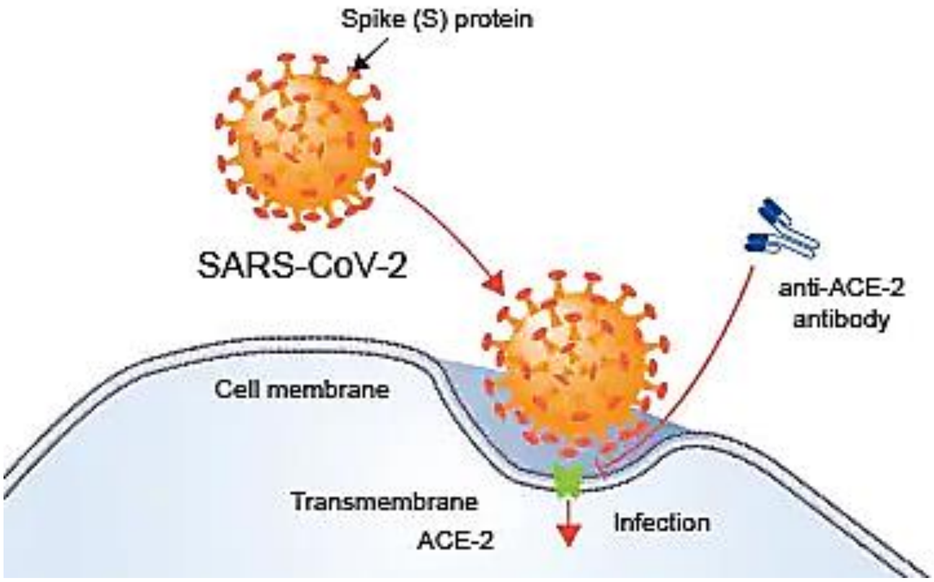

Figure 2. ACE-2 is the host cell receptor responsible for mediating infection by SARS-CoV-2, the novel coronavirus responsible for COVID-19 (Zu et al., 2020).

2.8. Diagnosis of COVID-19

It is very important to make a prompt diagnosis of COVID-19 to prevent the spread of the virus. It is generally acknowledged that computed tomography (CT), is the method that provides accurate results when determining whether COVID-19 is present in a patient. The contrast medium CT scan, on the other hand, is made up of hundreds of slices, each of which can be challenging to interpret, which can lead to diagnostic delays. With the assistance of artificial intelligence (AI), and more specifically deep learning, the diagnosis of COVID-19 based on these scans could potentially be simplified and completed in a timelier manner. The molecular diagnostic test and the imaging diagnostic test are two of the most important tests that can be used to establish whether an individual has COVID-19 (Minglei et al., 2022).

The Reverse Transcription-Polymerase Chain Reaction (RT-PCR), is a molecular diagnostic test that is typically used to determine the presence of COVID-19 (Minglei et al., 2022). On the other hand, RT-PCR testing for COVID-19 has the potential to produce a false negative result due to an insufficient amount of viral material in the specimen. In spite of these limitations, this laboratory test that is currently being used is still considered to be the most reliable method for identifying COVID-19 (Minglei et al., 2022).

In order to have an accurate and timely diagnosis of thrombosis and thromboembolic complications in hospitalized COVID-19 patients, it is necessary to take into consideration the patient's medical history, the outcomes of laboratory tests that reflect hemostasis, the findings of the physical examination, and/or the findings of focused imaging investigations (Gsecka et al., 2021).

Patient lower respiratory tract RT-PCR analysis were done. Feces and nasal and oral swabs were also collected. Nucleic acid test findings depend on illness progression, testing methodologies, and reagents. Sample collecting procedure can also affect outcomes. In addition, several factors might alter nucleic acid test results, making it difficult to draw conclusions (Wiley, 2022).

In conclusion, the current SARS-COV-2 tests use nasopharyngeal or oral swabs to detect the genetic material of the virus by RT-PCR test. The tests are unable to distinguish between people who contracted an infection, recovered, and then overcame it. For the detection of COVID-19, ELISA method which is based on antibody detection for immunoglobulin M (IgM) and immunoglobulin G (IgG) antibody, viral protein of specific interest and patient antibodies are "sandwiched" between reporter antibodies and patient antibodies, enabling the identification of functional patient antibodies (Sethuraman et al., 2020).

Chapter III

Methodology

3.1. Design of Study and participants

The study's sample collection occurred between December, 2020 and February, 2021. A total of 2500 Participants were included in the study, the study was conducted on participants living in all governorates of Jordan. Participants who had a positive result of COVID-19 RT-PCR test was (n=1500), control group (n=1000) consisted of Participants who have a negative result for COVID-19 RT-PCR test.

The samples were chosen using a straightforward random sampling procedure from the auditors living in all governorates of Jordan, staff and patients of the Diamond Medical Laboratory were invited to participate, this project was conducted at Diamond Medical Laboratory, Amman, Jordan. after obtaining the approval of the Institutional Research Board Committee (IRB) at Near East University (NEU).

3.2. Nasopharyngeal Swab Specimen Collection

Under aseptic conditions, important procedures have been followed for the volunteer doctors in collecting study samples. Followed by using of disinfectants, Personal protective equipment (PPE), and be careful not to be infected with the disease. All volunteers were asked to remove and replace the nose masks before taking a nasopharyngeal swab to reduce the risk of virus release causing coughing Furthermore, volunteers were washed their hands and use hand hygiene before taking the swab. After taking flocked swab from volunteer putted in RNA preservation solution tube. It is an inactivated virus solution tube and non-sterile, only used for the collection and transportation of virus samples was performed using Zybio kit.

3.3. Experimental design

A questionnaire from the auditors was used to conduct the first phase of this investigation living in all governorates of Jordan and the staff and patients of the

Diamond Medical Laboratory. The second section included Reverse transcription polymerase chain reaction (RT-PCR) analysis for the sample study.

3.3.1. Questionnaire

Both the face validity and the constituent of the questionnaire were carefully examined to see whether using it in the current study was appropriate. When evaluating the content validity of the questionnaire, experts who are familiar with the causes of COVID-19 and available treatments determined that the items were appropriate. Face validity was confirmed by a pilot study that examined the usefulness and intelligibility of the questionnaire items. The questionnaire's translation from forward to backward ensured that its scientific assumptions were preserved.

A questionnaire was designed to collect information from the study population and all volunteers were informed for the purpose of the study. The questionnaire was designed to contain Four parts that were reported in this study. The first section included demographic variables (gender: male, female; age (years); level of education, ranging from never been to school, to postgraduate; marital status: married, single; number of living people living in the household; and having children).

The second section included the reasons for being tested for COVID-19 two main questions:

1- Why are you giving sample for COVID-19 PCR test at the moment?
2- Do you have one or more of the following symptoms at the moment?

The final segment contained past positive COVID-19 diagnoses and included three primary questions.

1- If a previous COVID-19 diagnosis was positive, the following questions must be addressed.
- Did you spend time in the Intensive Care Unit?
- Has anyone in your family tested positive for COVID-19?
2- How many people in your family have tested positive for COVID-19?

3- Excluding your household, was anyone with whom you had contact (family, friend) diagnosed with COVID-19?

The Third portion addressed risk factors such as smoking, substance abuse and underlying illnesses.

The Fourth component on work conditions included employment status, style, if the work is performed inside, interaction with others as a prerequisite of the job, whether the workplace is congested, travel, and the use of disinfectants.

The questionnaire was translated into Arabic by English and Arabic language specialists.

3.3.2. Reverse transcription polymerase chain reaction

Nasopharyngeal swabs were collected by a trained physician from patients during a home visit. The collected swabs were stored in an ice box at 2–8 C until lab arrival. Viral nucleic acid extraction was performed using Zybio kits by EXM3000 Zybio machine which is a high-tech device that uses the magnetic bead method to separate and purify nucleic acids. Its advantages include more effective extraction, lower size, and safer operation. the extraction time takes 9 minutes for every 32 samples. After the viral nucleic acid extraction, COVID-19 would be identified in our laboratory (Diamond Lab) by QuantStudio 1 Real-Time PCR System using one of two kits. The first kit is the LiliFTM COVID-19 Multi Real-time RT-PCR Kit, which uses the reaction of a specific primer and fluorescent probe with a sample to identify the novel coronavirus using the probe method of Real-time RT-PCR. RNA-dependent RNA polymerase (RdRP) and envelop (E) gene, markers for finding novel coronaviruses, can be found using the LiliFTM COVID-19 Multi Real-time RT-PCR Kit. Additionally, the united states centers for disease control and prevention (US CDC) Nucleocapsid (N) gene and ribonuclease P (RNase P) gene, which can validate the accuracy of all test reactions, have been adopted and created for simultaneous detection. Zybio kits are the second kit; The Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Ribonucleic acid (RNA) prepared in step one was reverse-transcribed to generate complementary deoxyribonucleic acid (cDNA) in RT-PCR reaction system Additionally, it was combined with certain primers and probes (created using the conserved open reading frame (ORF1ab) and (N gene) sequences) for PCR amplification. Qualitative detection of SARS-COV-2 was realized by monitoring the change of fluorescence signal intensity during RT-PCR amplification. Uracil DNA glycosylase (UNG) and deoxyuridine triphosphate (DUTP) were aiming to reduce the potential for PCR amplification products contamination during detection. In the interim, it is possible to prevent false negative results in PCR amplification by combining exogenous positive control. Regarding these kits, the positive control used virus containing the SARS-CoV- 2 target fragment sequence while the negative control used 0.9% sodium chloride (Nacl).

