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Clinical Characteristics and Risk Factors for COVID-19 Deaths in West Bank

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Clinical Characteristics and Risk Factors for COVID-19 Deaths in West Bank

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Dedication

I apologize, but since the dedication part is my personal space, I prefer to express it in my mother tongue "Arabic," as no other language in the world can express what my soul feels.

الإهداء

قبل أن تُشير الساعة إلى انتهاء موعد الزيارة، دبّ في حيرتي الرّعب، كيف تلقّى تأشيرة دخول إلى قسم العناية المكثفة؟ ستّيني بجسد لم يعهد السّقم، جبل مقيّد كأسير حُرم وداع أمّه، أيقاتله فيروس بلا هوادة؟! وعلى حين غرّة، تجدّلت نبراته مع شهقاته، آخر ما حدّثني: "غادري ولا تؤجلي امتحاناتك!"، ولم تغادرني صرخات عُروقه وقسمات الوجوه من حوله؛ فركنتُ سريره عنوة، وخططت المقترح، خطيتُ على أشواك ناعمة، حملت الرّسالة على ظهري حتى تقوّس، حشدتّ عشرات المتغيرات صفًّا صفًّا، وما بدت أن تتوارى حتى لوّحت الثوابت استنكارًا وسط مسير أشقاه النصب من كل صوب، لم التشبّث هذا؟ لأنّي حتمًا لا أؤمن ببراثن العبثية، فلم تحطّ الأقدار أثقالها إلا لمسوّغ لم نبصره بعد، حتى سطعت الشّمس على أفكاري وسرعان ما أيقظتني صفعة من إمكانات الوطن لأعود أدراجي، ذاك الوطن الذي ما زال يتنفّس بمن يملؤون حويصلات رئتيهم بثرى الإعداد تحت الأرض، ومن يجودون بدمهم بين الزّقاق فوق الأرض، وما لليلي أن تنفّس حتى ألقى بقطعه على ضلوعي، بتّ أربّت على نفسي بكل من علّمني حرفًا، ودعوات أمّي الصّابرة تطوف حولي؛ لئلا يطوق القنوط علمي ، فالعلم الذي يسطّر بالإصرار يسجّل دومًا الانتصار، وإن عجز في موازنة طرفي معادلة لاستحالة التكافؤ ، فهل أوفي بحقّ أبي وأمي؟ أم بحقّ وطن احتضنني كي أرفعه، فارفع رأسك بفلذة كبدك بين رفاقك في البرزخ، إلى روحك أبي الحبيب، وروح جدّتي الغالية، وكل روح هنا مرّت وأنّت، وكل روح لوطنها ضحّت، أسأل الله لكم الرحمة، وأن يكون نتاج بحثي هذا همزة وصل بين قبركم وأجركم، وأتلو عليكم بردًا وسلامًا، أنتم السّابقون ونحن اللاحقون، إذ لا بُد من الغياب، لكن من منّا سيُحسن العتاد؟ ألا ونحن المعتبرون...!

Declaration

I certify that this thesis submitted for the degree of Master is the result of my own research, except where otherwise acknowledged and that this thesis (or any part of the same) has not been submitted for a higher degree to any other university or institution.

Name: Duha Issa Hammad Hamamdeh

Signed: 

Date: 23\5\2023

Acknowledgment

I am very grateful to **God**; without his guidance, I would not have achieved what I have, and without his facilitation, I would not have reached this point. I am also grateful to my loving **family**, who surrounded me with their sincere prayers.

This research had many challenges, so, I am pleased to express my appreciation and respect to my extraordinary research supervisor, **Dr. Asad Ramlawi**, who was like a father to me and never hesitated to guide and encourage me. Also, I offer my heartfelt thanks to **Al-Quds University** and the **Palestinian MOH**, who allowed me to conduct this research, and many thanks to all public health professors for their great support throughout the study period especially in the program of infectious disease prevention and control, **Dr. Nuha Sharif** and **Dr. Khaldoun Bader**.

