Deanship of Graduate Studies
Al-Quds University

Association Between ABO Blood Group System and the Severity of COVID-19 in the West Bank: A Case-control Study

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M.Sc. Thesis

Jerusalem – Palestine

1442 - 2021

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A thesis submitted in partial fulfillment of requirement for the degree of Master of Public Health - Deanship of Graduate studies - Al-Quds University

1442 – 2021

Deanship of Graduate Studies
Al-Quds University
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Thesis Approval

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1442 / 2021

Dedication

All life's challenges require striving. There are people who are closed to my heart, who have supported and helped me in this study. Therefore, this thesis is proudly dedicated to my precious family, who have been my source of creativity and have given me strength when I thought of giving up, who continually provide their endless love and support.

To my dearest friends and relatives who shared their encouragement for me to follow my dreams.

To my master mates in Gaza who encouraged and believed in me.

Ala' Hamdan Obeyat

Declaration

I certify that this thesis submitted to the degree of master is the result of my own research, except where otherwise acknowledged, and that this thesis or any of its parts has not been submitted for higher degree to any other university or institution.

Signature: Ala' Obeyat

Ala' Hamdan Mohammed Obeyat
Date: 12 / 08 / 2021

Acknowledgement

The power of Allah over all things

I would like to express my special appreciation to my supervisor **Dr. Maher Khdour** for his support, advice and guidance.

I extend this appreciation to all health directors in the governorates of the West Bank, especially **Mrs. Salma Khamaiseh** and **Dr. Wissam Sbeihat** in Jenin for their kindness, to all my teachers at **Al-Quds University** and the medical scientist **Mr. Issa Ghrouz** for their advice and guidance.

My greatest thanks are given to my supportive and encouraging **parents** whom without them I wouldn't have reached anything.

To my elder sister **Yara**: My role model and inspiration, the best teacher and translator, the one who helped and supported me through my study.

To my sister **Lara**: The chemist who is always there to wipe a tear or share a laugh.

To my sister **Tamara**: My favorite dentist who gave me strength and energy.

To my brother **Qassam**: The generous doctor who didn't skimp on helping and motivating me.

To my brother **Muhammad**: The wise, intelligent, and brilliant doctor who shared his valuable information with me.

To **my friends**: Who have endured my good and bad habits, my rock in difficult days, who have held my heart and believed in me and in my abilities.

Last but not least, to my beloved **Gaza**, my favorite city, for its strength and determination.

When I mention Gaza, I could never forget my teacher, advisor, and guide: **Dr Yehia Abed**, the wonderful person, who lit the candle of my life, all the words of thanks in the world are not enough for him.

And my dear **master mates from Gaza**, the strongest people I've seen in my life, who gave me support, encouragement and strength when they needed it the most.

Abstract

Background: A new coronavirus disease-2019 (COVID-19) outbreak was recorded in Wuhan, Hubei province and spread rapidly to all districts and communities in China nationwide, also spreading all over the map of world. In Palestine the number of cases is still continuous.

Study problem and justifications: Several studies have examined risk factors for COVID-19. And there was a conflict between the results and reports of researchers about whether the type of blood type had a role in influencing the risk of COVID-19. Therefore, the current study planned to find the effect of blood type on the severity of risk to infect with COVID-19 so that it can be taken as a reference towards adhering to prevention measures among people and the treatment mechanism towards COVID-19 by the decision makers.

Aim and Objectives: This study aimed to determine the association between ABO blood group system and the severity of COVID-19 in the West-Bank in Palestine. Its objectives are to determine the susceptibly to infect with COVID-19 in consonance with blood group, the severity of symptoms, the various risk factors of COVID-19 as sociodemographic variables, health status, smoking status, seasonal flu experience and COVID-19 infection experience as potential confounder variables. And demonstrate the COVID-19 composite outcomes according to their blood groups.

Methodology: A case control study design, consisted of 338 participants (169 cases and 169 controls) who had tested COVID-19 PCR during March/2021 in the West Bank, stratified according to their COVID-19 test result. Cases were who have COVID-19 positive test with symptoms and Control were who have COVID-19 negative test. A self-administrated questionnaire was used for data collection and filled by contacting the participants via their phone numbers.

Statistical Analysis: Data entered and analyzed using the Statistical Package for Social Science version 23(SPSS-23). Both descriptive and analytical analysis were carried out. Descriptive statistics used for representing the frequencies and percentages categorical variables whereas the continuous variables were represented by the means, and standard deviation. Chi-square test was used to compare two categorical variables association between blood group and COVID19, also between cases and controls. Binary logistic regression (Enter model) was used in the multivariate analysis to demonstrate the odds ratio.

Ethical Considerations: This study submitted to the school of public health research committee. Ethical approval of consent form was taken verbally from the participants, the

permission to conduct the study obtained from the MOH. Collected the consent form of all the participants verbally.

Results: The analysis of the study data revealed that the mean age of the participants was 38±16 (mean ± SD) years, the majority of the participant's blood group was "O" (37.9%), followed by "A" (36.7%), and (13.6%) of them were "B" and (11.8%) with "AB". Regarding the rhesus factor (RH), the majority of participants were positive RH with (80.2%) and (19.8%) of them were RH negative. The multivariate analysis compared blood group "A" versus others which showed that blood group B is more protective against COVID-19 than "A" (AOR= 0.40, CI= 0.223-0.27). "AB" is more protective towards COVID-19 by 31.6% more times ($P < 0.05$, AOR= 0.316, CI= 0.143-0.698). On the other hand, there is no difference between blood group A and blood group O ($P > 0.05$, AOR= 0.843, CI= 0.382-1.863) and no significant difference between blood groups according to the severity of symptoms or the composite outcomes of COVID-19. Also, being not vaccinated for seasonal flu increases the risk for COVID-19 infection by 1.97 times compared to people who gets vaccinated $P < 0.05$, AOR= 1.974, CI= 1.119-3.483).

Conclusion: This is the first study in Palestine that concerned with blood group and COVID19. The study confirmed the association between blood group and COVID-19 susceptibility to infect, but it showed that no association with the severity of symptoms or the composite outcomes of COVID-19. As blood group "A" showed high risk for COVID-19 than others blood group. Taken seasonal flu vaccination shown as a protective factor towards COVID-19, no association between study participants characteristics (gender, RH, health status, BMI, occupation exposure and COVID-19) except the "Age" which had been a confounder variable in the study. Furthermore, people with blood group A should strengthen prevention methods against COVID-19, taking into consideration the commitment of all other blood groups to safety and prevention measures, other studies should be conducted on a large sample size and assessing more confounder variables.

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List of abbreviations

ACE	**Angiotensin converting enzyme**
AOR	**Adjusted odds ratio**
BMI	**Body Mass Index**
CI	**Confidence interval**
COVID-19	**Coronavirus disease 2019**
ECMO	**Extracorporeal membrane oxygenation**
FUT2	**Fructosyltransferase 2**
ICU	**Intensive care unit**
IgG	**Immunoglobulin G**
MERS-CoV	**Middle East respiratory syndrome coronavirus**
MOH	**Ministry of health**
PCBS	**Palestinian Central Bureau of Statistics**
PCR	**Polymerase chain reaction**
RBC	**Red blood cells**
Rh factor	**Rhesus factor**
SARS-CoV	**Severe acute respiratory syndrome coronavirus**
SARS-CoV-2	**Severe acute respiratory syndrome coronavirus two**
WHO	**World Health Organization**

Chapter one

Introduction

1.1 Background

Coronavirus disease 2019 (COVID-19) is a pandemic respiratory infection caused by a new corona virus known as Severe Acute Respiratory Syndrome2 (SARS coronavirus 2) (Wu et al., 2020). The coronal form of the virus is roughly 125 nanometer in diameter and is encased in spikes (glycoproteins) that are almost 9 to 12 nanometer in diameter, the virus's morphology is similar to that of other coronaviruses, such as SARS-CoV and MERS-CoV (El-Shitany et al., 2021).

It began in the city of Wuhan (Central China) and quickly spread throughout the world, with growing rates of morbidity and mortality, pretense a major risk to public health globally (Wu et al., 2020). Moreover, on March 11, 2020, the World Health Organization (WHO) declared COVID-19 a pandemic. which extremely infectious virus can be without symptoms or with mild to serious symptoms and may be life-threatening to high-risk individuals such as the elderly, patients with immunosuppression and those with underlying medical problems as cardiovascular disease and cancer (WHO, 2020b), which transmitted through human to others among symptomatic and asymptomatic infected people (El-Shitany et al., 2021). A positive reverse transcriptase polymerase-chain-reaction (rt-PCR) performed on either nasopharyngeal or oropharyngeal swabs from suspicious people can confirm the presence of COVID-19 virus and chest radiographs (El-Shitany et al., 2021).

COVID-19 is continuous, for example, until 29/6/2021 there were 178 million confirmed cases in the world (WHO, 2021) and exceeded 300,000 confirmed cases and 3000 deaths in Palestine (MOH, 2021a). Therefore, this rising of cases enhances the scientists from all over the world to find the factors that might increase the risk of infection with the virus (Harvard Medical School, 2020).

Researchers have explored the mechanism to viral entrance into human hosts via endocytosis, histo-blood group antigen, cell surface and acetylcholine receptor in respiratory diseases, in addition to documented evidence of auto-antigenicity and reporting of hematological problems such as agglutinated of red blood cells by the serum from the others (Chakravarty, 2020). In 1901, Karl Landsteiner discovered the ABO blood group system and this encourage researchers to look for a connection between the ABO blood group system

and different diseases which suggested many bacterial and virus infections are associated with the ABO blood group system such as helicobacter pylori norovirus, hepatitis B virus and severe acute respiratory virus (SARS-CoV) (Alpoim et al., 2013).

Moreover, understanding the link between illnesses that have resulted in pandemics and blood types might be a helpful risk factor for predicting outcomes and developing effective ways to fight disease transmission in relation to blood group distributions (Shokri et al., 2021). In addition to the main uncertainties regarding blood type and MERS infection during the severe acute respiratory syndrome Covid (SARS-CoV) episode that began in late 2002 along with risk factors that may exacerbate disease severity and progression. (D'Adamo et al., 2020) This has often led to an increase in symptom severity to more questions than answers involving susceptibility to COVID-19 that have recently been linked to ABO blood groups in patients (D' Adamo et al., 2020).

In a meta-analysis which consisted of two case-control cohorts among 31,100 samples, the "A" blood group was shown to be related with a perilous of exacerbated COVID-19 infection but the "O blood group was found to be protective towards COVID-19 infection (Wu et al., 2020). Furthermore, people with AB group appear to have a greater risk of COVID-19 and death. Individuals with the O blood group were probable to have a riskless of COVID-19 severity whereas those with the B blood group were more likely to have a riskless of COVID-19 (Wu et al., 2020). On the other hand, a study conducted in Egypt and Saudi Arabia which showed that there is an association between blood group and being exposed to infection with COVID-19 as "O" group are more protective against COVID-19 whereas blood group "A" wasn't the highest risk (ElShitany et al., 2021).

1.2 Problem statement

Researchers have studied several factors affecting COVID-19 virus including the possible role of blood groups. As the most generally explored erythrocyte antigen framework and clear available component in a person's hereditary makeup (Mao et al., 2019), ABO blood group framework is utilized in clinical practice widely and evidence from previous studies conducted in Asia and Mediterranean Europe prompted the exploration that highlighted a higher risk of serious COVID-19 infection in individuals with the A group and relative safety in those with the O group, although there is still argumentative evidence (Valenti, et al., 2020). On the other hand, previous studies were not able to distinguish if the relationship between ABO and COVID-19 was clarified by an increased risk of COVID19 infection or

by heightened risk of continuation towards more serious symptoms (Valenti, etal., 2020). Therefore, this study will be conducted to find the association between ABO blood group system and the severity of COVID-19 in the West-Bank among Palestinians.

1.3 Study Justification

Blood types are genetic features that differ across cultures, possibly due to both the influence of the founder and biological evolution, the relation between the various of blood types and infectious disease vulnerability has represented with conspicuous examples Helicobacter pylori and the infection of Plasmodium falciparum (Ewald & Sumner, 2016). By varied process, including acting as receptors or misguide for infectious organisms and altering immune response in the construction of anti-ABO antibodies, blood group antigens may influence disease susceptibility, where as it may reveal a crucial role in driving the seriousness of the disease in patients diagnosed with coronavirus disease (COVID-19) (Laguipo, 2020).

Genetic study in patients with COVID-19 has demonstrated that persons with type O blood tend to be safe from serious illnesses and many with blood type A may suffer complications related viral infection (Laguipo, 2020).

The researchers have observed that individuals with A blood type had a 45 %greater chance of contracting the coronavirus and experiencing respiratory failure in comparative with other types of groups, whereas people with O blood group have a 35% reduced chance of contracting serious COVID-19 virus (Buchwald, 2020).

However, this requires the need to follow up on the validity of the association of people of different ABO group with infection of the COVID-19 virus as the cases are increasing in the world (WHO, 2021) and exceeded 300,000 cases in Palestine until 29/6/2021 which represented 13.43% among (20-29) years old, 11.28% among (30-39) years and 9.44% among (10-19) years (MOH, 2021a). (See figure 1.1 and figure 1.2)

This study will be the first in Palestine, through which it will investigate the association between ABO blood group and the severity of COVID-19. Although there are not enough studies on the association between blood type and the severity of infection with the Covid 19 virus, this study may benefit more in-depth studies in the future.