3.4. Statistical Analysis

Data were evaluated using descriptive statistics to determine the traits of the study population. There were percentages, a mean (M), and a standard deviation for the variables (SD). Data were compiled using Microsoft Excel, and statistical analysis was done using IBM SPSS Version 20 of the Statistical Package for the Social Sciences (v20). Using the Chi-Square test, the connection between the variables was examined.

3.5. Ethical Approval

The Institutional Research Board Committee (IRB) at Near East University granted approval for this investigation (NEU). Jordan's ministry of health also offers this service.

Chapter IV

Results

4.1. Features of the study population

The total number of completed surveys was 2500. Approximately, the male to Female ratio showed slightly female predominance (56.2%, n=1405). The mean age of participants at time of the study was 33.65 years with Standard deviation of 12.14 (33.65 ±12.14 years). The median of the age 30 years. The minimum and maximum ages were 10 , 80 years ,respectively. The participants belong to each age categories were noticed (24.0% of participants from 10-25 years of age category, 25.28% of participants from 25-30 years of age category, 26.8% of participants from 30-40 years of age category, and 23.92% of participants from 40-80 years of age category).

The vast majority of participants residence in Amman (85.92%, n=2148) having a Bachelor degree, (n=1297, 51.88%). Approximately half of participants were married (n=1274, 50.96%), and the remaining percentage (49.04%, n= 1226) was single. The highest proportion of the participants belong to the middle socioeconomic level (55.68%, n=1392) followed by low socioeconomic level (37.00%, n=925), and high socioeconomic level (7.32%, n=183). Approximately, 86.32% (n=2158) of participants do not belong to the medical sectors, whereas 13.68% (n=342) were health care providers distributed as a follow, (n=31, 1.24%) were nurses; (n=30, 1.2%) were a doctor; (n=10, 0.4%) were a pharmaceutical; and (n=13. 0.52%) were a laboratory technician as shown in Table 1.

Majority of participants were non-smokers (78.00%, n= 1950) whereas 19.16% of participants were smokers with smoking duration ranged from less than a year to 49 years.

Table 1.

General features of the study population.

Variables		Frequency	
		N	%
Gender	Male	1095	43.80
	Female	1405	56.20
Age category*	10-25 years	600	24.00
	25-30 years	632	25.28
	30-40 years	670	26.8
	40-80 years	598	23.92
Area of residence	Amman	2148	85.92
	Others	352	14.08
Educational level	Never went to school	286	11.44
	Primary School	249	9.96
	High School	605	24.2
	Pre-graduated	1297	51.88
	Post-graduated	63	2.52
Marital status	Single	1226	49.04
	Married	1274	50.96
Socioeconomic status	Low level	925	37.00

		Middle level	1392	55.68
		High level	183	7.32
Smoker		Yes	479	19.16
		No	1950	78.00
		Quit	71	2.84
Work sector	Healthcare provider	Doctor	30	1.2
		Nurse	31	1.24
		Pharmaceutical	10	0.4
		Laboratory technician	13	0.52
		Dentist	258	10.32
	Non health care provider	Unemployed/ student	923	36.92
		Not reported	1235	49.4

N: Number, %: Percentage, *Age categories were based on quartiles: The quartiles were determined based on age distribution and range for the whole study sample.

4.2. Prevalence of COVID-19 infection in the study population

The prevalence of COVID-19 infection among tested nasopharyngeal swabs was 60% resulted from 1500 samples out of 2500 samples as shown in the Figure 3. The participants were asked about the reason of COVID-19 testing; the highest proportion (67.32%) of participants were tested for COVID-19 because they had a symptom of COVID-19. This was followed by the history of contact with infected persons (29.64%) (Figure 4). Wide variety of different relationships with infected persons was reported; contacted with infected Friend (n=178, 24.02%), contacted with infected Colleague (n=137, 18.49%), and contacted with infected member of family as mother, father, uncle, aunt, brother and sister, (n=115, 15.52%) were the primary suspected sources of COVID-19 infection among participants (Table 2). Minority of participants (1.08%, n=27) reported a history of previous COVID-19 infection at the time of tested for COVID-19 during this study (Figure 5).

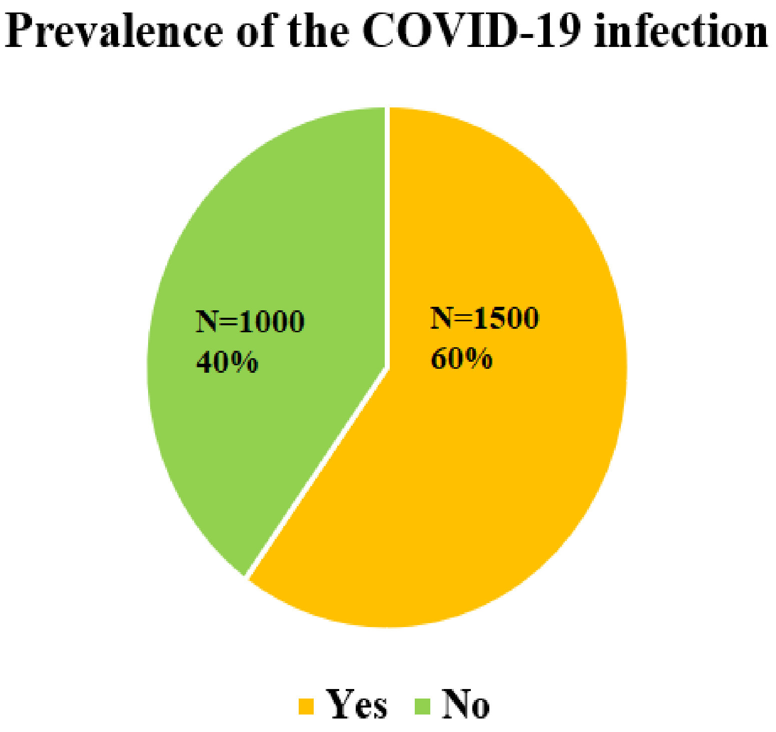

Figure 3: Prevalence of COVID-19 infection

.