I will not forget to thank **Dr. Rabee Adwan** who coordinated with private hospitals and provided his advice based on his experience with COVID-19 patients. Also, I would like to thank all the hospitals that facilitated my task, especially in the data collection and dump phase, **Dr. Mahmoud Kiswani** from Al-Makkased Hospital, **Dr. Ali Sabateen** and **Rami Zaghari** from Augusta Victoria Hospital, **Dr. Youssef Iyad** from the Al-Watani Hospital, **Dr. Ola Akkawi** from Ibn Sina Hospital, **Dr. Mays Al-Huwaiti** from Istishari Arab Hospital, **Mohammed Al-Zeer** from the National Rehabilitation Center.

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Abstract

Background: Many risk factors have been associated with severe outcomes and death from COVID-19 disease. In Palestine, the incidence of COVID-19 was 8.96%, the COVID-19 mortality rate was 0.1%, and deaths due to COVID-19 showed case fatality ratio of 1.04% until the 31st of December 2021. **Study Problem & Justification:** The mortality rate among the population in West Bank related to COVID-19 requires an accurate analysis of risk factors causing death, and MOH has published statistics about active, recovered, and fatal cases, but without any analysis of the exposures or causes. Therefore, we would like to conduct a study in Palestine to understand clinical characteristics and risk factors for deaths**. Aim & objectives:** This study aims to understand the clinical characteristics and risk factors for COVID-19 that resulted in death in West Bank. Its objectives are understanding the demographic characteristics, medical history, and complications of COVID-19 deaths. In addition, analyzing indicators of COVID-19 progression and evaluating the correlation between a medical intervention and deaths in different hospitals. **Study methodology:** A retrospective cohort study targeted the files of 1001 COVID-19 deaths 15 hospitals in West Bank from March 1, 2020 to December 31, 2021. Descriptive, univariate at p-value < 0.05, and multivariate analysis with (95% CI) were performed using SPSS software. **Results:** The mean age of sample was 68 years, with range 17-100 years, half of them were males (57.5%). A+ blood group was dominant (33.6%). The mean of stay duration in the hospital was 12.9 days, while the mean of survival days was 15.9 days. Also, 99.1% of patients received supplemental oxygen, 94.6% received non-invasive O2 while 56.3% received invasive O2, and the mean of initiation of giving the non-invasive O2 was one day from admission while the mean of initiation the intubation was 7 days from admission. All patients had signs and symptoms, 82.9% of patients had comorbidities. Pulmonary infiltrates were the most reported radiological finding with percentage of 60.2%. Also, on average, the first abnormal laboratory test results manifested by day 4 following the admission. In terms of medications, Dexamethasone was administrated to 82.7% of patients while Enoxaparin was received by 83.5% of them. Additionally, antibiotics were given to 97.1% of the patients, despite only 19.1% of them having co-infection. Also, the analysis showed a significant relationship through comparison between age and gender with the variables, and the findings indicated that individuals in the age range of 61-8- years, having diabetes, having cancer, and developing septic shock experienced a significant decrease (95% CI) in survival days, with reductions of

1.27 folds (127%), 1.202 folds (120%), 1.320 folds (132%), and 1.309 folds (130%) respectively. On the other hand, living in the southern West Bank, receiving intubation, having hypothyroidism, and receiving Tocilizumab experienced a significant increase (95% CI) in survival days, with increase of 0.799 folds (79.9%), 0.74 folds (74%), 0.46 folds (46%), 0.74 folds (74%) respectively. **Conclusion:** This study is the first one in Palestine that highlighted the COVID-19 deaths from all governorates of West Bank and identified their clinical characteristics and investigated the possible risk factors related to COVID-19 deaths attending the hospitals. Most of our findings were consistent with other international studies. Based on the findings of this study, it was observed that the old age, male, A+ blood group, comorbidities, and additional complications were related to COVID-19 mortality. Each of age and gender had an effect on some study variables. The indicators such as radiological investigation and laboratory tests showed abnormal findings that predicted to worse COVID-19 prognosis. In addition, the time factor clearly appeared in our study, as survival days, duration days in hospitals, and O2 supply timing as some variables significantly affected survival days since COVID-19 diagnosis. Therefore, the timely identification of COVID-19 severity by biomarkers would help to provide the appropriate intervention on time. Regarding intervention, the majority of hospitals adopted a similar treatment protocol, involving the administration of corticosteroids, anticoagulants, mineral and vitamin supplements, antivirals, and antibiotics. However, these treatments did not show a substantial impact on survival days, with the exception of Tocilizumab.