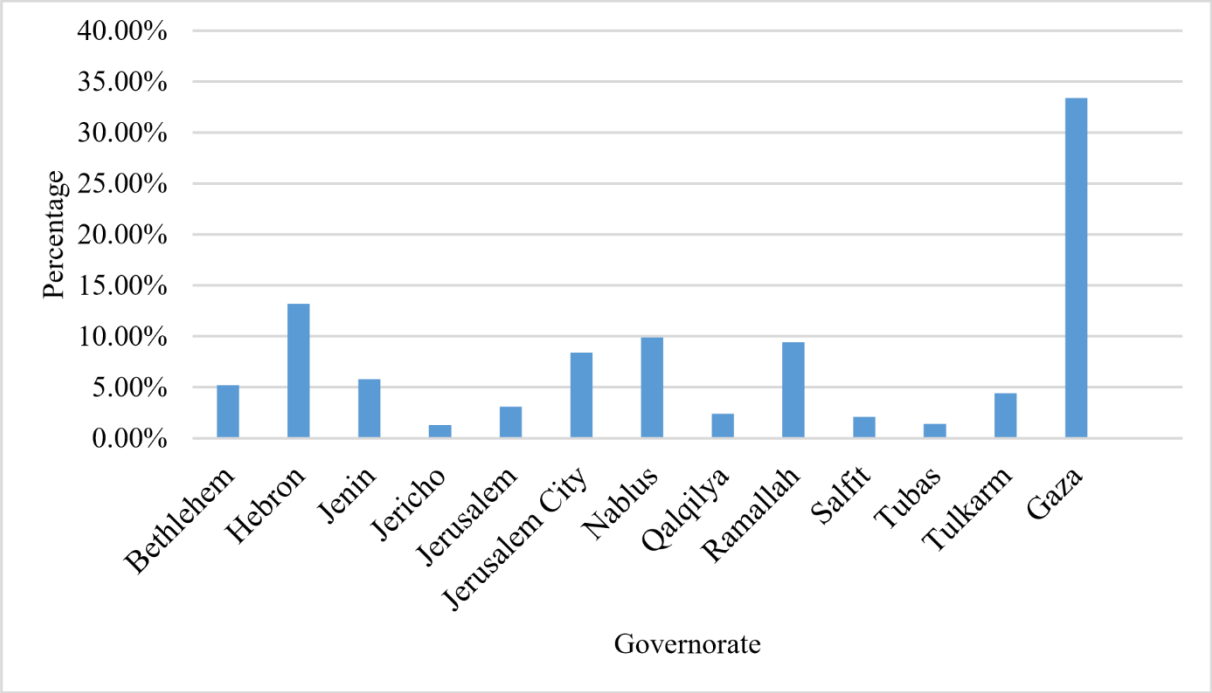

Figure 1.1: Distribution of total Distribution of total confirmed COVID-19 cases in Palestine between March 2020 - June 2021 years (MOH, 2021a)

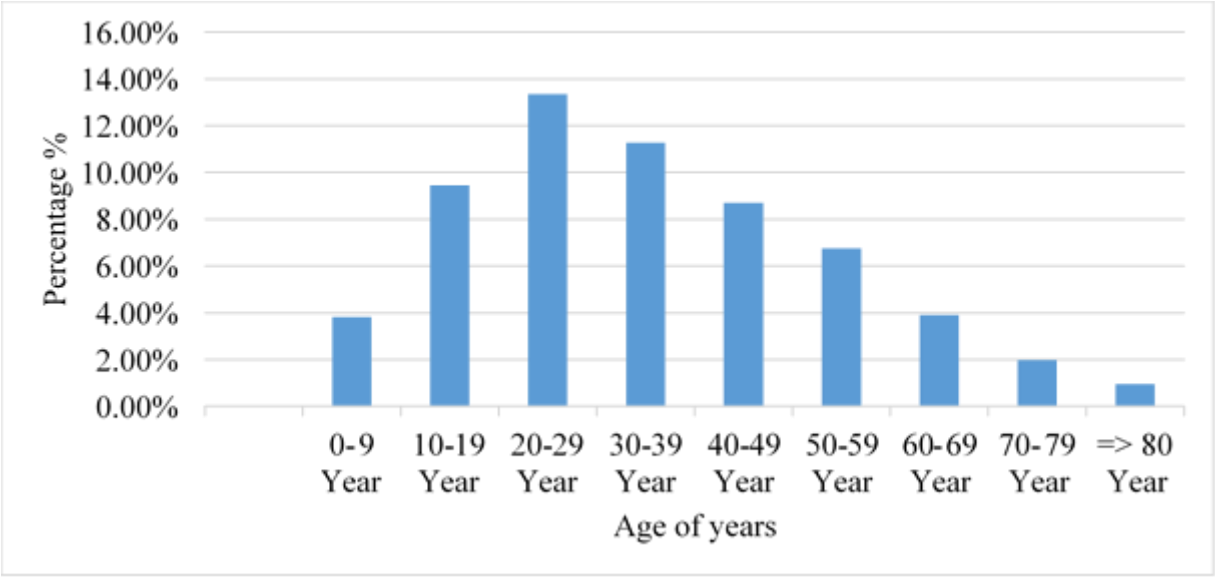

Figure 1.2: Distribution of confirmed COVID-19 cases by age group in Palestine between March 2020 – June 2021 years 2020-2021 (MOH, 2021a).

1.4 Expected outcome

The study on the association between ABO blood group system and the severity of COVID-19 in the West-Bank among Palestinian which can reduce the possibility of infection with Covid 19, increase close monitoring and strengthen treatment for the responsible blood group, also it may shed light on other factors affecting COVID-19 such as sociodemographic

data, health status, past seasonal flu experience, smoking status and taken the prevention measurement.

Thereafter, it would increase the awareness among people about the association between their blood group and their susceptibility to infection with COVID-19.

1.5 Study Aim

This study aimed to determine the association between ABO blood group system and the severity of COVID-19 in the West-Bank in Palestine.

1.6 Study Goal

To provide the susceptible blood groups more vigilant screening and proactive care which may help meet the objective of reducing the possibility of infection with the virus COVID-19 as a public health threat.

1.7 Study Objectives

1. To investigate the association between ABO blood group system and the susceptibility to be infected with COVID-19 among cases and controls.
2. To determine the association between study participants in regard with their sociodemographic characteristics.
3. To examine the association between different risk factors of COVID-19 as smoking, seasonal flu experience and health status with the susceptibility to be infected with COVID-19.
4. To examine the association between ABO blood group and the severity of symptoms among COVID-19 cases.
5. To identify ABO blood group distribution and sociodemographic characteristics among COVID-19 cases in the West-Bank.
6. To examine the association between the composite outcome of COVID-19 such as intensive care unit admission, intubation, oxygen therapy and complications with ABO blood group among cases.

1.8 Research Questions

1. Is there an association between ABO group system and susceptibility to infection with COVID-19?

2. Is there an association between sociodemographic characteristics of participants and the susceptibility to infection with COVID-19?

3. Is there an association between smoking, seasonal flu experience and health status with the susceptibility to infection with COVID-19?

4. Is there an association between ABO blood group and the severity of symptoms among COVID-19 cases?

5. Is there an association between the composite outcome of COVID-19 such as admission to intensive care unit, intubation, oxygen therapy and complications with ABO blood group among cases?

Chapter Two

Literature Review

2.1 Introduction

Scientists explained that blood groups may play a significant role in the infection of many infectious diseases, which made them search for the existence of relationships between infection with the COVID-19 and these groups, especially since their distribution is different among population (Barnkob et al., 2020). In this chapter, we are explained the conceptual framework of the study and discussed the association between ABO blood group and the severity of COVID-19.

2.2 Blood groups characteristics

An Austrian scientist Karl Landsteiner noticed in the first of 20th century that the red blood cells of certain individuals were agglutinated by serum from other individuals (Cooling, 2015). He made a notice of antiglobulin patterns and explained that blood could be broken into groups, as the term 'blood group' refers to the complete construction of the blood group containing antigens of the red blood cell (RBC) whose specificity is determined by a sequence of genes that can be allelic or very closely linked to the identical chromosome but the term “blood type” refers to a particular pattern of response within a specified mechanism to the testing of antisera (Rath et al., 2014). Therefore, the precursor to the ABO blood group antigens is H-antigen since it serves as a precursor, its absence indicates the absence of A and B antigens (Rath et al., 2014). There are four major blood groups determined on the surface of red blood cells by the presence or absence of two antigens, A and B. In addition to the A and B antigens, which can be present (+) or absent (–), there is a protein called the Rh component, producing the eight most common forms of blood (A+, A-, B+, B-, O+, O, AB+, AB) (American Red Cross, 2020).

In epidemiological research, blood groups are common targets because they are genetically defined characteristics with documented polymorphic expression across individuals and populations (Cooling, 2015). The ABO carbohydrate moieties of Landsteiner are inherited genetically and previous studies indicated a link between the composition of ABO blood, cardiovascular disease and cancers, as well as typing and susceptibility to certain infections, including coronavirus SARS (Latz, etal., 2020).

2.3 COVID-19 Characteristics

SARS-CoV-2 nucleic acid identification in nasal, throat, or other respiratory system samples using real-time polymerase chain reaction screening and next-generation sequencing is the primary method for clinical diagnosis of COVID-19 (Masoud & Dyal, 2020).

Cough, fever, and lethargy are the most frequent COVID-19 clinical signs, as the elderly people and those with chronic diseases are more susceptible for serious symptoms, it spreads primarily through the respiratory tract, where it binds with high affinity to the angiotensin converting enzyme 2 (ACE2) receptor which compatible with SARS-CoV (Masoud & Dyal, 2020). Also, studies showed that aging, higher body mass index, smokers, race, gender and people who received seasonal flu vaccine shot must be controlled for confounding effects to assess the severity of COVID-19 (Henderson, 2021).

According to the previous studies, the main characteristic variables which described the COVID-19 outcomes were admission to intensive care unit, respiratory failure and needed the mechanical ventilation, respiratory distress and death (Henry & Lippi, 2020). The researchers found various relationships between these variables and COVID-19 which categorized as the followings:

2.3.1: Age

Although persons of all ages are at risk of catching COVID-19, older people are at a higher risk of developing serious illness due to physiological changes associated with aging and probable underlying health problems such as cancer, diabetes mellitus and hypertension (WHO, 2020b).

2.3.2: Gender

Although males and females are both susceptible to SARS-CoV-2, males are more likely to have higher severity and death, a characteristic shared by SARS 2003 and the Middle East Respiratory Syndrome (MERS), based on existing of gender differences in respiratory viral infections such as smoking, are most likely linked to the poor management and consequences of COVID-19 in men, also females have more intense and stronger innate and immunological responses than men (Mi et al., 2020).

However, males have higher levels of pro-inflammatory cytokines and chemokines as the primary cytokine storm receptor, high homogeneity expressed in male lung epithelial cells, implying that males are more vulnerable to cytokine storm, which can contribute to COVID-

19 worsening in addition to, males have greater cell type-specific ACE2 receptor expression in type two alveolar epithelial cells than females (Mi et al., 2020).

2.3.3: Body Mass Index

Patients who are over weighted are at risk for chronic inflammation, which alters immunological and thrombogenic responses to pathogens as well as decreased pulmonary function caused by excess weight (CDC, 2021).

CDC assessed this association between body mass index and risk for unfavorable outcomes of COVID-19 among 148,494 patients with COVID-19 at 238 United States hospitals between March and December 2020 as the results showed that half of patients (50.8%) were obese and (28.3%) were overweight and there is significant difference between obesity and overweight and invasive mechanical ventilation especially among who aged 65 and older, displaying a dose response relationship as BMI increases as the estimated risk of intrusive mechanical ventilation increased over the whole BMI range, from 15 kg/m2 to 60 kg/m2 and compromised immunological function with reducing lung capacity and reserve which made breathing more demanding (CDC, 2021).

2.3.4: Occupation

According to the findings of four contact tracing case-control studies, people working in healthcare, social care, or hospitality were more likely to be COVID cases than those working in other occupations as they are in the direct contact with people (Scientific Advisory Group for Emergencies, 2021).

2.3.5: Seasonal flu vaccine

CDC confirmed that flu vaccination reduces the risk for acute respiratory infectious diseases and they conducted a study on hospitalized flu patients during 2013-2014 divided into two groups according to receiving seasonal flu vaccine and not as the results showed that unvaccinated patients were 2-5 times more likely to die than who vaccinated (CDC, 2017).

However, the researchers examined the medical records of almost 27,000 individuals who were tested for COVID-19 infection at Michigan Medicine between March and mid-July of 2020. Four percent of the almost 13,000 people who had a flu vaccine the previous year tested positive for COVID-19 and 5% of the 14,000 people who had not had a flu vaccine tested positive for COVID-19 (Henderson, 2021).

2.3.6: Smoking status

There are challenges about the relationship of smoking and COVID-19 among researchers which summarized into the followings:

In patients who need hospital care for Covid-19, a review by the World Health Organization revealed that smoking is linked to more severe disease and an increased risk of mortality (Heart Matters Magazine, 2021). On the other hand, people who presently smoke may be less likely to get infected with coronavirus, according to a new evidence assessment conducted by London researchers which revealed that nicotine inhibits the virus's ability to enter cells via interfering with ACE2 receptors (Heart Matters Magazine, 2021).

However, researchers stated that smoking has been linked to overexpression of ACE2, the SARS-CoV-2 virus's receptor in the lungs and shows that the effects are mixed, with upregulation in epithelial cells and downregulation in alveolar type 2 cells. Internalization of ACE2 as a result of viral infection may result in unopposed ACE inhibitor action and high angiotensin 2 levels, contributing to endothelial damage and the coagulopathy and micro thrombosis seen in severe COVID-19 patients (Hopkinson et al., 2021).

2.4 Blood group and COVID-19 infection

The first evidence of a link between blood groups and coronavirus infections dates back to 2005, when Cheng et al. investigated the relationship between ABO blood groups and the risk of SARS-CoV infection among 45 health-care workers who were not protected by appropriate equipment during exposure to affected patients, according to this study those with “O” blood type had a reduced risk of contracting COVID-19 than those with non-O groups (odds ratio [OR] = 0.18; 95% confidence interval [CI]: 0.04–0.81; p = 0.03) (Shokri et al., 2021).

Antigens of the ABO blood groups are found not only on erythrocytes, but also on the mucosal membranes of the gastrointestinal tract, respiratory, and reproductive systems, as well as in their secretions the FUT2 gene, which encodes the fructosyltransferase 2 enzyme, controls the expression of such antigens on epithelial cell surfaces and secretions (Shokri et al., 2021).

It was recently discovered that the receptor binding domain (RBD) of the SARS-CoV-2 spike protein had only a low affinity for binding to A, B, and H antigens on RBCs, but a high affinity for binding to blood group A antigen when exposed to blood group antigens expressed on respiratory epithelial cells (Shokri et al., 2021). Moreover, many studies assess the susceptibility to be infected with COVID-19 which summarized in Table 2.1.

A retrospective cross-sectional study conducted for two groups the first one contained 726 COVID-19 patients and the second one contained 2399 subjects in who hadn't diagnosed with COVID-19 as 707 from them selected randomly for comparing results in Arab community (Saudia Arabia and Egypt), aimed to determine the impact of blood group on COVID-19 and the results showed that there is significant difference between cases and controls in regard blood group, as whom with blood group "O" was lower in COVID-19 cases than controls (204, or 28%, versus 253, 36%) whereas there is insignificantly higher distribution between cases and controls in regard blood group "A" (35% versus 29%) respectively and non-significant difference between cases and controls in regard RH (P. value= 0.191) (El-Shitany et al., 2021).

A case control study conducted among 105 cases and 103 control in Wuhan who had tested for COVID-19 PCR between January and March 2020 aimed to investigate the association between blood group and the risk of COVID-19 as the results showed that there is a significant difference between blood group and the risk to infection with COVID-19, especially the females with "A" blood group (Fan et al., 2020).

Another case control study conducted among 186 of cases with COVID-19 and 1881 healthy controls in Turkey to identify the association between blood group and COVID-19 infection and its outcomes as the results showed that blood group "A" is significantly difference more frequent among cases compared to the controls and blood group "O" was significantly lower among cases compared to controls (24.8% vs. 37.2%, P: 0.001; OR: 1.8), for the both blood groups "B" and "AB" there no differences for catching COVID-19 (Goker et al., 2020).

A case control study conducted among 2153 COVID-19 cases and 3694 healthy controls in Wuhan to explore the association between blood group and risk for COVID-19 as the results revealed the significant difference between cases and controls 38.0% vs. 32.2% (P <0.001) as the risk among blood group "A" higher in cases than controls (Li et al., 2020).

Whereas, a population-based cohort study among 225,556 patients in Canada who had tested for COVID-19 between January until June 2020 to determine whether the type of blood group and rh are associated with the risk of COVID-19 by comparing blood group "O" with other types of blood group and the results showed that the people with "O" blood group may be associated with the lower level of risk to infect with COVID-19 (AOR, 0.89 [CI, 0.84 to 0.94]) (Ray et al., 2021).

2.5 Blood group and the severity of COVID-19 symptoms

The severity of COVID-19 makes challenges between studies which summarized in Table 2.2. El-Shitany et., al's retrospective cross-sectional study conducted for two groups the first one contained 726 COVID-19 patients and the second one contained 2399 subjects in who hadn't diagnosed with COVID-19 as 707 from them selected randomly for comparing results in Arab community (Saudia Arabia and Egypt), aimed to determine the impact of blood group on COVID-19 and the results showed that there is significant difference between cases and controls in regard risk for COVID-19 but not significant with fever, headache, shortness of breath, cough, bone ache, gastrointestinal symptoms and hospitalization. On the other hand, there is statistically significant between blood groups and the need to use mechanical ventilation, myalgia, and the recovery time from COVID-19 as blood group "A" represented the highest percentage experienced with low oxygen saturation (70.2%) and blood group "B" showed that no one had experienced of low oxygen saturation (0%). Despite of that, blood group "O" represented the highest percentage for whom required mechanical ventilation (2.9%) and no one with blood group "A" required it (0%) (El-Shitany et al., 2021).