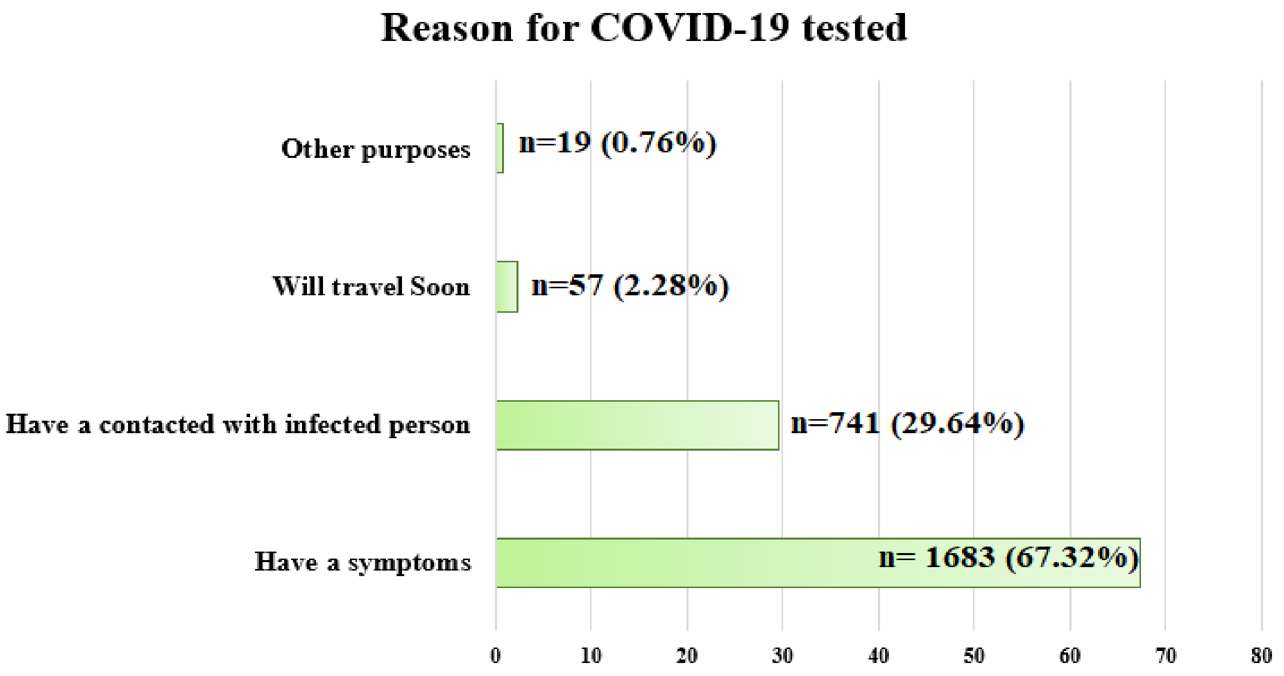

Figure 4: The reasons that required a COVID -1 9 PCR

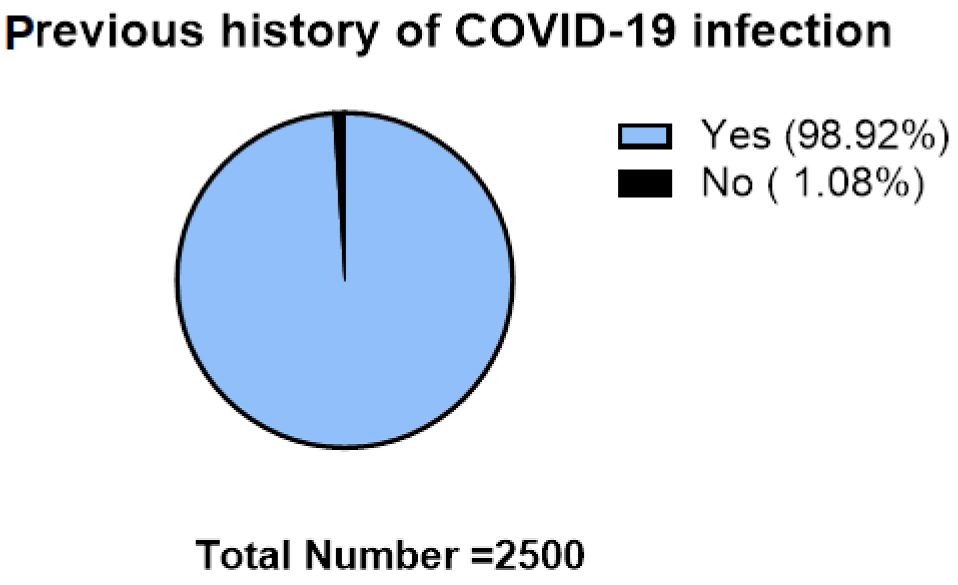

Figure 5: Proportion of participants with a previous history of COVID-19 infection

Table 2.

Frequency of contacted infected COVID-19 patients with tested participants.

Relationship	Frequency	
	N	%
Friend	178	24.03
Colleague	137	18.49
Uncle	115	15.53
Brother	83	11.20
Cousin	37	4.99
Sister	34	4.59
Mother	29	3.92
Relatives	24	3.24
Aunt	19	2.56
Father	15	2.02
Infected patient	10	1.35
Uncle wife	9	1.21
Neighbor	9	1.21
Husband father	8	1.08
Customer	6	0.81
Son	6	0.81
Grandmother	5	0.67
Wife	4	0.54

Sister of husband	4	0.54
Grandfather	2	0.27
Father's friend	2	0.27
Employee	3	0.40
Daughter	2	0.27
Total	741	100%

4.3. Complications of COVID-19 infection

4.3.1. Signs and symptoms caused by COVID-19 infection

Among 1500 participants with COVID-19 infection, 95.3% (n= 1430) of the participants reported different signs and symptoms caused by COVID-19 infection (Figure 6). Different signs and symptoms with different frequency and percentage were reported in Table 3. The Commonest symptoms were loss of taste or smell, shortness or difficulty of breath, and muscle or joint pain (71.9%, 65.2%, and 60.6%), respectively.

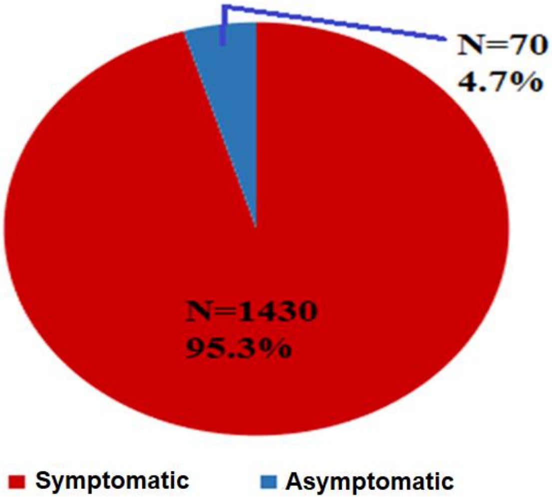

Figure 6: The percentage appearance of symptoms during COVID -19 infection between study samples

Table 3.

Reported symptoms among symptomatic COVID-19 patients.

Reported symptoms		Frequency	
		N	%
Fever	Yes	539	37.7
	No	891	62.3
Fatigue	Yes	314	22.0
	No	1116	78.0
Dry cough	Yes	261	18.3
	No	1169	81.7
Loss of taste or smell	Yes	1028	71.9
	No	402	28.1
Shortness or Difficulty of breath	Yes	932	65.2
	No	498	34.8
Muscle or joint pain	Yes	867	60.6
	No	563	39.4
Nasal congestion or runny nose	Yes	154	10.8
	No	1276	89.2
Sore throat	Yes	182	12.7
	No	1248	87.3

N: Number, %: Percentage, the percentage was calculated by divided the number of the cases from the total number of participants reported with symptoms (1430 participants)

4.3.2. ICU administration

One quarter (25.9%, n=7) of the participants who had COVID-19 previously was administrated to ICU as shown in Figure 7.

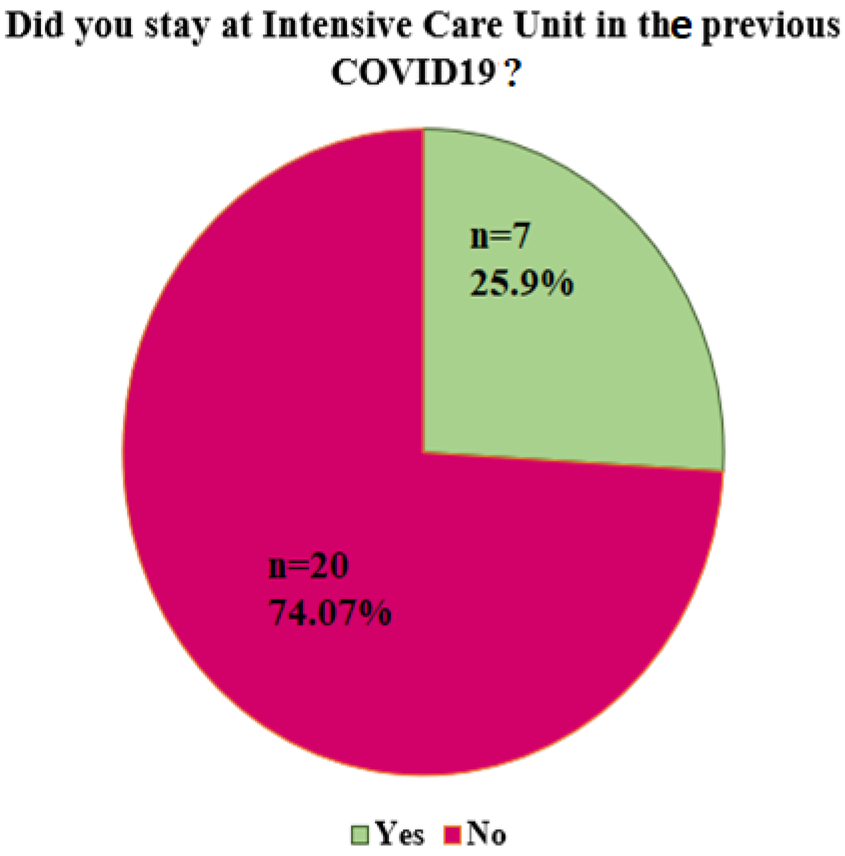

Figure 7: ICU administration due to previous COVID-19 infection

4.4. Evaluation of level of knowledge and awareness of participants during COVID-19 pandemic

There are different protective procedures that can be applied to decrease the probability of COVID-19 infection including; reducing the contact with people, keeping away from close and crowded places, working online and in door, cleaning hands using alcohol based, and washing hands with soap and water. High level of knowledge and awareness were noted among studied population. To avoid contact with people (n=1593, 63.72%), using a mask when found in crowded places (n=1098, 43.92%), and cleaning hands using alcohol-based (n=2139, 85.56%), and washing hands with soap and water (n=2153, 86.12%) were reported in high rate proportion in comparison with other negative practices and items that indicate poor knowledge about COVID-19 infection (Figure 8).

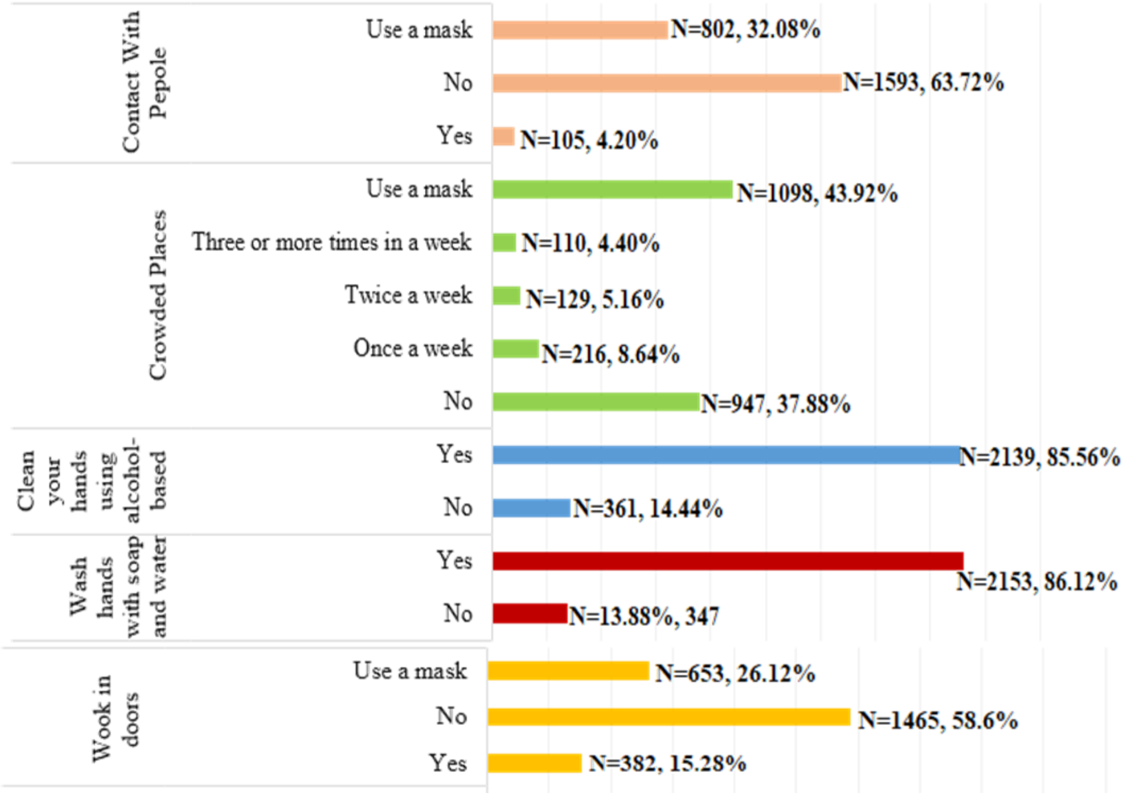

Figure 8: Knowledge, awareness, and protective measures of COVID-19

The participants with previous COVID-19 infection were reported with significant avoid the crowded places rather than participants without previous COVID-19 infection (*p*<0.001) and hands cleaning using alcohol-based (*p*=0.014). Other protective measures showed no significant improvement between participants with history of previous COVID-19 infection and participants without previous COVID-19 infection (Table 4).

Table 4.

A previous COVID-19 infection's effects on knowledge and practice improvements involving preventative measures.

Protective practice		Previously infection with COVID-19		*p*-Value
		Yes	No	
Contact With People	Yes	0	105	0.236
	No	18	1571	
	Use a mask	9	596	
Wash hands with soap and water	Yes	26	2127	0.093
	No	1	346	
Crowded Places	No	2	845	<0.001*
	Once a week	0	216	
	Twice a week	0	127	
	Three or more times in a week	0	33	

	Use a mask	25	973	
Total number of people working	1-5	2	294	0.264
	6-10	4	153	
	11-30	2	121	
	30-50	0	7	
Work In Door	Yes	7	375	0.139
	No	16	1450	
	Use mask while working	4	529	
Clean your hands using alcohol-based	Yes	27	2112	0.014*
	No	0	361	

4.5. Risk factors for COVID-19 infection in Jordan

4.5.1. Impact of history of previous COVID-19 on recurrent COVID-19 infection in Jordan

The participants who did not have a history of previous COVID-19 infection were at higher risk to COVID-19 infection in comparison to participants with previous infection of COVID-19 ($p \leq 0.001$). The date of previous infection among the participants ranged from less than one month ago to three months ago, the previous infection within 3 months ago shows a protective role against current COVID-19 infection with no significant differences between the reported duration of infection (Table 5).

Table 5.

Impact of history of previous COVID-19 on recurrent COVID-19

Items		Current COVID-19 infection		*p*-Value
		Yes	No	
Have you previously been diagnosed with COVID-19 infection?	Yes	0	27	≤0.001*
	No	1500	973	
When were you previously diagnosed with COVID-19 infection?	Less than 1 month ago	0	2	0.862
	1months ago	0	4	
	2 months ago,	0	8	
	3 months ago,	0	13	
Did you stay at Intensive Care Unit in the previous COVID19	Yes	0	4	0.026*
	No	1500	996	

4.5.2. COVID-19 infection among high-risk groups in Jordan

The participants were asked about different underlying disease or working as healthcare provider. Having a chronic disease is significantly associated with increase the probability of COVID-19 infection ($p \leq 0.001$). Chronic neurological disease (p-value 0.028), chronic kidney disease (p-value 0.003), chronic liver disease (p-value 0.028), chronic heart disease (p= 0.013), chronic lung disease (p= 0.010), and hypertension (p= 0.003) are significantly associated with increased probability of covid-19 infection. Having a sign of common cold is significantly associated with increase the risk of infection with COVID-19 ($p \leq 0.001$), as it was indicated in Table 6.

Table 6.

Impact of underlying conditions on COVID-19 infection

Items		current COVID-19 infection		*p*-Value
		Yes	No	
Cancer	Yes	10	5	0.403
	No	1490	995	
Chronic neurological disease	Yes	7	0	0.028*
	No	1493	1000	
Chronic kidney disease	Yes	15	1	0.003*
	No	1485	999	
Chronic liver disease	Yes	7	0	0.028*
	No	1493	1000	
Chronic heart disease	Yes	20	4	0.013*
	No	1480	996	
Chronic lung disease	Yes	9	0	0.010*
	No	1491	1000	
Hypertension	Yes	126	55	0.003*
	No	1374	945	
Organ or bone marrow transplantation	Yes	3	0	0.216
	No	1497	1000	

Health care/Non health care Provider	Healthcare provider	32	2	0.035*
	non health care provider	565	948	
Have Common Cold	Yes	167	63	≤0.001*
	No	1123	937	
	one week	25	4	
	less than two weeks	2	0	
	two weeks	1	1	
	three weeks	2	0	
	one month	56	40	
	more than one month	38	18	

4.5.3. Influence of a precautionary approach on COVID-19 infection in Jordan

Following a protective measure including; contact with people, wash hands with soap and water, clean your hands using alcohol-based, crowded places, work in door, and did not travel in the last year are strongly associated with reduce and eliminate the risk of COVID-19 infection ($p \leq 0.001$) among non-infected participants (Table 7).

Table 7.

Impact of follow a protective measures COVID-19 infection.

Items		current COVID-19 infection		*p*-Value
		Yes	No	
Contact With People	Yes	102	3	≤0.001*
	No	961	628	
	Use a mask while Contact with People	238	367	
Wash hands with soap and water	Yes	1182	971	≤0.001*
	No	318	29	
Clean your hands using alcohol-based	Yes	1155	984	≤0.001*
	No	345	16	
Crowded Places	No	521	326	≤0.001*
	Once a week	206	10	
	Twice a week	124	3	
	Three or more times in a week	32	1	
	Use a mask	340	658	
Work In Door	Yes	150	232	≤0.001*
	No	858	608	

	Use mask while working	373	160	
In the last one year did you travel	No	1204	987	≤0.001*
	Yes	101	12	

4.5.4. Status of social life during COVID-19 in Jordan

Living with group of people more than ten in the same house was strongly associated with current COVID-19 infection at the time of the study (*p*≤0.001). Having children younger than 18 years, and working with high number of people were associated with increased probability of COVID-19 (*p*=0.010, and 0.003) (Table 8).

Table 8.

Status of social life during COVID-19 in Jordan

		current COVID-19 infection		*p*-Value
		Yes	No	
Number of people living in your house	1-5	475	1219	≤0.001*
	6-10	294	236	
	More than 10	14	1	
children category	Less than 18 years	402	277	0.010*
	Equal or more than 18 years	16	5	
	Both category	50	18	
Do you have children?	Yes	39	48	0.292
	No	638	678	
Total number of people working	1-5	173	123	0.003*
	6-10	29	128	
	11-20	39	73	
	21-35	8	3	
	more than 35	5	2	

Chapter V

Discussion

The purpose of the present study was to estimate the incidence of COVID-19 cases in Jordan during a specific time frame, and to determine the prevalence of COVID-19 cases in Jordan. and COVID-19 risk factors in the Jordanian population.

In our study, the positivity rate in Jordan was (60%) during December, 2020 and February, 2021, this prevalence is higher than that reported elsewhere. In the previous study for (Setiadi W et al., 2022) the Prevalence and epidemiological characteristics of COVID-19 after one year of pandemic in Jakarta and neighboring areas, Indonesia found that the peak prevalence of infection was in March 2020 (26.3%) and was followed by January 2021 (23.9%) and February 2021 (21.8%). Out of 64,364 specimens, 10,130 (15.7%) were proven to be positive for SARS-CoV-2, The specimens from Jakarta, West Java, and Banten had positive rates of 16.3%, 13.3%, and 16.8%, respectively. While, in another descriptive analytical study (Marzieh Araban et al., 2021) for patients with COVID-19, Saveh, Islamic Republic of Iran, showed that 3181 patients in total , 1422 (44.7%) patients tested positive for COVID-19 based on laboratory data (PCR results), while 1759 (55.3%) patients tested negative.as well as, (Louis Jacob et al., 2021) From March 2020 to March 2021, approximately 14% of symptomatic patients tested for COVID-19 were tested positive with COVID-19 in German general practices.