A nested prospective observational study conducted among 123 critically ill patients with COVID-19 in Canda to determine whether blood group associated with the severity of symptoms of COVID-19 as the results showed that high proportion from people who with blood group "A" and "AB" had a respiratory failure which recommended to use the mechanical ventilation (P. value = 0.02) and had longer duration at intensive care unit) P. value= 0.03) (Hoiland et al., 2020).

On the other hand, a case control study conducted among 107,796 participants had tested COVID-19 PCR from March to November 2020 in Utah, Idaho and Nevada, aimed to find the correlation between ABO blood group and risk for COVID-19 and the severity after infection, as they are adjusted for age, gender and RH factor and the results showed that blood group wasn't associated with the risk either the severity of symptoms (Anderson et al., 2021).

Another cross-sectional study conducted among 507 COVID-19 patients admitted to the king Fahad Hospital in Saudi Arabia to determine whether blood group associated with COVID-19 susceptibly and severity as the cases were who within medical history as smoking history and any chronic disease and had diagnosed with COVID-19 PCR. However, the results found that "A" not differ statistically from "O" with age, gender and BMI nor with smoking

status while there was a significant increase in chronic diseases such as hypertension, diabetes melilites, ischemic heart disease, cerebrovascular accident, and bronchial asthma, with significant increase in the sever and critical patients with blood group "A" than "O", also people with blood group "A" had the significant increase to need mechanical ventilation (24/2, 16/1, respectively) (Samra et al., 2021).

Likewise, A retrospective cohort study conducted among 227 COVID-19 patients hospitalized to tertiary hospital care in New York between March 8th to July 31st, 2020 aimed to examine the ABO blood group susceptibly and severity of COVID-19 infection as the results revealed that blood group not associated with the susceptibly for catching COVID-19 (P. value=0.93) nor with the severity of COVID-19 for required to intensive care unit (P. value= 0.66) or require renal replacement therapy (P. value =0.09) (Mullins et al., 2021).

2.6 Blood group and COVID-19 outcomes

Studies found variation in the results between blood group and COVID-19 outcomes. Table 2.3 summarized the studies which concerned of the association between blood group and COVID19 outcomes.

A cohort study conducted in five major hospitals in state of Massachusetts from march to April 2020 aimed to determine if there is a correlation between ABO blood type and the severity of COVID-19 among 7648 patients in all the hospitals undergoing COVID-19 research and the results showed there 37.5 % of them were admitted to hospital, 9.5 % were admitted to ICU, 8.4% were intubated and 6.9% of them died, in addition to 34.2% of them had A blood group, 15.6% were blood type B, 4.7% of them were AB blood group and 45.5% of them were O blood group in regard with the researchers found that ABO blood type not associated with COVID-19 disease severity defined as intubation or death, whereas the lowest frequency for whom diagnosed with the disease was represented by "O" group (Latz et al., 2020).

A case control study conducted by (Fan et al., 2020) on 105 COVID-19 cases and 103 controls in Zhong nan Hospital of Wuhan University from January until March 2020 to assess the considering lymphopenia (low of lymphocyte count) as a feature of COVID-19 and the results showed that the average level of lymphocyte count was the lowest with blood type A in patients compared with other blood types (Fan et al., 2020).

Critically ill patients with COVID-19, shock from a variety of etiologies is prevalent and associated with high mortality due to inadequate oral intake and high-grade fever causing

insensitive losses, hypovolemic shock can be present in earlier stages of hospitalization, likely along with associated diarrhea (Fox et al., 2020).

Moreover, the heart may be impaired in some patients, and this may happen in people with or without a previous cardiovascular diagnosis. In patients hospitalized with COVID-19, evidence of myocardial injury, as defined as an elevated troponin level, is normal, with putative causes including stress cardiomyopathy, hypoxic injury, ischemic injury caused by cardiac microvascular or epicardial coronary artery disease), and systemic inflammatory response syndrome (cytokine storm) (Bonow et al., 2020).

Another case control study in Turkey aimed to assess the relationship between ABO groups and COVID-19 infection among 179 patients with confirmed COVID-19 and 5200 healthy control patients and the results showed that A blood group is the most common with cases of COVID 19 than control group and found that patient with A blood group had a longer stay in intensive care unit with higher mortality rate than others (Aktimur, etal., 2020).

Also, an ecological study conducted among 86 Asian, European, African and American countries to investigate the association between blood group or Rh factor and the COVID-19 outcomes including the morbidity and mortality cases as the results showed that A, B, Rh- are associated significantly with COVID-19 as blood group A- had the most seriousness outcomes and hospitalization rates (Ansari-Lari & Saadat, 2020).

2.7 RH blood group system and COVID-19

Few studies examine the association between RH factor and COVID-19. Table 2.4 shows the literature studies the association between RH factor and COVID-19.

A population cohort study conducted on 225,556 COVID-19 patients in Canda between January until December 2020 as the results showed thar negative RH factor seemed protective against COVID-19 infection especially for those who were O− (adjusted relative risk, 0.79 [CI, 0.73 to 0.85] (Ray et al., 2021).

Another case control study conducted on 5668 COVID-19 patients and 5668 health controls in Iraq demonstrated that people with negative RH are more susceptible to COVID-19 than people with positive RH blood type (OR = 2.38, 95% CI (2.03, 2.79), p= 0.0001) and there is no evidence for association between gender and blood type among COVID-19 patients (X2 = 4.97, df = 7, p = 0.664), also clinical symptoms such as (fever, cough, dyspnea,

anosmia ageusia, loss of appetite, muscle ache, cyanosis, rhinorrhea, sore throat, diarrhea, nausea, and vomiting) have no significant correlation with blood types (Majeed et al., 2021).

An ecological study conducted among 86 Asian, European, African and American countries to investigate the association between blood group or Rh factor and the COVID-19 outcomes including the morbidity and mortality, the results showed that there is an association between RH negative factor and the COVID-19 risk (Ansari-Lari & Saadat, 2020).

A retrospective cohort study conducted among 841,317 who had tested for COVID-19 PCR in Denmark aimed to identify the association between blood group, Rh factor and risk for COVID19 as the results showed that there was significant difference between blood group and risk for COVID-19 either, there wasn't significant difference between blood group or Rh factor and the hospitalization outcome or death (Barnkob et al., 2020).

2.8 Possible mechanisms discuss the association between blood group and COVID-19

2.8.1: ABO antigens as receptors for COVID-19 cell entry

Viral interaction with ACE-2 to enhance cell entrance may occur with other host molecules, such as blood group antigens, which influences the susceptibility of different blood group carriers to SARS-CoV-2 infection (Wu et al., 2021).

A recent in vitro investigation found that when SARS-CoV-2 was exposed to ABO antigens produced in respiratory epithelial cells, receptor binding domain preferred to bind to A antigen over B and H antigens (P 0.001). This indicates the possible significance of epithelial cell antigens in the development of SARS-CoV-2 infection (Wu et al., 2021).

2.8.2 Antibodies against ABO antigens and neutralization of COVID-19 particles

Guillon et al. revealed in 2008 that natural anti-A antibodies might block the attachment of SARS-CoV spike protein to ACE2. As a result, one may think that both blood types O and B should give protection, however numerous investigations have shown that blood type B had no effect on COVID-19 risk (Guillon et al., 2008).

For example, Gerard et al., found that patients with anti-A antibodies (blood types O and B) were considerably under-represented in COVID-19 as compared to A and AB then they introduced the possibility to see if there was a difference between groups O and B anti-A antibodies (Gerard et al., 2020). As a consequence, the frequency of group O carriers was substantially lower in COVID-19 patients but the prevalence of group B carriers was

significantly greater, this suggests that anti-A from O blood groups is more protective than anti A from B blood groups (Gerard et al., 2020).

Differences in the nature of anti-A antibodies from blood groups O and B are responsible for the main immunoglobulin isotypes of anti-A antibodies, which are IgG in blood group O and IgM in blood group B (Almadhi et al., 2021).

2.8.3 Blood group phenotypes and COVID-19 progression

Individuals with blood type O have lower amounts of von Willebrand and VIII factors, which may contribute to a lower risk of cardiovascular disease (Valenti et al., 2020)

COVID-19 coagulopathy and vasculopathy are known to be significant factors to the development of acute respiratory distress syndrome. As a result, the decreased risk of illness development observed in blood type O patients is thought to be a result of this occurrence (Valenti et al., 2020). Furthermore, blood type O carriers have reduced amounts of angiotensin converting enzyme (ACE), which is responsible for converting angiotensin one to angiotensin two (Valenti et al., 2020). Angiotensin 2 may increase inflammatory reactions as well as elevated blood pressure. As a result, low levels of ACE in group “O” patients infected with SARS-CoV-2 may be associated with milder symptoms (Valenti et al., 2020).

2.9 Summary of the previous studies on Blood group and COVID-19

Table 2.1: Blood group and COVID-19 infection

Authors	Location	Study design	Sample size	Main results
(El-Shitany et al., 2021)	Saudia Arabia and Egypt	Retrospective cross-sectional study	726 COVID-Versus 707 controls didn't diagnose with COVID-19	Blood group "O" more protective towards COVID-19. No significant difference between blood group "A" and COVID-19 risk.
(Fan et al., 2020)	Wuhan	Case control	105 cases 103 controls	There is significant difference between blood group and COVID-19 as female with "A" blood group showed the highest risk.
(Goker et al., 2020)	Turkey	Case control	186 of cases with COVID19 and 1881 healthy controls	There is significant difference in "A" blood group and "O" blood group. A" high frequency among cases "O" high frequency among controls. No significant difference in "B" and "AB".
(Li et al., 2020)	Wuhan	Case control	2153 COVID-19 cases and 3694 healthy controls	Blood group "A" high risk for COVID-19.

Table 2.2: Blood group and the severity of COVID-19 symptoms

Authors	Location	Study design	Sample size	Main results
(El-Shitany et al., 2021)	Saudia Arabia and Egypt	Retrospective cross-sectional study	726 COVID-Versus 707 controls didn't diagnose with COVID-19	Significant difference with "A" the most suffering from low oxygen saturation and "O" showed the most required mechanical ventilation
(Hoiland et al., 2020)	Canada	Nested prospective observational study	123 critically ill patients with COVID19	Association with "A" and "AB" high require to use mechanical ventilation
(Anderson et al., 2021)	Utah, Idaho and Nevada	Case control	107,796 participants had tested COVID-19 PCR from March to November 2020	Blood group not associated with the risk of COVID-19 either the severity of symptoms
(Samra et al., 2021)	Saudia Arabia	Cross sectional	507 COVID-19 patients admitted to the king Fahad Hospital	There is significant difference of severe symptoms and critical illness among blood group "A" and "O".
Mullins et al., 2021)	New York	Retrospective cohort study	227 COVID-19 patients hospitalized to tertiary hospital care between March - July 2020	No significant difference with risk nor the severity
(Majeed et l., 2021)	Iraq	Case control	5668 COVID-19 patients and 5668 health	No association between clinical symptoms and blood group

Table 2.3: Blood group and COVID-19 Outcomes

Authors	Location	Study design	Sample size	Main results
(Latz et al., 2020)	Massachusetts state	Cohort study	7648 COVID-19 patients	ABO group wasn't associated with the severity of COVID19 disease, and lowest frequency of cases whom with "O"
(Fan et al., 2020)	Zhong nan Hospital of Wuhan University	Case control	105 COVID-19 cases 103 health controls	The average level of lymphocyte count was the lowest with blood type A
(Aktimur, etal., 2020)	Turkey	Case control	179 COVID-19 patients 5200 health controls	There is significant difference between blood group and COVI-19 With significantly increased the duration in intensive care units among blood group "A"
(Ansari-Lari & Saadat, 2020).	Asia Europe Africa and America	Ecological study	86 countries	A, B, Rh- are associated significantly with COVID-19 A- had the most seriousness outcomes and hospitalization rates

Table 2.4: RH blood group system and COVID-19

Authors	Location	Study design	Sample size	Main results
(Ray et al., 2021).	Canda	Cohort study	225,556 subjects who tested for COVID-19 between January until June 2020	Negative RH factor seemed protective against COVID-19 infection especially for those who were O–
(Majeed et al., 2021)	Iraq	Case control	5668 COVID-19 patients and 5668 health	Negative RH are more susceptible to COVID-19.
(Ansari-Lari & Saadat, 2020).	Asia, Europe Africa and America	Ecological study	86 countries	There is an association between RH negative factor and the COVID-19 risk
(Barnkob et al., 2020).	Denmark	Retrospective cohort study	841,317 who had tested for COVID-19 PCR	No significant difference between RH factor and hospitalization outcome or death

2.10 Conceptual Framework

In this part we discussed the conceptual framework (Figure 2.1) that used in the study based on the literature review and defined the major theoretical and operational definitions of the study as the followings:

2.10.1: Theoretical Definitions

Allele: Is one of two or more versions of a gene which inherits two alleles for each gene, one of them from each parent and the combination of alleles possess the genotype as the ABO blood group system, which whom with "AB" have one allele for A and another one for B despite of that neither are with blood group "O" (Rogers, 2019).

Antigen: Is any substance that suppose the immune system to produce antibodies in response to it when the immune system couldn't recognize the substance to fighting it (Medline plus, 2019).

Angiotensin one: A peptide hormone for constricting the blood vessels, created and released by the liver, circulated in plasma and broken by the renin which is an enzyme produced by the kidney to form angiotensin one (Merriam Webster, 2019b).

Angiotensin converting enzyme: A proteolytic enzyme that converts angiotensin from its physiologically inactive form to its active vasoconstrictive form (Merriam Webster, 2019a).

Angiotensin two: A vasoactive octapeptide which stimulates a vascular smooth muscle, enhances produce aldosterone, and enhances the sympathetic nervous system, it is produced as a result of an angiotensin converting enzyme (Merriam Webster, 2019b).

Secretor status: The appearance or absence of water-soluble ABO blood group antigens in bodily fluids such as saliva (Azad et al., 2018).

Fructosyltransferase 2: A gene demonstrate the secretor status which encodes the alpha fructosyltransferase as that an enzyme transfer fucose sugar (C6H12O5) to nucleotide sugar (Azad et al., 2018).

Factor 8: A glycoprotein clotting factor which is essential for clotting the blood in plasma (Merriam Webster, 2019c).

Willebrand: A large glycoprotein clotting factor distributed in blood plasma that mediates platelet aggregation to collagen at sites of tissue destruction, binds to and protects factor 8 from deterioration, and is deficient or defective in von Willebrand disease patients (Merriam Webster, 2019d).

2.10.2: Operational Definitions

The following definitions according to the study conceptual framework.

COVID-19 patient: An individual with a positive detection of SARS-CoV antibodies to serum positive polymerase chain reaction (PCR) for COVID-19 (CDC, 2020).

Participant characteristics: A group of characteristics involving a mixed of factors affected by age, gender, blood group, RH factor, smoking status, occupation exposure, seasonal flu experience and health status. Each of the characteristics reviewed in the literature review of the study.

ABO Blood Group: Identification of human blood on the basis of the biological properties of red blood cells (erythrocytes), as evidenced by the presence or absence of red cell surface antigens A and B. Thus, persons may have type (A, B, O, AB blood) (Kritz & Huang, 2020).

Rhesus Factor (RH): Is an inherited protein originates on the surface of red blood cells, if blood has the protein the Rh is positive but when protein is unavailable the Rh will be negative (Mayo clinic, 2020).

Severity of Symptoms: This refers to the degree of symptoms which could be (Mild, moderate, severe, critical illness) (WHO, 2020a).