The most prevalent symptoms were fever, fatigue, dry cough, loss of taste or smell, shortness or difficulty of breath, muscle or joint pain, nasal congestion or runny nose, and sore throat. Such symptoms were described in other studies such as the study of (Nishiura et al., 2020; Elnasser et al., 2021; Iqbal et al., 2021). These symptoms were associated with the disease and their intensity were developed as the intensity of the infection increased.

There are many Studies were done in 2020. The first study reflects the Chinese community Database, 3600 patients were contributed into this study, the most common symptoms seen were fever (83.3%), cough (60.3%) and fatigue (38.0%) ,(Xiaoyi, et al.2020). The second study indicates that fever was the commonest symptom (77%), followed by cough (63%), fatigue (21.0%) and diarrhea (5%),(Yu, Chengcheng, et al2020). . On the contrary of the third study. The commonest symptom was cough followed by fever then diarrhea with the following percentages (92%), (83%) and (17%) respectively (Liu, Yingxia, et 2020). Comparing with the previous studies, our study shows that fever is the most common symptom with (37.7%) followed by fatigue with (22.0%) and cough with (18.3%)

The results revealed that slightly more than a quarter of the participants with previous COVID-19 infection was administrated to ICU. However, hospitalization depends on the presence of symptoms and their severity. Previous studies showed that some symptoms such as diarrhea were associated with COVID-19 patients (Díaz et al., 2020). In general, patients who had high risk factors were more likely to be hospitalized when infected with COVID-19 (Ghaebi et al., 2021).

A cross-sectional survey was done on 1241 truck drivers in India, the main part of the study reflects the level of knowledge and awareness of the drivers during the pandemic covid19. whereas the study results showed that (69%) of the truck drivers constantly sanitize their hands using alcohol, (89%) of them wear masks in the public area and (70%) of them leave safe distances and stay away from other people (Sood, Ishaana, et al,. 2022). According to our results. There were a high level of knowledge, awareness and protective measures among participants. As an example, avoided contact with people (63.72%), use a mask when found in crowded places (43.92%), and clean hands using alcohol-based (85.56%), and wash hands with soap and water (86.12%)

The participants with prior COVID-19 infection were significantly more likely to avoid crowded places and clean their hands with alcohol (p=0.001) than those without prior COVID-19 infection (p=0.014). Other protective measures did not differ significantly between participants with a history of prior COVID-19 infection and those without a history of prior infection. These findings can be explained by the cumulative experience of previous exposure to the infection, and it appears that patients learn from self-experience and social media-based instructions. However, media played a variety of roles during the pandemic and sometimes disseminated false information (Cinelli et al., 2020).

The results showed that previous history of COVID-19 was significantly beneficial to gain the patients autoimmunity against the virus which less likely to be currently infected with COVID-19 compared with those patients who were not previously infected (Min et al., 2021; Smits et al., 2021).

The data of the present study showed that having a chronic disease is significantly associated with increasing the probability of COVID-19 infection ($p \leq 0.001$). Chronic diseases seem to be a predisposing factor facilitating the existence and pathogenesis of COVID-19 (Haybar et al., 2020).

Chronic neurological disease ($p=0.028$), chronic kidney disease ($p=0.003$), chronic liver disease ($p=0.028$), chronic heart disease ($p=0.013$), chronic lung disease ($p=0.010$), and hypertension ($p= 0.003$) are significantly associated with increase probability of COVID-19. Having a sign of common cold is significantly associated with increasing the risk of infection with SARS-CoV-2 ($p \leq 0.001$). This clinical picture means that the existence of chronic diseases weakens the body defense mechanisms and makes the body vulnerable to the develop COVID-19. Several studies reported the existence of various comorbidities to be associated with worse outcomes of the disease (He et al., 2020; Murthy et al., 2020; Verity et al., 2020).

Following protective measures such as contact with people, wash hands with soap and water, clean your hands using alcohol-based, crowded places, work in door, and did not travel in the last year are strongly associated with reduce and eliminate the risk of SARS-CoV-2 infection ($p \leq 0.001$) among non-infected participants. It has been reported that minimizing contact with infected people leads to lower the number of infected persons (Bi et al., 2020; Guidetti et al., 2022).

The data of the present study showed that living with group of people more than ten in the same house was strongly associated with current SARS-CoV-2 infection ($p \leq 0.001$).

Working associated with many people and having young children, as they spend most of their time outside and interact with people of all ages, which makes them exposed to continuous risks of infection ($p= 0.010$, and 0.003). These findings can be explained by taking into consideration that as the number of people residing in close quarters rises, the spread of disease would also rise. (Dunton et al., 2020).

Chapter VI

Conclusion

Identification of COVID-19 in Jordan using RT-PCR as a specific method allowed accurate identification of the virus and this procedure was a reliable and effective technique. According to the findings of the survey which was useful to know the Jordanian lifestyle during COVID-19 pandemic, there was a low level of commitment of using personal protection measures such as wearing masks and washing hands with alcohol-based disinfectants. There was a significant association between COVID-19 and crowded areas, regardless of whether those areas were at home or at work.

References

Adhikari, S. P., Meng, S., Wu, Y. J., Mao, Y. P., Ye, R. X., Wang, Q. Z., ... & Zhou, H. (2020). Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. *Infectious diseases of poverty*, 9(1), 1-12.

Aljaberi, M. A., Alsalahi, A., Juni, M. H., Noman, S., Al-Tammemi, A. A. B., & Hamat, R. A. (2021). Efficacy of interventional programs in reducing acculturative stress and enhancing adjustment of international students to the new host educational environment: A systematic review and meta-analysis. *International journal of environmental research and public health*, 18(15), 7765.

Alqassieh, R., Suleiman, A., Abu-Halaweh, S., Santarisi, A., Shatnawi, O., Shdaifat, L., ... & Bsisu, I. (2021). Pfizer-BioNTech and Sinopharm: a comparative study on post-vaccination antibody titers. *Vaccines*, 9(11), 1223.

Al-Qudah, M., Al-Shaikh, A. A., Haddad, H., Alolayyan, M., Zawaneh, Y., Matalka, M., & Matalka, I. (2022). Impact of COVID-19 Exclusive Allocation Strategy on Quality of Healthcare: A Study from Jordan, 2020. *Health security*, 20(3), 193-202.

Anderson, F. M., Hatch, S. L., Comacchio, C., & Howard, L. M. (2017). Prevalence and risk of mental disorders in the perinatal period among migrant women: a systematic review and meta-analysis. *Archives of women's mental health*, 20(3), 449-462.

Anderson, J. R., Bothell, D., Byrne, M. D., Douglass, S., Lebiere, C., & Qin, Y. (2004). An integrated theory of the mind. *Psychological review*, 111(4), 1036.

Anthony, S. J., Johnson, C. K., Greig, D. J., Kramer, S., Che, X., Wells, H., ... & Goldstein, T. (2017). Global patterns in coronavirus diversity. *Virus evolution*, 3(1), vex012.

Ashour, H. M., Elkhatib, W. F., Rahman, M. M., & Elshabrawy, H. A. (2020). Insights into the recent 2019 novel coronavirus (SARS-CoV-2) in light of past human coronavirus outbreaks. *Pathogens*, 9(3), 186

Assiri, A., Al-Tawfiq, J. A., Al-Rabeeah, A. A., Al-Rabiah, F. A., Al-Hajjar, S., Al-Barrak, A., ... & Memish, Z. A. (2013). Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. *The Lancet infectious diseases*, 13(9), 752-761.

Azevedo, J. P., Hasan, A., Goldemberg, D., Geven, K., & Iqbal, S. A. (2021). Simulating the potential impacts of COVID-19 school closures on schooling and learning outcomes: A set of global estimates. *The World Bank Research Observer*, 36(1), 1-40.

Bi, Q., Wu, Y., Mei, S., Ye, C., Zou, X., Zhang, Z., ... & Feng, T. (2020). Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. *The Lancet infectious diseases*, 20(8), 911-919.

Biggs, H. M., Behravesh, C. B., Bradley, K. K., Dahlgren, F. S., Drexler, N. A., Dumler, J. S., ... & Traeger, M. S. (2016). Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain spotted fever and other spotted fever group rickettsioses, ehrlichioses, and anaplasmosis—United States: A practical guide for health care and public health professionals. Morbidity and Mortality Weekly Report: Recommendations and Reports, 65(2), 1-44.

Blinova, I., Niskanen, J., Kajankari, P., Kanarbik, L., Käkinen, A., Tenhu, H., ... & Kahru, A. (2013). Toxicity of two types of silver nanoparticles to aquatic crustaceans Daphnia magna and Thamnocephalus platyurus. *Environmental Science and Pollution Research*, 20(5), 3456-3463.

Caso, D., Guidetti, M., Capasso, M., & Cavazza, N. (2022). Finally, the chance to eat healthily: Longitudinal study about food consumption during and after the first COVID-19 lockdown in Italy. *Food Quality and Preference*, 95, 104275.

Chang, L. (2004). Epidemiology and quality of life in functional gastrointestinal disorders. Alimentary pharmacology & therapeutics, 20, 31-39.

Chen, Z., Wu, Q., Chen, J., Ni, X., & Dai, J. (2020). A DNA aptamer based method for detection of SARS-CoV-2 nucleocapsid protein. *Virologica Sinica*, 35(3), 351-354.

Cinelli, M., Quattrociocchi, W., Galeazzi, A., Valensise, C. M., Brugnoli, E., Schmidt, A. L., ... & Scala, A. (2020). The COVID-19 social media infodemic. *Scientific reports*, 10(1), 1-10.

Cohen, E. E., Rosen, F., Stadler, W. M., Recant, W., Stenson, K., Huo, D., & Vokes, E. E. (2003). Phase II trial of ZD1839 in recurrent or metastatic squamous cell carcinoma of the head and neck. Journal of clinical oncology, 21(10), 1980-1987.

De Groot, R. S., Blignaut, J., Van Der Ploeg, S., Aronson, J., Elmqvist, T., & Farley, J. (2013). Benefits of investing in ecosystem restoration. *Conservation Biology*, 27(6), 1286-1293.

De Wit, E., Van Doremalen, N., Falzarano, D., & Munster, V. J. (2016). SARS and MERS: recent insights into emerging coronaviruses. *Nature Reviews Microbiology*, 14(8), 523-534.

Dhama, K., Sharun, K., Tiwari, R., Dadar, M., Malik, Y. S., Singh, K. P., & Chaicumpa, W. (2020). COVID-19, an emerging coronavirus infection: advances and prospects in designing and developing vaccines, immunotherapeutics, and therapeutics. *Human vaccines & immunotherapeutics*, 16(6), 1232-1238.

Díaz, A. L., Prados, J. S. F., Canosa, V. F., & Martínez, A. M. M. (2020). Impactos del confinamiento por el COVID-19 entre universitarios: Satisfacción Vital, Resiliencia y Capital Social Online. *RISE,* 9(1), 79-104.

Dunton, G. F., Do, B., & Wang, S. D. (2020). Early effects of the COVID-19 pandemic on physical activity and sedentary behavior in children living in the US. *BMC public health*, 20(1), 1-13.

Ellis, T. M., Barry Bousfield, R., Bissett, L. A., Dyrting, K. C., Luk, G. S., Tsim, S. T., ... & Peiris, J. M. (2004). Investigation of outbreaks of highly pathogenic H5N1 avian influenza in waterfowl and wild birds in Hong Kong in late 2002. *Avian Pathology*, 33(5), 492-505.

Elnasser, Z., Obeidat, H., Amarin, Z., Alrabadi, N., Jaradat, A., & Almomani, R. (2021). Prevalence of COVID-19 among blood donors: The Jordan University of Science and Technology experience. *Medicine*, 100(41).

Fehr, A. R., & Perlman, S. (2015). Coronaviruses: an overview of their replication and pathogenesis. *Coronaviruses*, 1-23.

Geers, D., Shamier, M. C., Bogers, S., den Hartog, G., Gommers, L., Nieuwkoop, N. N., ... & GeurtsvanKessel, C. H. (2021). SARS-CoV-2 variants of concern partially escape humoral but not T cell responses in COVID-19 convalescent donors and vaccine recipients. *Science immunology*, 6(59), eabj1750.

Guan, W. J., Ni, Z. Y., Hu, Y., Liang, W. H., Ou, C. Q., He, J. X., ... & Zhong, N. S. (2020). Clinical characteristics of coronavirus disease 2019 in China. *New England journal of medicine*, 382(18), 1708-1720.

Gurung, M., Li, Z., You, H., Rodrigues, R., Jump, D. B., Morgun, A., & Shulzhenko, N. (2020). Role of gut microbiota in type 2 diabetes pathophysiology. *EBioMedicine*, 51, 102590.

Gussow, A. B., Auslander, N., Faure, G., Wolf, Y. I., Zhang, F., & Koonin, E. V. (2020). Genomic determinants of pathogenicity in SARS-CoV-2 and other human coronaviruses. *Proceedings of the National Academy of Sciences*, 117(26), 15193-15199.

Han, H., Best, A. J., Braunschweig, U., Mikolajewicz, N., Li, J. D., Roth, J., ... & Blencowe, B. J. (2022). Systematic exploration of dynamic splicing networks reveals conserved multistage regulators of neurogenesis. *Molecular Cell*, 82(16), 2982-2999.

Harwood, R., Allin, B., Jones, C. E., Whittaker, E., Ramnarayan, P., Ramanan, A. V., ... & Yardley, I. (2021). A national consensus management pathway for paediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS): results of a national Delphi process. *The Lancet Child & Adolescent Health*, 5(2), 133-141.

Haybar, H., Kazemnia, K., & Rahim, F. (2020). Underlying chronic disease and COVID-19 infection: a state-of-the-art review. *Jundishapur Journal of Chronic Disease Care*, 9(2).

He, J. H. (2020). A short review on analytical methods for a fully fourth-order nonlinear integral boundary value problem with fractal derivatives. *International Journal of Numerical Methods for Heat & Fluid Flow*, 30(11)

He, J., Tao, H., Yan, Y., Huang, S. Y., & Xiao, Y. (2020). Molecular mechanism of evolution and human infection with SARS-CoV-2. *Viruses*, 12(4), 428.

Hijawi, B., Abdallat, M., Sayaydeh, A., Alqasrawi, S., Haddadin, A., Jaarour, N., ... & Alsanouri, T. (2013). Novel coronavirus infections in Jordan, April 2012: epidemiological findings from a retrospective investigation. *EMHJ-Eastern Mediterranean Health Journal*, 19 (supp. 1), S12-S18, 2013.

Hilgenfeld, R., & Peiris, M. (2013). From SARS to MERS: 10 years of research on highly pathogenic human coronaviruses. *Antiviral research*, 100(1), 286-295.

Huang, X. D., El-Alawi, Y., Penrose, D. M., Glick, B. R., & Greenberg, B. M. (2004). A multi-process phytoremediation system for removal of polycyclic aromatic hydrocarbons from contaminated soils. *Environmental pollution*, 130(3), 465-476.

Ijeoma, U. F., Aderonke, S. O., Ogbonna, O., Augustina, M. A., & Ifeyinwa, C. N. (2011). Antinociceptive and anti-inflammatory activities of crude extracts of Ipomoea involucrata leaves in mice and rats. *Asian Pacific journal of tropical medicine*, 4(2), 121-124.

Imai, N., Dorigatti, I., Cori, A., Donnelly, C., Riley, S., & Ferguson, N. (2020). Report 2: Estimating the potential total number of novel Coronavirus cases in Wuhan City, China.

Jacob, L., Loosen, S. H., Kalder, M., Luedde, T., Roderburg, C., & Kostev, K. (2021). Impact of the COVID-19 pandemic on cancer diagnoses in general and specialized practices in Germany. *Cancers*, 13(3), 408.

Kalinsky, K., Barlow, W. E., Gralow, J. R., Meric-Bernstam, F., Albain, K. S., Hayes, D. F., ... & Hortobagyi, G. N. (2021). 21-gene assay to inform chemotherapy benefit in node-positive breast cancer. *New England Journal of Medicine*, 385(25), 2336-2347.

Kameritsch, P., Singer, M., Nuernbergk, C., Rios, N., Reyes, A. M., Schmidt, K., ... & Beck, H. (2021). The mitochondrial thioredoxin reductase system (TrxR2) in vascular endothelium controls peroxynitrite levels and tissue integrity. *Proceedings of the National Academy of Sciences*, 118(7), e1921828118.

Kang, L., Li, Y., Hu, S., Chen, M., Yang, C., Yang, B. X., ... & Liu, Z. (2020). The mental health of medical workers in Wuhan, China dealing with the 2019 novel coronavirus. *The Lancet. Psychiatry*, 7(3), e14.

Kang, L., Ma, S., Chen, M., Yang, J., Wang, Y., Li, R., ... & Liu, Z. (2020). Impact on mental health and perceptions of psychological care among medical and nursing staff in Wuhan during the 2019 novel coronavirus disease outbreak: A cross-sectional study. Brain, behavior, and immunity, 87, 11-17.

Kessler, R. C., Demler, O., Frank, R. G., Olfson, M., Pincus, H. A., Walters, E. E., ... & Zaslavsky, A. M. (2005). Prevalence and treatment of mental disorders, 1990 to 2003. *New England Journal of Medicine*, 352(24), 2515-2523.

Ki, M. (2015). 2015 MERS outbreak in Korea: hospital-to-hospital transmission. *Epidemiology and health*, 37.

Kimball, A., Hatfield, K. M., Arons, M., James, A., Taylor, J., Spicer, K., ... & Zane, S. (2020). Asymptomatic and presymptomatic SARS-CoV-2 infections in residents of a long-term care skilled nursing facility—King County, Washington, March 2020. *Morbidity and Mortality Weekly Report*, 69(13), 377.

Koelle, K., Martin, M. A., Antia, R., Lopman, B., & Dean, N. E. (2022). The changing epidemiology of SARS-CoV-2. *Science*, 375(6585), 1116-1121.