Mild symptoms: Include low grade fever (not more than 100 degrees Fahrenheit), cough, sore throat, malaise, headache, muscle pain, congestion or runny nose, loss of taste or smell, and diarrhea without shortness of breath (WHO, 2020a).

Moderate symptoms: A patient might start to show evidence of lower respiratory disease, fever of about 101-102 degrees Fahrenheit, chills with repeated shaking, but they still have good oxygenation on room air in addition to any of the mild symptoms (WHO, 2020a).

Severe symptoms: Include shortness of breath (generally breathing quickly over 30 times a minute), chest discomfort, confusion/unresponsiveness and oxygenation level is less than 94%, and that generally means that patient needs supplemental oxygen (WHO, 2020a).

Critical illness: Include the signs of respiratory failure and need a breathing machine and patients may experience other organ dysfunction and shock which require to intensive care unit (WHO, 2020a).

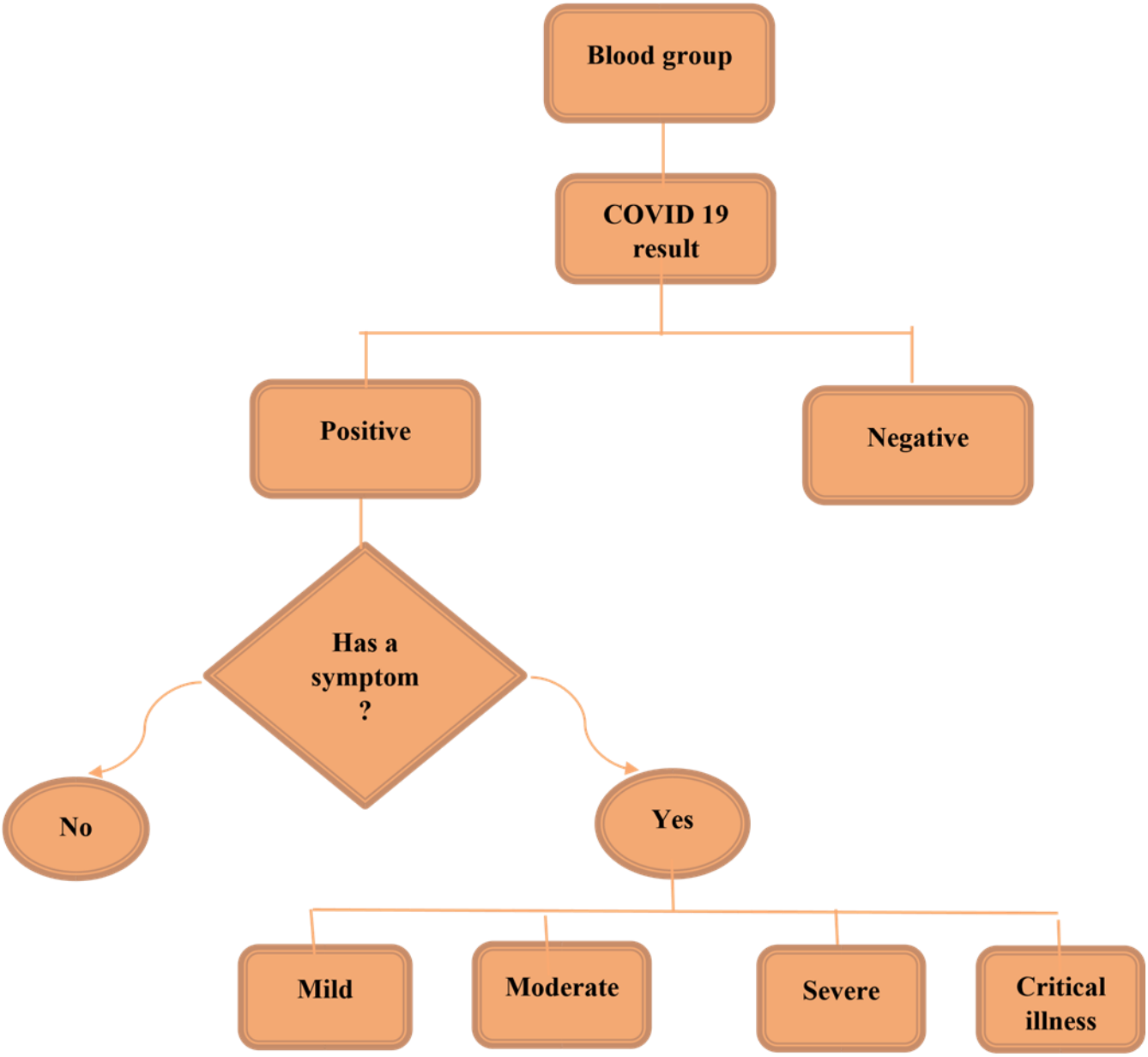

Figure 2.1: Conceptual frame work of the association between ABO group system and the severity of COVID-19

Chapter Three

Methodology

3.1 Introduction

This chapter described the methodology used in this study includes study setting, study design, sampling process that used in this study, selection criteria, statistical analysis and study instrument. Furthermore, the ethical considerations had been taken.

3.2 Study setting and population characteristics

The study conducted at all the governorates in the West Bank who had tested for COVID-19 during 1/3/2021 until 31/3/2021 which enfolded in Table 3.1 (Bethlehem, Hebron, Jericho, Ramallah, Nablus, Jenin, Qalqilya, Salfit, Tubas, Tulkarm, Jerusalem).

West Bank characteristics: West Bank is the term given by Jordan to the remaining part of Palestine (within the borders of the British Mandate) that did not fall after the Nakba, and which it annexed to it after the Battle of Jerusalem at the Jericho Conference in 1951, and its area constitutes approximately 21% of the area of historical Palestine (from the river to the sea) about 5860 km² (Marfeh, 2021).

This area includes geographically the Nablus Mountains, the Jerusalem Mountains (including the eastern part of the city of Jerusalem), the Hebron Mountains and the western Jordan Valley. The Jordanian authorities named it the West Bank because it is located to the west of the Jordan River, while most of the territory of the Hashemite Kingdom of Jordan is located east of the river (Marfeh, 2021) which showed in the figure 3.1.

Bethlehem governorate: It is located in the south of the West Bank has a population about of 229884, covers an area of 575 square kilometers and includes five main cities, seventy villages and three Palestinian refugee camps (PCBS, 2020).

Hebron governorate: It is located in the south of the West Bank, bordered on the north by the Bethlehem Governorate between the Green Line and the Dead Sea on the other sides. It is the largest of the West Bank governorates in terms of area and population, with an area of 1,060 km² which represented by 16% of the lands of the West Bank and a population of 762541 in 2020 (PCBS, 2020).

Jericho governorate: It is located in the middle of the West Bank, has a population estimated to be 52355, including more than 6000 Palestinian refugees living in the camps (PCBS, 2020).

Ramallah and Alberieh governorate: Located in the middle of the West Bank, with an area of 844 km² and a population of about 347818 (PCBS, 2020).

Nablus governorate: Nablus, located in the northern West Bank, is considered the center of the northern West Bank, as well as the capital of the Nablus Governorate, which includes 56 villages and has an estimated population of 407754 with an area of 28.6 km² (PCBS, 2020).

Jenin governorate: A governorate located in the northern West Bank of the Palestinian Authority and its center is the city of Jenin. The governorate constitutes an economic weight much greater than its population size; it has a population of about 332050. Its area is 583 km² and constitutes 9.7% of the total area of the West Bank, the Jenin camp is located to the west of Jenin and is home to 16,000 refugees (PCBS, 2020).

Qalqilya governorate: It is located in the south of the West Bank, with an area of 166 km² and a population of about 195341 (PCBS, 2020).

Salfit governorate: Its center is the city of Salfit, which is characterized by a unique geographic location due to its oversight of the occupied Palestinian coast, and its location at the side of the West Bank; To form a link within an extension linking the Palestinian coast with the Jordan Valley areas, located in the northwest of the West Bank, it constitutes an area of 3.6% of the area of the West Bank with an area of 27 km² and a population of about 80225 (PCBS, 2020).

Tubas governorate: It is located in the northeast of the West Bank, where it is bordered by the Jordan River and the Jordanian border to the east, Jenin and Nablus governorates to the west, Jericho governorate to the south, and the Green Line to the north. Its population reached 64507 (PCBS, 2020).

Tulkarm governorate: It is located in the north of the West Bank. The area of the province is about 300 km², has a population of 195341 people (PCBS, 2020).

Jerusalem governorate: It is located in the center of the West Bank and its population about 461666 with an area of 331.6 km² (PCBS, 2020).

Table 3.1: The distribution of PCR COVID-19 tests during March 2021 in the West Bank (MOH, 2021b).

Governate	Total of PCR COVID-19 test during March 2021
Bethlehem	14346
Hebron	30215
Jericho	3830
Ramallah & Albereh	28177
Qalqilia	6789
Nablus	25850
Jenin	17731
Salfit	6004
Tubas	3316
Tulkarm	12999
Jerusalem	7287
Total	156,544

Figure 3.1: Map of the West Bank Governorates (Albaba, 2016).

3.3 Study design

A Case control study was conducted which concerned with determining the association between ABO blood group system and the severity of COVID-19 in the West bank-Palestine. Furthermore, it is used to assess the potential links between exposure (ABO blood group) and outcome (COVID-19), not costly and enable us to study multiple exposure variables despite of the weakness points as this study couldn't explain the causation of the association and probability of having recall bias (Tenny et al., 2020).

3.4 Sampling process

The study used stratified systematic sampling. There is an electronic excel sheet program called district health information system for COVID-19 (DHIS). It is used by all health directorates to enter the contact information of patients conducting PCR test with the test result.

First, the researcher obtained the electronic excel sheet file for all governorates of the West Bank from the Palestinian Ministry of Health, then the data stratified according to their COVDI-19 PCR result into two groups as the first strata were positive and the second strata were negative. After that, the researcher selected the patients from each stratum

systematically using kth interval by dividing the entire population size by the desired sample size (Fleetwood, 2020).

Study Cases: The study cases who have positive PCR test for COVID-19 from the health electronic data during 1/3/2021 until 31/3/2021 which was equal to (169 controls).

Cases were defined by:

1. The final nasal or pharyngeal swab is positive result.
2. Only alive patients were selected
3. Have a contact information at the ministry of health register file as the phone number.
4. Know their ABO Blood group.
5. Have signs and symptoms.

Study Control group: The controls who have tested negative result for the COVID-19 PCR from the health electronic data during 1/3/2021 until 31/3/2021 which was equal to (169 cases).

1. It should be the final nasal or pharyngeal swab is negative result.
2. Only alive patients were selected.
3. Have a contact information at the ministry of health register file as the phone number.
4. Know their ABO Blood group.
5. Not infected with COVID-19 previously.

The selected controls were excluded if:

1. Had a positive result before the last one.
2. Those who refused to participate in the study
3. Don't know their ABO blood group

The selected cases were excluded if:

1. Asymptomatic patients.
2. Who died.
3. Patients with critical condition couldn't answer the questionnaire.
4. Don't know their ABO blood group
5. Those who refused to participate in the study

In our study 9 cases and 9 controls were excluded from the study, as 13 of subjects didn't know their blood group and 5 refused to participate in the study.

3.5 Sample size determination

The sample size for a case control study was determined using the online software tool "Epitool" (AUVEST, n.d.). The following parameters were used in the calculation: With

95% confidence, the association between ABO blood group and COVID-19 has an 80% power and an estimated odds ratio of 2.0 and a case control ratio 1:1, A hypothetical assumption of risk (20%) was applied to the control group as stated in the literature for similar study which conducted in Saudi Arabia as the distribution of blood groups between Saudi Arabia and Palestine is similar, as the most prevalent of blood group are A and O (Skaik & El-Zyan, 2006).

Our target sample was about 338 (169 cases, 169 controls). To compensate for missing or non-responding cases, the researcher increased the number of cases to 186 and the number of controls to 186, generating a total sample size of 372 for the study.

34 pairs of cases and controls were excluded, 16 of them for piloting study and 18 were not continent with the selection criteria of the study to have a total of 338 sample size for the study.

3.6 Data Collection Procedure

Data collection took place in the period between 25/ March /2021 until 25/ April/ 2021.

Prior to distributing the questionnaire, a meeting with the director of the medical support professions in the Palestinian Ministry of Health was conducted in order to obtain the permission to have access for the contact information for the confirmed cases and controls whether they are in COVID-19 centers or their homes for each governorate in the West Bank. The health electronic files available to those with a positive PCR and a negative PCR were used and communicated with them via phone numbers with duration about ten minutes.

Those who were not unable to answer the questions by the phone were interviewed in their hospitals or COVID-19 centers if possible.

3.7 Study Instrument

After reviewing the literatures of the similar studies, a questionnaire was modified and developed based on the aims and objectives of the study and its conceptual framework (Appendix 3). In regard the smoking status was adopted from the WHO Stepwise questionnaire with mild modifications to be acceptable with the study factors.

It consisted of the following parts:

Section A: Socio-demographic data. Questions 1.1 to 1.10.1

Section B: Smoking Status. Questions 2.1 to 2.15.

Section C: Seasonal Flu. Questions 3.1 to 3.6.

Section D: Medical History of PCR COVID-19. Questions 4.1 to 4.5.

Section E: The Experience of COVID-19 Cases. Questions 5.1 to 5.9.1.

The first 4 section of variables for all the participants

The 5th section just for the cases.

the Severity of COVID-19 of the study was defined as the following based on the reviewed literature (WHO, 2020a).

The Risk: The susceptibility to have positive result of COVID-19 PCR.

Severity of symptoms: Categorized into: (Mild, Moderate, Severe, Critical illness) which defined according to WHO definitions as mentioned in the conceptual framework.

COVID-19 outcomes: Categorized into: (Require mechanical ventilation, Admission to intensive care unit, Complication's post COVID-19).

3.8 Pilot study of the questionnaire

This study validated and piloted after its development. The piloting done on 16 COVID 19 patients to examine the methodology of the study, the advisability of the research instrument, and to identify difficulties and challenges that participant might face in the instrument content and structure so that they can be amended prior to the data collection process, as some changes were made to the format of the questionnaire to improve the specific language, and their data were not included in the study. For data entry and analysis Statistical Package for Social Sciences (SPSS version 23.0) was used. The questionnaire reliability measurement revealed a Cronbach alpha of each section was done which confirmed that the study tool is reliable as the result of the piloting data analysis described in table 3.2.

Table 3.2: Cronbach alpha level for each section of the piloting study questionnaire

Questionnaire section	Cronbach alpha result
Section A: Socio-demographic data. Questions	0.81
Section B: Smoking Status.	0.78
Section C: Seasonal Flu.	0.91
Section D: Medical History of PCR COVID-19.	0.80
Section E: The Experience of COVID-19 Cases	0.83

3.9 Validity and Reliability

The study instrument was evaluated by eight experts. The experts included epidemiologists, researchers, statisticians, and field experts (Appendix 1). They were asked to perform content validity in order to evaluate how well the items in each section can measure what

needs to be measured and to improve instrument relevancy. All feedback and suggestions for instrument modification were evidenced.

3.10 Statistical analysis

The Statistical Package for Social Science version 23 was used to enter and analyze data (SPSS23). Analytical and descriptive analysis were both performed. Descriptive statistics were used to display frequencies and percentages for categorical variables, as well as means and standard deviation for continuous variables. The frequency and percentage of categorical variables were used to summarize them. The Chi-square test was used to compare two categorical variables associated with blood group and COVID-19, as well as between cases and controls. The multivariate analysis utilized binary logistic regression (Enter Model). Our primary measure of association was the Adjusted Odds Ratios (AORs) with 95% confidence intervals (95% CI). Throughout the study, p-values less than 0.05 were considered significant.