Lan, S. H., Lai, C. C., Huang, H. T., Chang, S. P., Lu, L. C., & Hsueh, P. R. (2020). Tocilizumab for severe COVID-19: a systematic review and meta-analysis. *International journal of antimicrobial agents*, 56(3), 106103.

Li, C., Zhou, J., Song, J., Xu, J., Zhang, H., Zhang, X., ... & Sun, Y. (2021). Non-fullerene acceptors with branched side chains and improved molecular packing to exceed 18% efficiency in organic solar cells. *Nature Energy*, 6(6), 605-613.

Liu, C., Mendonça, L., Yang, Y., Gao, Y., Shen, C., Liu, J., ... & Zhang, P. (2020). The architecture of inactivated SARS-CoV-2 with postfusion spikes revealed by cryo-EM and cryo-ET. *Structure*, 28(11), 1218-1224.

Mebius, M. M., van Genderen, P. J., Urbanus, R. T., Tielens, A. G., de Groot, P. G., & van Hellemond, J. J. (2013). Interference with the host haemostatic system by schistosomes. *PLoS pathogens*, 9(12), e1003781.

Meo, S. A., Bukhari, I. A., Akram, J., Meo, A. S., & Klonoff, D. C. (2021). COVID-19 vaccines: comparison of biological, pharmacological characteristics and adverse effects of Pfizer/BioNTech and Moderna Vaccines. *Eur Rev Med Pharmacol Sci*, 1663-1669.

Minglei, L., Dingzhong, W., Wuduo, Z., Hui, X., Hengyi, X., Shihao, S., ... & Jianxun, Z. (2022). Simultaneous determination of multiple flavorings in infant formula by direct analysis in real time-mass spectrometry. *LWT*, 113586.

Mirza, M. U., & Froeyen, M. (2020). Structural elucidation of SARS-CoV-2 vital proteins: Computational methods reveal potential drug candidates against main protease, Nsp12 polymerase and Nsp13 helicase. *Journal of pharmaceutical analysis*, 10(4), 320-328.

Mittal, R., Ni, R., & Seo, J. H. (2020). The flow physics of COVID-19. *Journal of fluid Mechanics*, 894.

Mozaffarian, D., Benjamin, E. J., Go, A. S., Arnett, D. K., Blaha, M. J., Cushman, M., ... & Turner, M. B. (2015). Heart disease and stroke statistics—2015 update: a report from the American Heart Association. *Circulation*, 131(4), e29-e322.

Mulligan, M. J., Lyke, K. E., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., ... & Jansen, K. U. (2020). Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults. *Nature*, 586(7830), 589-593.

Murthy, S., Gomersall, C. D., & Fowler, R. A. (2020). Care for critically ill patients with COVID-19. *Jama*, 323(15), 1499-1500.

Muthu, V., Rudramurthy, S. M., Chakrabarti, A., & Agarwal, R. (2021). Epidemiology and pathophysiology of COVID-19-associated mucormycosis: India versus the rest of the world. *Mycopathologia*, 186(6), 739-754.

Nakajo, K., & Nishiura, H. (2021). Transmissibility of asymptomatic COVID-19: Data from Japanese clusters. *International Journal of Infectious Diseases*, 105, 236-238.

Narkiewicz, K., Bieniaszewski, L., Szczech, R., Gsecki, D., Winklewski, P., ZajC, I., ... & Krupa-Wojciechowska, B. (1993). 146 Analysis of the diurnal blood pressure profile in normotensive twins. *Journal of Hypertension*, 11, S460.

Nassar, M., Daoud, A., Nso, N., Medina, L., Ghernautan, V., Bhangoo, H., ... & Misra, A. (2021). Diabetes mellitus and COVID-19. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 15(6), 102268.

Nicola, M., Alsafi, Z., Sohrabi, C., Kerwan, A., Al-Jabir, A., Iosifidis, C., ... & Agha, R. (2020). The socio-economic implications of the coronavirus pandemic (COVID-19): A review. *International journal of surgery*, 78, 185-193.

Nishiura, H., Jung, S. M., Linton, N. M., Kinoshita, R., Yang, Y., Hayashi, K., ... & Akhmetzhanov, A. R. (2020). The extent of transmission of novel coronavirus in Wuhan, China, 2020. *Journal of clinical medicine*, 9(2), 330.

Omori, R., Mizumoto, K., & Nishiura, H. (2020). Ascertainment rate of novel coronavirus disease (COVID-19) in Japan. *International Journal of Infectious Diseases*, 96, 673-675.

Ou, X., Liu, Y., Lei, X., Li, P., Mi, D., Ren, L., ... & Qian, Z. (2020). Characterization of spike glycoprotein of SARS-CoV-2 on virus entry and its immune cross-reactivity with SARS-CoV. *Nature communications*, 11(1), 1-12.

Paden, C. R., Yusof, M. F. B. M., Al Hammadi, Z. M., Queen, K., Tao, Y., Eltahir, Y. M., ... & Al Muhairi, S. S. M. (2018). Zoonotic origin and transmission of Middle East respiratory syndrome coronavirus in the UAE. *Zoonoses and public health*, 65(3), 322-333.

Palefsky, J. M., Lee, J. Y., Jay, N., Goldstone, S. E., Darragh, T. M., Dunlevy, H. A., ... & Berry-Lawhorn, J. M. (2022). Treatment of anal high-grade squamous intraepithelial lesions to prevent anal cancer. *New England Journal of Medicine*, 386(24), 2273-2282.

Park, Y. J., Choe, Y. J., Park, O., Park, S. Y., Kim, Y. M., Kim, J., ... & Jeong, E. K. (2020). Contact tracing during coronavirus disease outbreak, South Korea, 2020. *Emerging infectious diseases*, 26(10), 2465.

Penttinen, P. M., Kaasik-Aaslav, K., Friaux, A., Donachie, A., Sudre, B., Amato-Gauci, A. J., ... & Coulombier, D. (2013). Taking stock of the first 133 MERS coronavirus cases globally–Is the epidemic changing?. *Eurosurveillance*, 18(39), 20596.

Perera, C., Zaslavsky, A., Christen, P., & Georgakopoulos, D. (2013). Context aware computing for the internet of things: A survey. *IEEE communications surveys & tutorials*, 16(1), 414-454.

Petit, C., Lacas, B., Pignon, J. P., Le, Q. T., Grégoire, V., Grau, C., ... & Torres-Saavedra, P. (2021). Chemotherapy and radiotherapy in locally advanced head and neck cancer: an individual patient data network meta-analysis. *The Lancet Oncology*, 22(5), 727-736.

Petrosillo, N., Viceconte, G., Ergonul, O., Ippolito, G., & Petersen, E. (2020). COVID-19, SARS and MERS: are they closely related?. *Clinical microbiology and infection*, 26(6), 729-734.

Petrosillo, N., Viceconte, G., Ergonul, O., Ippolito, G., & Petersen, E. (2020). COVID-19, SARS and MERS: are they closely related?. *Clinical microbiology and infection*, 26(6), 729-734.

Petrosillo, N., Viceconte, G., Ergonul, O., Ippolito, G., & Petersen, E. (2020). COVID-19, SARS and MERS: are they closely related?. *Clinical microbiology and infection*, 26(6), 729-734.

Rabi, F. A., Al Zoubi, M. S., Kasasbeh, G. A., Salameh, D. M., & Al-Nasser, A. D. (2020). SARS-CoV-2 and coronavirus disease 2019: what we know so far. *Pathogens*, 9(3), 231.

Rabi, F. A., Al Zoubi, M. S., Kasasbeh, G. A., Salameh, D. M., & Al-Nasser, A. D. (2020). SARS-CoV-2 and coronavirus disease 2019: what we know so far. *Pathogens,* 9(3), 231.

Rahimi, Z., Shirali, G. A., Araban, M., Mohammadi, M. J., & Cheraghian, B. (2021). Mask use among pedestrians during the Covid-19 pandemic in Southwest Iran: an observational study on 10,440 people. *BMC public health*, 21, 1-9.

Rehman, H. M., Mirza, M. U., Ahmad, M. A., Saleem, M., Froeyen, M., Ahmad, S., ... & Bhinder, M. A. (2020). A putative prophylactic solution for COVID-19: Development of novel multiepitope vaccine candidate against SARS-COV-2 by comprehensive immunoinformatic and molecular modelling approach. *Biology,* 9(9), 296.

Reusken, C., Mou, H., Godeke, G. J., van der Hoek, L., Meyer, B., Müller, M. A., ... & Koopmans, M. (2013). Specific serology for emerging human coronaviruses by protein microarray. *Eurosurveillance*, 18(14), 20441.

Riou, J., & Althaus, C. L. (2020). Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020. *Eurosurveillance,* 25(4), 2000058.

Rohilla, P., Jain, H., Chhikara, A., Singh, L., & Dahiya, P. (2022). Anticancer potential of Solanaceae plants: A review. South African Journal of Botany, 149, 269-289.

Singhal, T. (2020). A review of coronavirus disease-2019 (COVID-19). *The indian journal of pediatrics*, 87(4), 281-286.