3.11 Ethical consideration

The proposal was submitted to Al Quds University-School of public health research committee for discussion and approval and ethical approval obtained from Al Quds University Ethical Research committee (REC). Ethical approval of consent from, the permission to conduct the study obtained from the MOH (Appendix 2). Collected the consent form of all the participants verbally after explaining to them about respect, privacy, confidentiality, autonomy, no harm and the benefit of the research and how their participation was useful to know the association between ABO group system and susceptibility to infect with COVID 19.

Chapter Four

The Results

4.1 Introduction

This chapter represented the main study findings which achieve the study objectives as the first section concerned with the descriptive analysis of the cases and controls towards COVID-19 infection followed by the second section which presented the univariate analysis between cases and controls in regard with their blood group and the severity of COVID-19. The final section presented multivariate analysis for the significant variables between cases and controls.

4.2 Descriptive analysis

Our study composed of 338 participants (169 cases and 169 controls) with 95% response rate.

Table 4.1 shows the characteristics of the study participants. The most of our participants (46.4%) were living in the northern region (Nablus, Jenin, Qalqilya, Salit, Tubas, Tulkarm), whereas (60.7%) of them were married.

The mean age of our study participants was 38 years (The youngest was 14 years old) and (the oldest was 84 years). Males were slightly more than females in our study with (51.5%) of the participants.

The most of the participant's blood group was "O" (37.9%), followed by "A" (36.7%), and (13.6%) of them were "B" and (11.8%) with "AB". Regarding the rhesus factor (RH), the majority of participants were positive RH with (80.2%) and (19.8%) of them were RH negative.

For assessing the body mass index, the results showed that the majority of participants were within normal range represented with (43.2%), followed by (32.8%) of overweight, (21.3%) of the participants were obese. In the occupation section, (50%) of the participants were non-health employees and 9.8% of them were health care workers.

The health status of the participants showed that most of them (78.4%) didn't suffer from any chronic diseases. Only (12.7%) of them were diagnosed with diabetes mellitus, (11.8%) hypertension, (3%) Asthma, (0.3%) heart failure, (1.8%) cancer, and (2.1%) of them coronary artery disease.

Table 4.1: Description of study socio demographic characteristics

Variables		Count	Column %
Age years	Mean (SD) Min-Max	38 (15.96) 14-84	
Sex	Male	174	51.5%
	Female	164	48.5%
Area of residence	Northern West Bank *	157	46.4%
	Southern West Bank**	96	28.4%
	Middle West Bank***	85	25.1%
Blood group	A	124	36.7%
	B	46	13.6%
	AB	40	11.8%
	O	128	37.9%
Rhesus factor	Positive	271	80.2%
	Negative	67	19.8%
BMI	<18 Underweight	9	2.7%
	18-24.9 Normal	146	43.2%
	25-29.9 Overweight	111	32.8%
	>30 Obesity	72	21.3%
Marital status of participant	Single	114	33.7%
	Married	205	60.7%
	Divorced or widowed	19	5.6%
Occupation	Health Care Workers	33	9.8%
	Non-Health employee	169	50.0%
	Unemployed	136	40.2%
Having Chronic Disease	Yes	73	21.6%
	No	265	78.4%
Diabetes mellitus	Yes	43	12.7%
	No	295	87.3%
Hypertension	Yes	40	11.8%
	No	298	88.2%
Asthma	Yes	10	3.0%
	No	328	97.0%
Renal Failure	Yes	2	0.6%
	No	336	99.4%
Heart failure	Yes	1	0.3%
	No	337	99.7%
Cancer	Yes	6	1.8%
	No	332	98.2%
Coronary artery disease	Yes	7	2.1%
	No	331	97.9%

*Northern West Bank: Nablus, Jenin, Qalqilya, Salfeet, Tubas, Tulkarem, **Southern West Bank: Bethlehem, Hebron, ***Middle West Bank: Ramallah, Jericho, Jerusalem

Univariate Analysis

4.3 Participant's sociodemographic characteristics

Table 4.2.A summarized the results which were analyzed according to the Chi-square test as that there is no statistically significant difference when comparing cases and controls in gender (P value = 0.829), as males were more in number compared to females.

The tables also show that there is no significant difference between cases and controls regarding the area of residence (P value= 0.991) whereas the majority of the participants live in the northern West Bank. Comparing study cases and control group, table 4.2.A shows that there is a statistically significant difference between cases and controls according to their blood group (P< 0.05) as the majority of cases were with "A" blood group represented by 72(42.6%) and the majority of controls with "O" blood group represented by (45.6%).

The age showed significant association between Blood group and COVID-19 (P. Value= 0.05) which excluded from the analysis regarding highly potential for confounding effects in the study.

In regard the rhesus factor (RH) there is no significant difference between cases and controls as the majority of participants were with positive RH which represented by (81.1%) in cases and (79.3%) on controls.

No significant difference was observed in BMI (P value=0.739) as the majority of the participants fall within the normal range represented by (43.8%) in cases and (42.6%) in controls. In addition to, there is no significant difference between cases and controls (P value=0.343) with their marital status and the occupation status.

Comparing study cases and control group, table 4.2.B reveals that there are no statistically significant differences (P< 0.05) in any of the health status sections or having chronic diseases as the results between them absolutely equal represented by (21.9%) in cases and (21.3%) in controls.

Table 4.2.A: Univariate analysis for cases and controls according to their characteristics

		Cases and controls				P value of Chi Square
		Cases		Controls		
		Count	Column %	Count	Column %	
Sex	Male	86	50.9%	88	52.1%	0.828
	Female	83	49.1%	81	47.9%	
Area of residence	Northern West Bank	78	46.2%	79	46.7%	0.991
	Southern West Bank	48	28.4%	48	28.4%	
	Middle West Bank	43	25.4%	42	24.9%	
Blood group	A	72	42.6%	52	30.8%	0.019
	B	27	16.0%	19	11.2%	
	AB	19	11.2%	21	12.4%	
	O	51	30.2%	77	45.6%	
Rhesus factor	Positive	137	81.1%	134	79.3%	0.682
	Negative	32	18.9%	35	20.7%	
BMI	<18 Underweight	6	3.6%	3	1.8%	0.739
	18-24.9 Normal	74	43.8%	72	42.6%	
	25-29.9 Overweight	55	32.5%	56	33.1%	
	>30 Obesity	34	20.1%	38	22.5%	
Marital status of participant	Single	51	30.2%	63	37.3%	0.343
	Married	109	64.5%	96	56.8%	
	Divorced or widowed	9	5.3%	10	5.9%	
Occupation	Health Worker	12	7.1%	21	12.4%	0.132
	Non-Health employee	82	48.5%	87	51.5%	
	Unemployed	75	44.4%	61	36.1%	

Table 4.2.B: Continued Univariate Analysis for cases and controls according to their health status

		Cases and controls				P value of Chi Square
		Cases		Controls		
		Count	Column %	Count	Column %	
Having Chronic Disease	Yes	37	21.9%	36	21.3%	0.895
	No	132	78.1%	133	78.7%	
Diabetes mellitus	Yes	22	13.0%	21	12.4%	0.870
	No	147	87.0%	148	87.6%	
Hypertension	Yes	21	12.4%	19	11.2%	0.736
	No	148	87.6%	150	88.8%	
Asthma	Yes	7	4.1%	3	1.8%	0.199
	No	162	95.9%	166	98.2%	
Renal Failure	Yes	2	1.2%	0	0.0%	0.156
	No	167	98.8%	169	100.0%	
Heart failure	Yes	1	0.6%	0	0.0%	0.317
	No	168	99.4%	169	100.0%	
Cancer	Yes	4	2.4%	2	1.2%	0.410
	No	165	97.6%	167	98.8%	
Coronary artery disease	Yes	4	2.4%	3	1.8%	0.703
	No	165	97.6%	166	98.2%	

4.4 Smoking Status

Table 4.3 shows that the majority (70.4%) of our cases are non- smokers compared to (55.6%) of our controls. On the other hand, (27.8%) of the smoking cases compared to (38.5%) of the smoking controls are current smokers.

When comparing study cases and control groups, manufactured cigarettes were the most commonly used type of smoking, followed by shisha, table 4.3 reveals that there are statistically significant differences ($P < 0.05$) in the smoking, current smokers, age of smoking initiation. Also, the cases and controls did not differ statistically according to their past smoking history and non-smoked tobacco use. Second hand smoking which contained the indoor and work smoking reveals that there is statistical significance difference ($P < 0.05$) between cases and controls, as the indoor smoking presented that (49.7%) of the cases exposed to indoor smoking compared to (66.9%) from the controls. (47.9%) of the cases exposed to work smoking compared with (59.2%) from the controls.

Table 4.3: Association between Smoking and COVID-19

		Cases and controls				P value of Chi Square
		Cases		Controls		
		Count	Column %	Count	Column %	
Smoking	Yes	50	29.6%	75	44.4%	0.005
	No	119	70.4%	94	55.6%	
Current smoker	Yes	47	27.8%	65	38.5%	0.038
	No	122	72.2%	104	61.5%	
Age of smoking initiation	< 18 years	26	15.4%	40	23.7%	0.019
	≥ 18 years	24	14.2%	35	20.7%	
Manufactured cigarettes smoked (Weekly)	<20 cigarettes	5	3.0%	3	1.8%	0.105
	≥ 20 cigarettes	26	15.4%	41	24.3%	
	I don't smoke	138	81.7%	125	74.0%	
Shisha sessions smoked (Weekly)	<7 sessions	14	8.3%	24	14.2%	0.206
	≥7 sessions	4	2.4%	5	3.0%	
	I don't smoke shisha	151	89.3%	140	82.8%	
Quit smoking	Yes	56	33.1%	56	33.1%	0.886
	No	103	60.9%	105	62.1%	
	I don't smoke	10	5.9%	8	4.7%	
Past daily Smoking	Yes	48	28.4%	54	32.0%	0.550
	No	38	22.5%	42	24.9%	
	I don't smoke	83	49.1%	73	43.2%	
Non smoked tobacco	Yes	7	4.1%	0	0.0%	0.08
	No	162	95.9%	169	100.0%	
Non smoked tobacco daily	Yes	3	1.8%	0	0.0%	0.082
	No	166	98.2%	169	100.0%	
Ever used non smoked tobacco	Yes	5	3.0%	3	1.8%	0.474
	No	164	97.0%	166	98.2%	
Ever used Non smoked tobacco daily	Yes	5	3.0%	1	0.6%	0.099
	No	164	97.0%	168	99.4%	
Indoor smoking	Yes	84	49.7%	113	66.9%	0.001
	No	85	50.3%	52	30.8%	
	I don't smoke	0	0.0%	4	2.4%	
Work smoking	Yes	81	47.9%	100	59.2%	0.036
	No	76	45.0%	53	31.4%	
	I don't smoke	12	7.1%	16	9.5%	

4.5 Seasonal Flu

Comparing study case and control group, table 4.4.A shows that there are no statistically significant differences between case and control group in regard with suffering from seasonal flu or with the symptoms that may have when infected except complaining of muscle aches

(P< 0.05), as the results presented that (50.3%) of the COVID-19 patients had muscle aches when they got seasonal flu in the past compared to (38.5%) of the controls.

As for the people who received the flu vaccination this year, the results showed that there is no statistically significant difference between cases and controls but it showed a statistical significance difference (P< 0.05) between the cases and controls based on who had taken the flu vaccination in the previous years represented by (5.9%) (8.3%) respectively.

Table 4.4.B showed that there is no statistical difference between cases and controls based on suffering from the side effects of the flu vaccination except the fever and cough (P< 0.05) which represented (0.0%) in cases and (2.4%) among controls in the both symptoms.

Table 4.4.A: Seasonal Flu experience with COVID-19

		Cases and controls				P value of Chi Square
		Cases		Controls		
		Count	Column %	Count	Column %	
In past years, did you suffer from seasonal flu?	Yes	131	77.5%	137	81.1%	0.421
	No	38	22.5%	32	18.9%	
Sore throat	Yes	89	52.7%	97	57.4%	0.382
	No	80	47.3%	72	42.6%	
Fever	Yes	64	37.9%	77	45.6%	0.152
	No	105	62.1%	92	54.4%	
Runny or congested nose	Yes	108	63.9%	114	67.5%	0.492
	No	61	36.1%	55	32.5%	
Muscles aches	Yes	85	50.3%	65	38.5%	0.029
	No	84	49.7%	104	61.5%	

Table 4.4.B: Continued Seasonal Flu vaccine side-effects with COVID-19

		Cases and controls				P value of Chi Square
		Cases		Controls		
		Count	Column %	Count	Column %	
Headache	Yes	85	50.3%	79	46.7%	0.514
	No	84	49.7%	90	53.3%	
General body weakness	Yes	80	47.3%	74	43.8%	0.512
	No	89	52.7%	95	56.2%	
Diarrhea	Yes	25	14.8%	21	12.4%	0.526
	No	144	85.2%	148	87.6%	
Nausea	Yes	23	13.6%	16	9.5%	0.233
	No	146	86.4%	153	90.5%	
Vomiting	Yes	20	11.8%	11	6.5%	0.09
	No	149	88.2%	158	93.5%	
In past years, did you get the flu vaccination?	Yes	39	23.1%	58	34.3%	0.022
	No	130	76.9%	111	65.7%	
Did you receive the flu vaccination this year?	Yes	25	14.8%	34	20.1%	0.197
	No	144	85.2%	135	79.9%	
Did you suffer from side effects of the flu vaccination?	Yes	10	5.9%	14	8.3%	0.397
	No	159	94.1%	155	91.7%	
Redness or swelling	Yes	5	3.0%	11	6.5%	0.124
	No	164	97.0%	158	93.5%	
Headache	Yes	2	1.2%	3	1.8%	0.652
	No	167	98.8%	166	98.2%	
Fever	Yes	0	0.0%	4	2.4%	0.044
	No	169	100.0%	165	97.6%	
Cough	Yes	0	0.0%	4	2.4%	0.044
	No	169	100.0%	165	97.6%	
Muscle aches	Yes	6	3.6%	5	3.0%	0.759
	No	163	96.4%	164	97.0%	

4.6 COVID-19

The table 4.5.A shows that there is no statistically significant difference between cases and controls in regard with the reason of doing the test as the majority of participants had indirect contact (55%) in cases and (51.5%) in controls. There is a statistically significant difference ($P< 0.05$) in the times they needed to do this test before as the majority of cases and controls

needed to do the test less than three times (69.8%) (53.8%) respectively. Also, statistical significance differences appeared between the cases and controls (P< 0.05) in the need to re-examine the last sample to confirm the result as (17.2%) of the cases and (32.5%) of the controls needed to repeat the test. With regard towards taken the prevention measures between the cases and controls, the table 4.5.B showed that there is no statistically significant difference between them except the avoiding direct contact with infected people and washing hands with soap, water or alcohol continuously. The majority of participants revealed that they are always avoiding direct contact with infected people which represented by (66.3%) in the cases and (52.7%) in the controls. Also, they are always washing their hand continuously represented by (59.2%) (38.5%) in the cases and controls respectively.

Table 4.5.A: Characteristics of the COVID-19 experience

		Cases and controls				P value of Chi Square
		Cases		Controls		
		Count	Column %	Count	Column %	
PCR COVID-19 result	Positive	169	100.0%	0	0.0%	-------
	Negative	0	0.0%	169	100.0%	
The reason for doing test	Direct Contact	76	45.0%	82	48.5%	0.513
	Indirect Contact	93	55.0%	87	51.5%	
How many times have you done this test?	< 3 times	118	69.8%	91	53.8%	0.003
	≥ 3 times	51	30.2%	78	46.2%	
In the last Test, was there a need for a re-test?	Yes	29	17.2%	55	32.5%	0.001
	No	140	82.8%	114	67.5%	
Keep at least 6 feet distance between people	Always	68	40.2%	75	44.4%	0.239
	Often	55	32.5%	46	27.2%	
	Sometimes	33	19.5%	31	18.3%	
	Rarely	3	1.8%	10	5.9%	
	Never	10	5.9%	7	4.1%	

Table 4.5.B: Continued characteristics of the COVID-19 experience

		Cases and controls				P value of Chi Square
		Cases		Controls		
		Count	Column %	Count	Column %	
Wearing a face mask, the correct way by covering the nose and mouth	Always	86	50.9%	77	45.6%	0.599
	Often	46	27.2%	49	29.0%	
	Sometimes	23	13.6%	32	18.9%	
	Rarely	8	4.7%	5	3.0%	
	Never	6	3.6%	6	3.6%	
Avoiding Crowdedness in the public places	Always	70	41.4%	65	38.5%	0.588
	Often	53	31.4%	48	28.4%	
	Sometimes	29	17.2%	36	21.3%	
	Rarely	14	8.3%	13	7.7%	
	Never	3	1.8%	7	4.1%	
Wash hands with soap, water or alcohol continuously	Always	100	59.2%	65	38.5%	0.0001
	Often	45	26.6%	45	26.6%	
	Sometimes	12	7.1%	42	24.9%	
	Rarely	10	5.9%	13	7.7%	
	Never	2	1.2%	4	2.4%	
Avoid direct contact with infected people	Always	112	66.3%	89	52.7%	0.005
	Often	34	20.1%	39	23.1%	
	Sometimes	8	4.7%	23	13.6%	
	Rarely	12	7.1%	8	4.7%	
	Never	3	1.8%	10	5.9%	

4.7 COVID-19 characteristics among cases

Table 4.6 summarized the COVID-19 characteristics among cases as the majority of cases were being treated at home represented by (72.2%), (17.2%) in COVID centers, (7.7%) in hospitals and (7.7%) in other health care centers. However, the majority of them had mild symptoms (53.2%). In regard with the duration of symptoms, the majority of cases (68.6%) took more than 7 days. Also, more than the half of cases (59.2%) didn't know the source of infection as 10% of them infected from their workplace, (4.1%) from the family and (26.6%) from others.

Table 4.6: COVID-19 Characteristics among cases

Variable		Count	Column %
Place of treatment	Home	122	72.2%
	COVID-Centers	29	17.2%
	Hospital	13	7.7%
	Other health centers	5	3.0%
Symptoms	Mild	90	53.2%
	Moderate	39	23.1%
	Severe	11	6.5%
	Critical	29	17.2%
The duration of symptoms (days)	< 7days	53	31.4%
	≥ 7 days	116	68.6%
Did you know the source of infection?	Yes	69	40.8%
	No	100	59.2%
Source of infection	Work place	17	10.1%
	Family	7	4.1%
	Other	45	26.6%

4.8 ABO Blood group and prevention measurement towards COVID-19

The table 4.7 shows that there is an extent of the commitment of the participants in the study towards prevention methods, as no statistically significant differences appeared between prevention measures and infection with the COVID-19, with the exception of wearing the mask correctly ($P < 0.05$).

Table 4.7: The association between ABO blood group COVID-19 cases and the prevention measurement methods

		Blood group								P value of Chi Square
		A		B		AB		O		
		Count	Column (%)	Count	Column (%)	Count	Column (%)	Count	Column (%)	
Keep at least 6 feet distance between people	Always	50	40.3%	13	28.3%	16	40.0%	64	50%	0.091
	Often	34	27.4%	18	39.1%	13	32.5%	36	28.1%	
	Sometimes	30	24.2%	9	19.6%	6	15.0%	19	14.8%	
	Rarely	4	3.2%	5	10.9%	1	2.5%	3	2.3%	
	Never	5	4.8%	1	2.2%	4	10.0%	6	4.7%	
Wearing a face mask, the correctly	Always	64	51.6%	20	43.5%	15	37.5%	64	50.0%	0.003
	Often	24	19.4%	10	21.7%	21	52.5%	40	31.3%	
	Sometimes	24	19.4%	11	23.9%	1	2.5%	19	14.8%	
	Rarely	7	5.6%	2	4.3%	0	0.0%	4	3.1%	
	Never	5	4.0%	3	6.5%	3	7.5%	1	0.8%	
Avoiding crowdedness in the public places	Always	50	40.3%	15	32.6%	16	40.0%	54	42.2%	0.629
	Often	31	25.0%	15	32.6%	14	35.0%	41	32.0%	
	Sometimes	29	23.4%	8	17.4%	4	10.0%	24	18.8%	
	Rarely	10	8.1%	6	13.0%	4	10.0%	7	5.5%	
	Never	4	3.2%	2	4.3%	2	5.0%	2	1.6%	
Wash hands with soap, water or alcohol continuously	Always	60	48.4%	20	43.5%	20	50%	65	50.8%	0.190
	Often	27	21.8%	17	37.0%	15	37.5%	31	24.2%	
	Sometimes	26	21.0%	5	10.9%	4	10.0%	19	14.8%	
	Rarely	9	7.3%	2	4.3%	0	0.0%	12	9.4%	
	Never	2	1.6%	2	4.3%	1	2.5%	1	0.8%	
Avoid direct contact with infected people	Always	75	60.5%	24	52.2%	22	55.0%	80	62.5%	0.469
	Often	30	24.2%	11	23.9%	8	20.0%	24	18.8%	
	Sometimes	11	8.9%	5	10.9%	3	7.5%	12	9.4%	
	Rarely	7	5.6%	2	4.3%	5	12.5%	6	4.7%	
	Never	1	0.8%	4	8.7%	2	5.0%	6	4.7%	

4.9 ABO Blood group and the severity of COVID-19

First, we assessed the severity of symptoms as the 4.8 table shows that there is no significant difference between the ABO blood group and the severity of symptoms, as the results showed that patients with blood group B (13%) had the highest critical symptoms, follow by blood group AB (12.5%) while blood group O (4.7%) had the lowest critical symptoms followed by blood group A (9.7%). Also, there was no significant difference according to the duration of symptoms as blood group “B” reached the longest duration than others represented by (41.3%) followed by blood group “A” represented by (40.3%).

Then, we assessed the outcome by the need for oxygen therapy, ICU admission, complications and the need to use mechanical ventilation as the results showed that there is no association between ABO blood group and complications post COVID-19 (P > 0.05) the highest percent were in the musculoskeletal complications represented by (4.8%) among blood group "A". The highest percentage of blood type that needed oxygen and intubation was among blood group "B" represented by (19.6%) (13%) respectively which revealed by the longest duration represented by (8.7%) on mechanical ventilation more than 7 days.

Table 4.8.A: The association between ABO blood group and the severity of COVID-19

				Blood group						P value of Chi Square
		A		B		AB		O		
		Count	Column %	Count	Column %	Count	Column %	Count	Column %	
Severity of Symptoms	Mild *	36	29.0%	15	32.6%	11	27.5%	28	21.9%	0.317
	Moderate **	15	12.1%	3	6.5%	3	7.5%	14	10.9%	
	Severe ***	5	4.0%	3	6.5%	0	0.0%	4	3.1%	
	Critical ***	12	9.7%	6	13.0%	5	12.5%	6	4.7%	
The duration of symptoms (days)	< 7days	21	16.9%	8	17.4%	4	10.0%	16	12.5%	0.154
	≥ 7 days	50	40.3%	19	41.3%	16	40.0%	36	28.1%	
Cardiovascular complications		2	1.6%	2	4.3%	1	2.5%	1	0.8%	0.456
Immune complications		3	2.4%	3	6.5%	3	7.5%	3	2.3%	0.260
Musculoskeletal complications		6	4.8%	0	0.0%	2	5.0%	4	3.1%	0.456
Digestive complications		5	4%	0	0.0%	3	7.5%	4	3.1%	0.300
Reproductive complications		2	1.6%	0	0.0%	0	0.0%	5	3.9%	0.254
Respiratory complications		13	10.5%	7	15.2%	5	12.5%	10	7.8%	0.520
Urinary complications		0	0.0%	1	2.2%	0	0.0%	3	2.3%	0.281
Nervous complications		4	3.2%	1	2.2%	0	0.0%	1	0.8%	0.394
Intensive care unit admission		11	8.9%	5	10.9%	5	12.5%	4	3.1%	0.105

Table 4.8.B: Continued The association between ABO blood group and the severity of COVID-19

		Blood group								P value of Chi Square
		A		B		AB		O		
		Count	Column %	Count	Column %	Count	Column %	Count	Column %	
Oxygen therapy		17	13.7%	9	19.6%	5	12.5%	9	7.0%	0.117
Mechanical Ventilation (Intubation)		9	7.3%	6	13.0%	3	7.5%	4	3.1%	0.121
Duration on Mechanical Ventilation (days)	< 7days	1	0.8%	2	4.3%	0	0.0%	1	0.8%	0.108
	≥ 7 days	8	6.5%	4	8.7%	3	7.5%	2	1.6%	

*Mild: Headache, Muscle ache, Diarrhea, Cough, loss of taste or smell, Fever, Nose congestion, Sore throat, General body weakness, Nausea, Vomiting *Moderate: Shortness of breath on room air. ***Severe: Require oxygen supplements ****Critical illness: Required mechanical ventilation and intensive care admission

4.10 Multivariate analysis

All the significant variables at (P <0.05) in the univariate analysis were included in the multivariate analysis except for the variables with small numbers such as the side-effects of Flu vaccine which summarized in table 4.9.

We compared blood group “A” against other blood groups, based on AOR and CI the results showed significant differences between Blood group “A” and B. It showed that the B is more protective against COVID-19 (AOR= 0.40, CI= 0.223-0.27). Also, there is a significant difference between blood group “A” and “AB” as the second one more protective towards COVID-19 by 31.6% more times (P <0.05, AOR= 0.316, CI= 0.143-0.698). On the other hand, there is no difference between blood group A and blood group O (P> 0.05, AOR= 0.843, CI= 0.382-1.863) which revealed that blood group “O” 0.84 time more protective that blood group “A”.

Smoking showed no significant differences between smokers and nonsmokers(P> 0.5), but the table show a trend for protection against COVID-19 for who not smoking. The table 4.9 also show that being not vaccinated for seasonal flu increases the risk for COVID19 infection by 1.97 times compared to people who gets vaccinated.

Table 4.9: Multivariate Forward non conditional model analysis of the associated variables with COVID-19

Variable		Sig	AOR**	95% C.I.***	
				Lower	Upper
Blood group	A	.003			
	B	.002	.400	.223	.720
	AB	.004	.316	.143	.698
	O	.673	.843	.382	1.863
Smoking	Yes	Ref.****	Ref.	Ref.	Ref
	No	.493	.545	.096	3.100
Current smoker	Yes	Ref.	Ref.	Ref.	Ref
	No	.180	.379	.092	1.566
Age of smoking initiation	< 18 years	.055			
	≥ 18 years	.064	6.109	.898	41.575
In past years, did you get the flu vaccination?	Yes	Ref.	Ref.	Ref.	Ref
	No	.019	1.974	1.119	3.483
How many times have you done this test?	< 3 times	Ref.	Ref.	Ref.	Ref
	≥ 3 times	.023	.531	.308	.916
In the last Test, was there a need for a re-test to confirm the result?	Yes	Ref.	Ref.	Ref.	Ref
	No	.098	1.679	.909	3.102
Wash hands with Soap, Water or alcohol continuously	Always	.0001			
	Often	.044	.136	.020	.946
	Sometimes	.120	.216	.031	1.492
	Rarely	.965	.956	.129	7.108
	Never	.271	.322	.043	2.419
Avoid direct contact with sick people and others	Always	.042			
	Often	.204	.379	.085	1.692
	Sometimes	.206	.367	.078	1.734
	Rarely	.858	1.168	.212	6.430
	Never	.055	.186	.034	1.037

All variables that were significant ($P < 0.05$) in univariate analysis were included in a multivariate model: i.e., Blood group, Smoking, current smoker, Flu vaccination

**Adjusted odds ratio. ***Confidence interval. ****Ref: Reference.

Chapter Five

Discussion

5.1 Introduction

This chapter summarized the core findings and compared to other studies. Also, the results interpreted and discussed. The limitation we faced during the study were represented and study conclusion and recommendations were represented in the final section.

5.2 Summary of the results

The univariate analysis of the study data revealed significant differences between study cases and control group in the type of blood group and didn't show any other significant difference in the socio demographic factors. It also showed significant difference in smoking, current smokers, age of smoking initiation, indoor smoking and working smoking. In the health status section, there were no significant differences between cases and controls. In the seasonal flu experience section, the results showed that there were significant differences between cases and control in whom complained from muscle aches, received flu vaccination in the past and who complained from cough and fever as a side effect of the vaccine. Also, there was a significant difference between cases and controls in their COVID-19 experience as the number repetition time of PCR test and the prevention measurement were taken by them as avoiding the direct contact with infected people and washing their hands continuously.

On the other hand, the multivariate analysis of the study data represented the comparing results via group A and other blood group as participants with blood group "as the results showed that Blood group B and AB were more protective than Blood group A towards COVID-19. Also, who received flu vaccination were more protected towards COVID-19.

5.3 Study Participants characteristics and Blood Group Type with Risk of COVID-19

This contained participants sociodemographic factors, smoking status, BMI, occupation exposure and seasonal flu experience as we had made unadjusted odds ratio for each variable which showed non-significant difference for exception any confounding effects except the "Age" which had been a confounder variable. We discussed the main findings in those variables as the followings:

Gender

Males composed (51.5%) and females composed (48.5%) of our study sample and the results showed that there is no significant difference between cases and controls in risk with COVID19 (P. value= 0.828> 0.05) as this result is consistent with studies from Egypt, Saudia

Arabia, China, Italy, Spain, France, Germany, and Switzerland (El-Shitany et al., 2021; Ad'hiah et al., 2020; Jin et al., 2020; Mukherjee & Pahan, 2021). Few of the studies that studied gender with blood type and the severity of the COVID-19, where we shed light on it in search of it being confounder.

This study had a limitation for doing the gender matching related to the difficulty for access the difference according to gender which need to expand.

Area of residence

Our study showed that cases and controls did not differ significantly based on their residency. As no difference between them for COVID-19 measurement methods taken. No previous studies concerned with the area of residence which furthered to conduct more studies concerned with the governmental rules for reposing to COVID-19 pandemic.

Blood group

In our multivariate analysis we compared blood group "A" versus another blood groups as the results showed that blood group AB (0.4%) was more protective and blood group B (0.2%) was more protective and there was no difference between blood group O and blood group A (CI= 0.382-1.863, AOR= 0.843) which is consistent with a case control study conducted among 105 cases and 103 control in Wuhan who had tested for COVID-19 PCR as the results showed that there is a significant difference between blood group and the risk to infection with COVID-19, especially the females with "A" blood group (Fan et al., 2020). Also, similar with another case control study conducted among 186 of cases with COVID-19 and 1881 healthy controls, as the results showed that blood group "A" is significantly more frequent among cases compared to the controls (Goker et al., 2020).

On the other hand, our results contrasted with a population-based cohort study results among 225,556 patients in Canada who had tested for COVID-19 between January until June 2020 as the researchers compared blood group "O" with other types of blood group and the results showed that the people with "O" blood group may be associated with lower risk to infection with COVID-19 (AOR, 0.89 [CI, 0.84 to 0.94]) (Ray et al., 2021).