Says, F. E., Ayuob, N., Fahmy, A. R., Fayez, F. E., Hasanian, M., & El Deek, B. (2013). Experience of establishment of multiple mini structure interview as part of student admission policy at faculty of medicine, King Abdulaziz University, 2011–2012. *Medical teacher,* 35(sup1), S74-S77.

Sciberras, J., Camilleri, L. M., & Cuschieri, S. (2020). The burden of type 2 diabetes pre-and during the COVID-19 pandemic–a review. *Journal of Diabetes & Metabolic Disorders,* 19(2), 1357-1365.

Sethuraman, N., Jeremiah, S. S., & Ryo, A. (2020). Interpreting diagnostic tests for SARS-CoV-2. *Jama*, 323(22), 2249-2251.

Setiadi, W., Rozi, I. E., Safari, D., Daningrat, W. O. D., Johar, E., Yohan, B., ... & Wascove team. (2022). Prevalence and epidemiological characteristics of COVID-19 after one year of pandemic in Jakarta and neighbouring areas, Indonesia: A single center study. *PloS one*, 17(5), e0268241.

Shah, A. S., Gribben, C., Bishop, J., Hanlon, P., Caldwell, D., Wood, R., ... & McAllister, D. A. (2021). Effect of vaccination on transmission of SARS-CoV-2. *New England Journal of Medicine*, 385(18), 1718-1720.

Shang, J., Wan, Y., Luo, C., Ye, G., Geng, Q., Auerbach, A., & Li, F. (2020). Cell entry mechanisms of SARS-CoV-2. *Proceedings of the National Academy of Sciences*, 117(21), 11727-11734.

Shereen, M. A., Khan, S., Kazmi, A., Bashir, N., & Siddique, R. (2020). COVID-19 infection: Emergence, transmission, and characteristics of human coronaviruses. *Journal of advanced research*, 24, 91-98.

Shi, J., Chan, C., Pang, Y., Ye, W., Tian, F., Lyu, J., ... & Yang, M. (2015). A fluorescence resonance energy transfer (FRET) biosensor based on graphene quantum dots (GQDs) and gold nanoparticles (AuNPs) for the detection of mecA gene sequence of Staphylococcus aureus. *Biosensors and Bioelectronics*, 67, 595-600.

Sohrabi, C., Alsafi, Z., O'neill, N., Khan, M., Kerwan, A., Al-Jabir, A., ... & Agha, R. (2020). World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). *International journal of surgery*, 76, 71-76.

Sood, I., Chinnakaran, A., Majumdar, A., & Sabherwal, S. (2022). Assessment of COVID-19-related awareness, knowledge, prevention practices and challenges faced by truck drivers in major transport cities of India: a cross-sectional survey. *BMJ open*, 12(2), e052543.

Stone, N. J., Robinson, J. G., Lichtenstein, A. H., Bairey Merz, C. N., Blum, C. B., Eckel, R. H., ... & Wilson, P. W. (2014). 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart

Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*, 63(25 Part B), 2889-2934.

Tan, J. H., Chin, W., Shaikh, A. L., & Zheng, S. (2021). Pancreatic pseudocyst: Dilemma of its recent management. *Experimental and Therapeutic Medicine*, 21(2), 1-1.

Tang, Z., Liu, Z. H., Wang, H., Dang, Z., & Liu, Y. (2021). Occurrence and removal of 17α-ethynylestradiol (EE2) in municipal wastewater treatment plants: Current status and challenges. *Chemosphere*, 271, 129551.

Thompson, M. G., Stenehjem, E., Grannis, S., Ball, S. W., Naleway, A. L., Ong, T. C., ... & Klein, N. P. (2021). Effectiveness of Covid-19 vaccines in ambulatory and inpatient care settings. *New England Journal of Medicine*, 385(15), 1355-1371.

Tlili, A., Huang, R., Shehata, B., Liu, D., Zhao, J., Metwally, A. H. S., ... & Burgos, D. (2022). Is Metaverse in education a blessing or a curse: a combined content and bibliometric analysis. *Smart Learning Environments*, 9(1), 1-31.

Triggle, C. R., Bansal, D., Ding, H., Islam, M. M., Farag, E. A. B. A., Hadi, H. A., & Sultan, A. A. (2021). A comprehensive review of viral characteristics, transmission, pathophysiology, immune response, and management of SARS-CoV-2 and COVID-19 as a basis for controlling the pandemic. *Frontiers in immunology*, 12, 631139.

Van der Hoek, L. (2007). Human coronaviruses: what do they cause?. *Antiviral therapy*, 12(4_part_2), 651-658.

Van Ditmarsch, H., van Der Hoek, W., & Kooi, B. (2007). Dynamic epistemic logic (Vol. 337). Springer Science & Business Media.

Van Doremalen, N., Bushmaker, T., Morris, D. H., Holbrook, M. G., Gamble, A., Williamson, B. N., ... & Munster, V. J. (2020). Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *New England journal of medicine*, 382(16), 1564-1567.

Verity, R., Okell, L. C., Dorigatti, I., Winskill, P., Whittaker, C., Imai, N., ... & Ferguson, N. M. (2020). Estimates of the severity of coronavirus disease 2019: a model-based analysis. *The Lancet infectious diseases*, 20(6), 669-677.

Vijgen, L., Keyaerts, E., Moës, E., Thoelen, I., Wollants, E., Lemey, P., ... & Van Ranst, M. (2005). Complete genomic sequence of human coronavirus OC43: molecular clock analysis suggests a relatively recent zoonotic coronavirus transmission event. *Journal of virology*, 79(3), 1595-1604.

Voysey, M., Clemens, S. A. C., Madhi, S. A., Weckx, L. Y., Folegatti, P. M., Aley, P. K., ... & Bird, O. (2021). Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. *The Lancet*, 397(10277), 881-891.

Weiss, S. R., & Leibowitz, J. L. (2011). Coronavirus pathogenesis. Advances in virus Whitelaw, S., Mamas, M. A., Topol, E., & Van Spall, H. G. (2020). Applications of digital technology in COVID-19 pandemic planning and response. *The Lancet Digital Health*, 2(8), e435-e440.

Widjaja, G., Jalil, A. T., Rahman, H. S., Abdelbasset, W. K., Bokov, D. O., Suksatan, W., ... & Ahmadi, M. (2021). Humoral immune mechanisms involved in protective and pathological immunity during COVID-19. *Human Immunology*, 82(10), 733-745.

Woo, P. C., Lau, S. K., Chu, C. M., Chan, K. H., Tsoi, H. W., Huang, Y., ... & Yuen, K. Y. (2005). Characterization and complete genome sequence of a novel coronavirus, coronavirus HKU1, from patients with pneumonia. *Journal of virology*, 79(2), 884-895.

Wu, C., Chen, X., Cai, Y., Zhou, X., Xu, S., Huang, H., ... & Song, Y. (2020). Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA internal medicine*, 180(7), 934-943.

Xiang, Y. T., Yang, Y., Li, W., Zhang, L., Zhang, Q., Cheung, T., & Ng, C. H. (2020). Timely mental health care for the 2019 novel coronavirus outbreak is urgently needed. *The lancet psychiatry*, 7(3), 228-229.

Xu, Z., Bennett, M. T., Tao, R., & Xu, J. (2004). China's Sloping Land Conversion Program four years on: current situation and pending issues. *International Forestry Review*, 6(3-4), 317-326.

Zaki, A. M., Van Boheemen, S., Bestebroer, T. M., Osterhaus, A. D., & Fouchier, R. A. (2012). Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *New England Journal of Medicine*, 367(19), 1814-1820.

Zhang, B., Xie, Y., Lan, Z., Li, D., Tian, J., Zhang, Q., ... & Liu, Y. (2022). SARS-CoV-2 nucleocapsid protein has DNA-Melting and strand-Annealing activities with different properties from SARS-CoV-2 Nsp13. *Frontiers in Microbiology*, 13.

Zhao, Q., Meng, M., Kumar, R., Wu, Y., Huang, J., Deng, Y., ... & Yang, L. (2020). Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A systemic review and meta-analysis. *International journal of infectious diseases*, 96, 131-135.

Zhao, Y., Fang, C., Zhang, Q., Zhang, R., Zhao, X., Duan, Y., ... & Yang, H. (2022). Crystal structure of SARS-CoV-2 main protease in complex with protease inhibitor PF-07321332. *Protein & cell*, 13(9), 689-693.

Zhong, N. S., Zheng, B. J., Li, Y. M., Poon, L. L. M., Xie, Z. H., Chan, K. H., ... & Guan, Y. (2003). Epidemiology and cause of severe acute respiratory syndrome (SARS) in Guangdong, People's Republic of China, in February, 2003. *The Lancet*, 362(9393), 1353-1358.

Zhu, L., She, Z. G., Cheng, X., Qin, J. J., Zhang, X. J., Cai, J., ... & Li, H. (2020). Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. *Cell metabolism*, 31(6), 1068-1077.

Zu, Z. Y., Jiang, M. D., Xu, P. P., Chen, W., Ni, Q. Q., Lu, G. M., & Zhang, L. J. (2020). Coronavirus disease 2019 (COVID-19): a perspective from China. *Radiology*, 296(2), E15-E25.