Conversely with a retrospective cross-sectional study conducted in (Saudia Arabia and Egypt) for two groups the first one contained 726 COVID-19 patients and the second one contained 2399 subjects who hadn't diagnosed with COVID-19 as 707 from them were selected randomly for comparing the results which showed that there is significant difference between cases and controls in regard blood group, as those with blood group "O" had lower in COVID-19 cases than controls (204, or 28%, versus 253, 36%) whereas there is

insignificantly higher distribution between cases and controls in regard blood group "A" (35% versus 29%) respectively and non-significant difference between cases and controls in regard RH (P. value= 0.191) (El-Shitany et al., 2021). This difference could be attributed to the differences of the sample size, the comparative design and the distribution of blood group among geographical areas.

The role of blood group on COVID-19 susceptibility has been theorized to be partly related to a differential aggregation of virus glycoprotein receptors on host cell surface, which is induced by ABO(H) determinants via interactions (carbohydrate-carbohydrate) with these receptors' glycan motif, and which may interfere with virus binding and entry into target cells (Silva-Filho et al., 2020). Other cells and tissues, such as lymphocytes, endothelial cells, platelets, gastric mucosa, and bone marrow, express the carbohydrate structures of ABO(H) blood groups, which are not limited to the surface of red blood cells (Rath et al., 2014). Furthermore, blood type antigens may be found in the secretions (saliva) of around 80% of people (ABO secretors) (Rath et al., 2014).

Rhesus factor

Our study showed that there is no significant difference between cases and controls similar to the findings in a retrospective cohort study conducted among 841,317 who had been tested for COVID-19 PCR in Denmark as the results showed that there was significant difference between blood group and risk for COVID-19 and there wasn't significant difference between blood group or Rh factor and the hospitalization outcome or death (Barnkob et al., 2020).

The results in our study conversely with the results in a case control study conducted on 5668 COVID-19 patients and 5668 controls in Iraq which demonstrated that people with negative RH are more susceptible to COVID-19 than people with positive RH blood type (OR = 2.38, 95% CI (2.03, 2.79), p= 0.0001) (Majeed et al., 2021).

Another an ecological study conducted among 86 Asian, European, African and American countries to investigate the association between blood group or Rh factor and the COVID-19 outcomes including the morbidity and mortality, the results showed that there is an association between RH negative factor and the COVID-19 risk (Ansari-Lari & Saadat, 2020).

Also, contrasted with the results which conducted among 225,556 COVID-19 in Canada which concluded that the Rhesus-negative (Rh−) blood type was protective against COVID-19 slightly, especially for those who were o negative aRR, 0.74 [CI, 0.66 to 0.83]; ARD, −8.2 per 1000 [CI, −10.8 to −5.3] (Ray et al., 2021).

Moreover, these differences could be contributed to the variety of sample size and distribution of Rh factors among countries as in Palestine the negative rh is a rare factor.

The followings factors were assessed to be a confounder variable as the results were not associated with the COVID-19 outcome which demonstrated they aren't confounder variables in our study.

Body Mass Index

No significant difference between COVID-19 patients in regard with their BMI was observed in our study which agreed with the results in the study conducted on 1067 patients in South-East Asia (Smith et al., 2018). Furthermore, no genome-wide association studies have shown if other genes linked in higher BMI are situated on the same chromosomal area as ABO or that ABO gene exerts regulatory control over them (Smith et al., 2018). As a result, it's reasonable to conclude that a genetic foundation for connecting ABO to BMI is insufficient. The various findings addressing the link between ABO/Rh status and BMI, in our opinion, may be influenced by local variables that alter population phenotype or change in sample size rather than real genetic impact (Smith et al., 2018).

Flu

Our study showed that there is no significant difference between cases and controls according to their past seasonal flu experience but there is a significant difference between cases and controls in whom received flu vaccine previously ($P< 0.05$) except the current year.

In the multivariate analysis the results showed that people who didn't receive flu vaccination are more susceptible to infection with COVID-19 by 1.97 more times than those who received it which is consistent with the results among 27201 COVID-19 patients as those who got an influenza vaccination had a 24% lower chance of testing positive for COVID-19 than those who did not, people who choose to get vaccinated against the flu may be more health-conscious and much more likely to follow COVID-19 prevention guidelines than those who do not (Conlon et al., 2021).

Others have pointed out that overall behavior, rather than the shot, may have made people in the former group less likely to become ill in his study, these kinds of studies, which look for links between behavior and outcomes, can't prove cause and effect. On the other hand, an increasing amount of evidence shows that this happens as a result of a process known as "trained innate immunity." Vaccines stimulate the adaptive immune system, causing the

body to produce antibodies that can detect and attack a specific disease if it is met again (Moyer, 2020).

Smoking

In patients who need hospital care for Covid-19, a review by the World Health Organization revealed that smoking is linked to more severe disease and an increased risk of mortality (Heart Matters Magazine, 2021).

The univariate analysis revealed that there is a significant difference between cases and controls as whom current smokers were more protective towards COVID-19. Although the multivariate analysis showed no significant difference.

On the other hand, people who presently smoke may be less likely to get infected with coronavirus, according to a new evidence assessment conducted by London researchers. According to one study, nicotine inhibits the virus's ability to enter cells via interfering with ACE2 receptors (Heart Matters Magazine, 2021).

Contrasted with a study conducted on over 2.4 million participants by (Hopkinson et al., 2021) which showed that current smokers were more likely to report symptoms that pointed to a COVID-19 diagnosis: classic symptoms adjusted OR (95 % Ci) 1.14 (1.10 to 1.18); >5 symptoms adjusted OR (95 % Ci) 1.29 (1.26 to 1.31); >10 symptoms adjusted OR (95 % Ci) 1.50 (1.42 to 1.58). Therefore, they stated that smoking has been linked to overexpression of ACE2, the SARS-CoV-2 virus's receptor in the lungs, however a recent meta-analysis shows that the effects are mixed, with upregulation in epithelial cells and downregulation in alveolar type 2 cells. Internalization of ACE2 as a result of viral infection may result in unopposed ACE inhibitor action and high angiotensin 2 levels, contributing to endothelial damage and the coagulopathy and micro thrombosis seen in severe COVID-19.1 patients (Hopkinson et al., 2021).

Moreover, these variations of results may be due to the distribution of smokers approximately among cases and controls which related to the small sample size.

5.4 Association between ABO blood group and the Severity of Symptoms

Our study results showed that the most critical symptoms were among blood group B 6 (13%) and the highest distribution with moderate symptoms were be among blood group B also (32.6%) despite that, there is no association between ABO blood group and the severity of symptoms which corresponded with (Mullins, etal., 2020) among 227 COVID-19 patients as the results showed the risk of severe COVID-19 infection didn’t differ significantly according to ABO blood types.

Our findings are similar to a case control study conducted among 107,796 participants had tested COVID-19 PCR from March to November 2020 in Utah, Idaho and Nevada, as they are adjusted for age, gender and RH factor and the results showed that there is no association between blood group and the risk or the severity of symptoms (Anderson et al., 2021).

Likewise, A retrospective cohort study conducted among 227 COVID-19 patients hospitalized to tertiary hospital care in New York between March 8th to July 31st, 2020 as the results showed that there is no significant difference between blood group and the susceptibility to infection with COVID-19 (P. value=0.93) nor with the severity ofCOVID-19 for required to intensive care unit (P. value= 0.66) or require renal replacement therapy (P. value =0.09) (Mullins et al., 2021).

Conversely with a retrospective cross-sectional study conduce in Arab community (Egypt and Saudia Arabia) which showed that there is significant difference between cases and controls in regard risk for COVID-19 but not significant with fever, headache, shortness of breath, cough, bone ache, gastrointestinal symptoms and hospitalization. On the other hand, there is statistically significant difference between blood groups and the need to use mechanical ventilation, myalgia, and the recovery time from COVID-19 as blood group "A" showed the highest percentage experienced with low oxygen saturation (70.2%) and blood group "B" showed that no one had experienced of low oxygen saturation (0%). Despite of that, blood group "O" showed the highest percentage for whom required mechanical ventilation (2.9%) and no one with blood group "A" required it (0%) (El-Shitany et al., 2021). This difference could be attributed to the difference of the sample size and distribution of blood groups.

5.5 Association between ABO blood group and COVID-19 outcomes

Our study revealed that there is no significant difference between ABO blood group and COVID-19 outcomes which contained the intubation, need to intensive care unit admission, need to oxygen therapy or complications which is consistent with a study conducted in five major hospitals in state of Massachusetts from March to April among 7648 patients in all the hospitals undergoing COVID-19 research and the results showed there 37.5 % of them were admitted to hospital, 9.5 % were admitted to ICU, 8.4% were intubated and 6.9% of them died, in addition to 34.2% of them had A blood group, 15.6% were blood type B, 4.7% of them were AB blood group and 45.5% of them were O blood group in regard with the researchers found that there was no association between ABO blood type and COVID-19

disease severity defined as intubation or death and blood type O had the lowest frequency of disease positivity (Latz et al., 2020).

In contrasted with a case control study conducted among 179 patients with confirmed COVID19 and 5200 healthy control patients in Turkey and the results showed that A blood group is the most common with cases of COVID 19 than control group and found that patient with A blood group had a longer stay in intensive care unit with higher mortality rate than others (Aktimur, etal., 2020).

And contrasted with an ecological study conducted among 86 Asian, European, African and American as the results showed that A, B, Rh- are associated significantly with COVID-19 as blood group A- had the most serious outcomes and hospitalization rates (Ansari-Lari & Saadat, 2020).

In our study, blood group doesn't matter the severity of COVID-19 or the outcomes due to the classifications of our study as the majority of participants were recovered at home (72.2%) and there is a small sample size required the hospital care (7.7%).

Furthermore, the outcomes of this study, as well as the few other publications in this sector, indicate a wide range of data, making a conclusion about a link between blood type and COVID19 challenging. On the other hand, this discrepancy in data, might imply that some unknown underlying component, rather than the blood group or kind of antibodies present.

5.6 Study Strengths and Limitations

Our study had several strengths which summarized as the followings:

1. The first study in Palestine
2. It was included multiple variables might be a confounder.
3. The using of case control study design
4. It was able to measure the risk of COVID-19 infection, the severity of symptoms, as well as the outcomes of infection.
5. Using a valid and reliable study tool.

Study Limitations:

1. Limited resources, and previous studies concerning of ABO group and COVID-19.
2. Limited Financial Support.
3. Self-reported behaviors are known to differ from actual behavior in the COVID-19 precautions measurement.
4. Recall bias of remembering a specific severity of symptoms.

5. Possibility of misclassification of cases and controls due to the false negative or positive results.
6. Difficulty of doing matching
7. Limited resources concerning with possible confounders.
8. Lock down restriction.
9. Couldn't study the using of drugs during the pandemic related to difficulty of access to a review concerned with and the differences between types of drugs in each area.
10. Couldn't matching with gender and age related to the incorrect data entry to the excel sheet file for the name of whom tested for COVID-19 PCR.

5.7 Conclusion

The current is the first study that investigated the possibility of an association between ABO blood group and different factors towards COVID-19 susceptibility and severity in Palestine. In order to answer the study questions a case control study design was conducted. The study has identified the possible association between ABO blood group and COVID-19 in the West Bank.

Moreover, blood group "A" increased risk to infection with COVID-19. The majority of the study's findings were expected and comparable to those of other global studies, but some unexpectedly contradicted the literature. Blood group, Smoking, Flu vaccination, taken the prevention measurement appeared to be associated with COVID-19 regardless the direction of the factor effect. Other factors were not associated with ABO blood group such as BMI, health status, occupation, severity of COVID-19 and the outcomes except the age which showed the confounding effects.

5.8 Recommendations

Recommendation for people at risk of COVID-19 according to their blood group

- Providing more attention for people with "A" blood group and strengthen the protection methods towards COVID-19 and this doesn't mean that people with other blood types reduce prevention methods, as they are also at risk.

Recommendations for policy makers and health care team:

- Considering of ABO blood type in the treatment of COVID-19 infection might be beneficial.
- Conducting educational programs to aware the people about the possibility of linking blood type to infection.

- Providing awareness and advice on the importance of vaccination as the seasonal flu vaccine.

Recommendations for public health researchers:

- Conducting more detailed researches with larger sample size, including more risk factors and assessing the confounder effects.
- Conducting more studies about smoking and the susceptibility to infection with COVID- 19Conducting additional studies of pre-specified outcomes in hospitalized patients (especially those with severe COVID-19 illness to estimate the risk of COVID-19 based on blood type.

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Appendices

Appendix 1: The names of experts who evaluated the study instrument

Names of expert	Fields of expert
Dr. Dina Bitar	Researcher
Dr. Hatem Eideh	Microbiologist
Dr. Hazem Agha	Public health nutritionist
Dr. Imad Matook	Biologist
Dr. Khalid Younes	Medical laboratory scientist
Dr. Nuha Sharif	Epidemiologist
Dr. Yehia Abed	Epidemiologist and statistician

Appendix 2: The ethical approval to start the study from the Ministry of Health

State of Palestine
Ministry of Health
General Directorate of Education in
Health and Scientific Research

دولة فلسطين
وزارة الصحة
الإدارة العامة للتعليم الصحي
والبحث العلمي

Ref.: .....
Date:.....

الرقم: عبد/ ٢٤٣/ ٢٠٢١
التاريخ: ٢٠٢١/٣/٢٥

الأخ مدير عام الادارة العام للمستشفيات المحترم ،،،

تحية واحترام...

الموضـــوع: تسهيل مهمة بحث

مرفق طلب تسهيل مهمة **الطالبة: آلاء حمدان عبيات– ماجستير صحة عامة/ علم اوبئة– جامعة القدس**، وباشراف د. ماهر الخضور، في عمل بحث بعنوان:

" Association Between ABO blood group and the severity of COVID-19 in the West-Bank: A Case Control Study "

من خلال للباحث بجمع معلومات عن طريق تعبئة استبانة من المرضى في مراكز فحص كورونا، وذلك في:

- **مراكز فحص كورونا جميع المحافظات**

حيث سيتم الالتزام باساليب واخلاقيات البحث العلمي.

على ان يتم الالتزام بجميع تعليمات واجراءات الوقاية والسلامة الصادرة عن وزارة الصحة بخصوص جائحة كورونا، وتحت طائلة المسؤولية.

على ان يتم تزويد الوزارة بنسخة من نتائج البحث، التعهد بعدم النشر.

مع الاحترام...

د. عبد الله القواسمي
مدير التعليم الصحي والبحث العلمي

نسخة: عميدة كلية الصحة العامة المحترمة/ جامعة القدس

P.O .Box: 14
Telfax.:09-2333901

Healtheducation.dep@gmail.com

ص.ب. 14
تلفاكس: 09-2333901

Appendix 3: The study questionnaire

عزيزي المشارك / المشاركة

تحية طيبة وبعد ,

أنا الطالبة آلاء عبيات من كلية الصحة العامة – الدراسات العليا – أقوم بعمل دراسة بحثية " رسالة الماجستير "حول " الارتباط بين نوع فصيلة الدم (ABO) وحَدَة الإصابة بفايروس كوفيد – 19- في الضفة الغربية في فلسطين وذلك إستكمالاً لمتطلبات التخرج من كلية الصحة العامة في جامعة القدس بهدف تحديد الارتباط بين نوع فصيلة الدم والإصابة بفايروس كوفيد -19- وحدّة الأعراض المتعاقبة معها وبناءً على ذلك , أطلب من حضرتكم بالتكرم في الاجابة على هذه الاستبانة بمنتهى الدقة والموضوعية .
شاكرة لكم على حسن تعاونكم, علماً بأن إج اباتكم ستكون سرية ولن تستخدم إلا لغرض البحث العلمي فقط .

للمزيد من المعلومات او للإستفسار يرجى التواصل عبر البريد الالكتروني :
Alaahamdanobeyat18@gmail.com

الموافقة على المشاركة في الدراسة:

1- موافق
2- غير موافق

- **تتكون الاستبانة من 5 أقسام**

الأقسام الأربعة الأولى لجميع المشاركين الخاضعين لفحص كوفيد 19 خلال شهر 3 -2021

القسم الخامس: مختص فقط بالمصابين بفايروس كورونا

الرقم التسلسلي : .....

القسم الأول : معلومات المريض		
الترميز	**السؤال**	**الاجابة**
1.1	العمر	..... بالسنوات
1.2	الجنس	1- ذكر 2- أنثى
1.3	مكان السكن	1- بيت لحم 2- الخليل 3- رام الله 4- أريحا 5- نابلس 6- جنين 7- طولكرم 8- قلقيلية 9- سلفيت 10-طوباس
1.4	فصيلة الدم	1- A 2- B 3- AB 4- O 5- لا أعلم
1.5	العامل الرايزيسي لفصيلة الدم	1- موجب 2- سالب 3- لا أعلم
1.6	الطول (سم)	.....
1.7	الوزن (كغم)	.....
1.8	الحالة الإجتماعية	1- أعزب / عزباء 2- متزوج / متزوجة 3- مطلق / مطلقة 4- أرمل/ أرملة
1.9	المهنة	.....
1.10	هل يوجد لديك أمراض مزمنة؟	1- نعم (اذهب إلى 1.10.1) 2- لا
1.10.1	حدد/ي ما هي الأمراض المزمنة لديك	.....
القسم الثاني : خصائص حالة التدخين		
الترميز	**السؤال**	**الاجابة**

2.1	هل تدخن التبغ او أي من منتجاته مثل السجائر، الغليون والنارجيلة ؟	1- نعم 2- لا (اذهب إلى 2.6)
2.2	هل انت حاليا مدخن للتبغ او أي من منتجاته ؟	1- نعم 2- لا
2.3	كم كان عمرك عندما بدأت التدخين ؟	العمر بالسنوات : ..... 99- لا أعلم
2.4	منذ متى وانت تدخن ؟	أو ..... سنوات أو ..... أشهر أو ..... أسابيع 99- لا أعلم
2.5.1W/2.5.1D 2.5.2W/2.5.2D 2.5.3W/2.5.3D 2.5.4W/2.5.4D 2.5.5W/2.5.5D 2.5.6W/2.5.6D	كم من المنتجات التالية تدخن أسبوعيا/ يوميا ؟	المنتجات — أسبوعياً — يومياً سجائر جاهزة .... سجائر محضرة يدوياً .... غليون .... سيجار .... أرجيلة .... غير ذلك ....
2.6	في الماضي، هل سبق وان دخنت أي نوع من أنواع التبغ ؟	1- نعم 2- لا (اذهب إلى 2.10)
2.7	هل سبق لك وان دخنت بشكل يومي بالماضي؟	1- نعم 2- لا
2.8	كم كان عمرك عندما توقفت عن التدخين ؟	العمر بالسنوات ..... 99-لا أعلم
2.9	منذ متى وانت متوقف عن التدخين ؟	أو ..... سنوات أو ..... أشهر أو ..... أسابيع 99- لا أعلم
2.10	هل سبق لك وان استخدمت أي من منتجات التبغ الغير مدخنة مثل الممضوغة وعلكة التبغ وغيرها؟	1- نعم 2- لا (اذهب إلى 2.13)
2.11	هل تستخدم منتجات الدخان الغير مدخنة بشكل يومي ؟	1- نعم 2- لا

2.12	هل سبق لك وان استخدمت أي من منتجات التبغ الغير مدخنة في الماضي ؟	1- نعم 2- لا (اذهب إلى 2.14)
2.13	هل سبق لك وان استخدمت أي من منتجات التبغ الغير مدخنة بشكل يومي في الماضي ؟	1- نعم 2- لا
2.14	خلال ال 30 يوما الماضية ، هل دخن احد داخل منزلك ؟	1- نعم 2- لا
2.15	خلال ال 30 يوماً الماضية، هل دخن احد بقربك في منطقة مغلقة مثل العمل ؟	1- نعم 2- لا 3- لا أعمل في منطقة مغلقة
القسم الثالث : الخصائص المتعلقة بالإنلفونزا الموسمية		
3.1	في الأعوام الماضية, هل عانيت من الإنفلونزا الموسمية؟	1- نعم (اذهب إلى 3.2) 2- لا
3.2	في الأعوام الماضية , عند إصابتك بالانفلونزا العادية هل عانيت من الأعراض الآتية ؟	1- إلتهاب الحلق 4- آلام في العضلات 7- إسهال 2- ارتفاع درجة الحرارة 5- صداع 8- غثيان 3- سيلان أو إنسداد الأنف 6- هزل عام في الجسم 9- قيء 10 - غير ذلك
3.3	في الأعوام الماضية , هل قمت بأخذ تطعيم الإنفلونزا؟	1- نعم 2- لا
3.4	هل تلقيت تطعيم الانفلونزا لهذا العام ؟	1- نعم (اذهب إلى3.5) 2- لا
3.5	هل عانيت من أعراض جانبية للتطعيم ؟	1- نعم (اذهب إلى 3.6) 2- لا
3.6	حدد هذه الأعراض التي عانيت منها	.....

القسم الرابع : التاريخ الطبي للخضوع لفحص كورونا خلال شهر 3 من عام 2021 عن طريق اختبار تفاعل البوليميراز المتسلسل (PCR) والالتزام بإجراءات الوقاية .		
4.1	ما هي نتيجة فحص كوفيد-19- ؟	1- إيجابية 2- سلبية
4.2	ما السبب أو الأسباب التي جعلتك تقوم بالفحص ؟	1- مخالط مباشر مع مريض مصاب 2- ظهور أعراض 3- لأمور خاصة بالعمل 4- فحص عشوائي 5- غير ذلك 99- لا أعلم
4.3	كم مرة قمت بعمل هذا الفحص؟	..... عدد المرات
4.4	في الفحص الآخير هل كان هناك حاجة لإعادة الفحص للتأكيد على النتيجة؟	1- نعم (اذهب إلى 4.4.1) 2- لا
4.4.1	كم عدد المرات التي احتجتها للتأكيد على النتيجة النهائية؟	..... عدد المرات

4.5	حدد مدى التزامك بإجراءات الوقاية والسلامة التالية :

اجراءات الوقاية والسلامة	دائماً	غالباً	أحياناً	نادراً	أبداً
1.الالتزام بالمسافة الامنة والتباعد الجسدي بمسافة 6 أقدام على الاقل					
2. ارتداء الكمامة بالطريقة الصحيحة عن طريق تغطية الانف والفم					
3. الحد من التجمعات في الأماكن العامة					
4. غسل وتعقيم اليدين بشكل متكرر					
5. تجنب الإتصال المباشر مع الأشخاص المرضى					

القسم الخامس : هذا الجزء متعلق بمصابين كورونا فقط خلال شهر 3 حول حدّة الأعراض وطبيعتها والمضاعفات المترتبة عليها		
5.1	ما هو مكان العلاج؟	1- المنزل 2- مراكز الكورونا 3- المستشفيات 4- مراكز صحية أخرى
5.2	ما هي الأعراض التي قد تعرضت إليها أثناء إصابتك	1- إرتفاع درجة الحرارة 2- السعال 3- التهاب في الحلق 4- هزل عام 5- صداع 6- آلام في العضلات 7- احتقان أو سيلان الأنف 8- فقدان الشم أو التذوق 9- ضيق في التنفس
5.3	ما المدة التي استغرقتها في الأعراض السابقة؟	..... أيام
5.4	هل تعلم ما هو مصدر العدوى؟	1- نعم (اذهب إلى 5.5) 2- لا
5.5	حدد مصدر العدوى	.....
5.6	هل عانيت من مضاعفات في إحدى الأجهزة التالية؟	1- جهاز الدوران (القلب والشرايين) 2- الجهاز المناعي 3- الجهاز الهيكلي والعضلي 4- الجهاز الهضمي 5- الجهاز التناسلي 6- الجهاز التنفسي 7- الجهاز البولي 8- الجهاز العصبي 9- لم أعاني من أي مضاعفات
5.7	هل احتجت الدخول إلى العناية المكثفة؟	1- نعم 2- لا
5.8	هل احتجت إلى استخدام مصدر أوكسجين مساعد؟	1- نعم 2- لا
5.9	هل احتجت إلى استخدام جهاز تنفس إصطناعي ؟	1- نعم (انتقل للسؤال 5.9.1) 2- لا
5.9.1	ما المدة التي استغرقتها على جهاز التنفس الإصطناعي؟	..... أيام

الملخص بالعربية

العلاقة بين نوع فصيلة الدم وحَدّة الإصابة بفايروس كوفيد في الضفة الغربية: دراسة الحالات والضوابط

إعداد : آلاء حمدان عبيات

إشراف : د. ماهر خضور

الملخص

خلفية الدراسة: تم تسجيل تفشي مرض فيروس كورونا الجديد في ووهان بمقاطعة هوبي وانتشر بسرعة إلى جميع المقاطعات والبلديات في الصين على الصعيد الوطني ، وانتشر أيضًا في جميع أنحاء العالم. وفي فلسطين عدد الاصابات والوفيات في تزايد واستمرار.

مشكلة الدراسة والمبررات: فحصت العديد من الدراسات عوامل الخطر لفايروس كوفيد المستجد. وكان هناك اختلاف بين نتائج وتقارير الباحثين حول ما إذا كان لنوع فصيلة الدم دور في التأثير على خطر الإصابة بالفايروس لذلك ، خططت هذه الدراسة لتقييم تأثير فصيلة الدم على حدةّ الإصابة بفايروس كوفيد المستجد في جميع محافظات الضفة الغربية بحيث يمكن اعتبارها كمرجع نحو الالتزام بإجراءات الوقاية بين الآخرين وتحديث آلية العلاج تجاه فايروس كوفيد 19 من قبل صناع القرار.

الأهداف الرئيسية: هدفت هذه الدراسة إلى تحديد العلاقة بين نظام فصائل الدم وحدة الإصابة بفايروس كوفيد 19 في الضفة الغربية في فلسطين. وتتمثل أهدافها في تحديد مدى قابلية الإصابة بالفايروس وفقًا لفصيلة الدم ، وشدة الأعراض ، وعوامل الخطر المختلفة كمتغيرات اجتماعية ديموغرافية ، والحالة الصحية ، وحالة التدخين ، وتجربة الأنفلونزا الموسمية وتجربة الإصابة بفايروس كوفيد 19 كمتغيرات محيرة محتملة. وإثبات النتائج المترتبة على حدةّ الإصابة بفايروس كوفيد 19 وفقًا لفصائل الدم.

منهجية الدراسة: الدراسة عبارة عن دراسة للحالات والضوابط ، تتألف من 338 مشاركًا 169 حالة و 169 ضابطة، الذين قاموا بعمل فحص كوفيد خلال شهر 3 من العام 2021 في جميع محافظات الضفة الغربية حيث تم تصنيفهم بناءً على نتيجة الاختبار. كانت الحالات عبارة عن ذوي النتيجة الإيجابية مع أعراض كوفيد 19. والضوابط عبارة عن الأشخاص ذوي النتيجة السلبي لفحص كوفيد 19 .تم جمع البيانات عن طريق استبيان الدراسة وتم تعبئته عن طريق الاتصال بالمشاركين عبر أرقام هواتفهم.

التحليل الإحصائي: تم إدخال البيانات وتحليلها باستخدام برنامج (SPSS- 23) تم إجراء كل من التحليل الوصفي والتحليلي. تم تمثيل الإحصاء الوصفي لإظهار التكرارات والنسب المئوية للمتغيرات الفئوية والمتوسطات والانحراف المعياري للمتغيرات المستمرة. تم استخدام اختبارمربع كاي لمقارنة ارتباط متغيرين معنويين بين فصيلة الدم واحتمالية الاصابة بفايروس كوفيد 19 ، وكذلك في المقارنة بين الحالات والضوابط. تم استخدام الانحدار اللوجستي الثنائي في

التحليل متعدد المتغيرات لإثبات نسبة الأرجحية ودرجة الثقة 95%واعتماد العوامل المؤثرة عند الدلالة الاحصائية .P<0.05

الاعتبارات الأخلاقية: قدمت هذه الدراسة إلى لجنة البحث العلمي والدراسات العليا في جامعة القدس , تم أخذ الإذن بإجراء الدراسة التي تم الحصول عليها من وزارة الصحة الفلسطينية .حيث تم جمع استمارة الموافقة من جميع المشاركين شفهيًا عن طريق التواصل معهم عبر الهاتف.

النتائج: أظهر تحليل بيانات حالات الدراسة أن متوسط عمر المشاركين كان 38 عاماً ، كانت الغالبية العظمى من المشاركين ذوي فصيلة الدم "O" بنسبة 37.9% تليها فصيلة الدم "A" بنسبة 36.7% ومن ثم فصيلة الدم "B" وفصيلة الدم "AB" حيث شكّلت نسبتهما 13.6% 11.8% على الترتيب. وأظهر التحليل متعدد التغيرات عند مقارنة فصيلة الدم "A" مع فصائل الدم الأخرى أنها الأكثر احتمالية للإصابة بفايروس كوفيد , كما أن فصيلة الدم "B" أقل عرضة للإصابة بفايروس كوفيد من فصيلة الدم "A" بمقدار 0.40 مرة وفصيلة الدم "AB" أقل عرضة للإصابة من فصيلة الدم "A" بمقدار 31.6% مرات . ولم يظهر أي اختلاف في احتمالية الإصابة والخطر بين فصيلة الدم "A" وفصيلة الدم "O" بالإضافة إلى كونه لم يوجد أي دلالات فروقية بين حدة الأعراض بناءً على نوع فصيلة الدم أو على المضاعفات والنتائج المترتبة على الإصابة بفايروس كوفيد .كما تبين أن أخذ تطعيم الانفلونزا الموسمية في الأعوام الماضية يقلل من خطر الإصابة بفايروس كوفيد بمقدار 1.97 مرة من الذين لم يقوموا بأخذ التطعيم .

الخلاصة: هذه هي الدراسة الأولى في فلسطين التي تهتم بالارتباط بين فصيلة الدم وخطورة كوفيد 19 حيث أكدت الدراسة الارتباط بين فصيلة الدم وقابلية الإصابة بفايروس كوفيد 19 ، لكنها أظهرت أيضًا أنه لا يرتبط بشدة الأعراض أو النتائج المرتبطة بفايروس كوفيد 19 .تبين أن الأشخاص ذوو فصيلة الدم "A" يمتلكون احتمالية الإصابة بفايروس كوفيد 19 أكثر من غيرهم من فصائل الدم الأخرى.

كما تبين أن أخذ تطعيم الانفلونزا الموسمية في الأعوام الماضية هو عامل وقائي تجاه كوفيد 19. لم يظهرعلاقة ارتباط بين خصائص المشاركين في الدراسة (الجنس، عامل ريزوس، والحالة الصحية ، ومؤشر كتلة الجسم ، والتعرض للمهنة وتجربة فايروس كوفيد 19) باستثناء "العمر" الذي كان متغيرًا مرتبطاً بكلا السبب والنتيجة في الدراسة وتبين أنه عامل محير في الدراسة. علاوة على ذلك ، يجب على الأشخاص ذوي فصيلة الدم A تعزيز طرق الوقاية ضد كوفيد 19 ، مع الأخذ بعين الاعتبارضرورة التزام جميع مجموعات الدم الأخرى بتدابير السلامة والوقاية وينبغي إجراء دراسات أخرى ذات حجم عينة أكبر وتقييم المتغيرات الأكثر إرباكًا لتحديد مدى تأثير فصائل الدم على حدة فايروس كوفيد 19 المستجد.