الخصائص السريرية وعوامل الخطر لدى وفيات كوفيد-19 في الضفة الغربية

إعداد الباحثة: ضحى عيسى حماد حمامده

المشرف: د. أسعد رملاوي

الملخص

الخلفية: ارتبطت العديد من عوامل الخطر بالنتائج الخطرة والوفاة بسبب مرض كوفيد-19، في فلسطين بلغ معدل الإصابة بكوفيد-19 8.96%، وبلغ معدل الوفاة 0.1%، أما معدل الوفيات إلى الحالات فقد بلغ 1.04% وذلك حتى تاريخ 31 كانون أول 2021.

مشكلة ومبررات الدراسة: معدل وفيات كوفيد-19 بين سكان الضفة الغربية يتطلب تحليلًا دقيقًا لعوامل الخطر والتي تسببت بالوفاة، كما أن وزارة الصحة الفلسطينية تقدم إحصائيات وصفية حول نسبة الحالات النشطة والمتوفاة والمتعافية دون تحليل للمسببات؛ لذا ستقوم دراستنا بتحليل الخصائص السريرية وعوامل الخطر لدى الوفيات.

الهدف الرئيسي والأهداف الفرعية: تهدف هذه الدراسة إلى فهم الخصائص السريرية للوفيات وعوامل الخطر المرتبطة بحدوث الوفاة في الضفة الغربية، كما تسعى إلى فهم الخصائص الديموغرافية، التاريخ المرضي، والمضاعفات لدى وفيات كوفيد-19، إضافة إلى تحليل مؤشرات تقدم المرض، وتقييم العلاقة بين التدخلات العلاجية والوفاة في مختلف المشافي.

المنهجية: دراسة جماعية بأثر رجعي تناولت ملفات 1001 حالة وفاة بسبب كوفيد-19، في 15 مشفى مستهدفًا في الضفة الغربية خلال الفترة الواقعة ما بين 1 آذار 2020 حتى 31 كانون أول 2021. كما تم تقديم تحليل وصفي، تحليل أحادي المتغير عند الدلالة الإحصائية (P-value < 0.05)، وتحليل متعدد المتغيرات بدرجة الثقة 95% عبر برنامج SPSS.

النتائج: أظهر التحليل أن معدل العمر للحالات بلغ 68 سنة حيث تراوحت الأعمار ما بين 17-100 سنة، وأكثر من نصف العينة كانت ذكورًا بنسبة 57.5%، وتبين أن فصيلة الدم الأكثر شيوعًا +A بنسبة 33.6%. وبلغ معدل مدة الإقامة في المشفى 12.9 يومًا، بينما بلغ معدل أيام البقاء على قيد الحياة 15.9 يومًا. إضافة إلى ذلك، تلقى 99.1% من المرضى الأكسجين، وتلقى 94.6% الأكسجين عبر القناع أو جهاز الضغط بينما تلقى 56.3% الأكسجين عبر جهاز التنفس الصناعي، وبلغ متوسط البدء بإعطاء الأكسجين عبر القناع أو جهاز الضغط يومًا واحدًا من الدخول إلى المشفى بينما بلغ متوسط البدء بالتنبيب 7 أيام من الدخول. وظهرت لدى جميع المرضى علامات وأعراض، ونسبة 82.9% من المرضى من أمراض مصاحبة. أما الارتشاح الرئوي فكان الأكثر تكرارًا في تقارير الأشعة الموثقة وبنسبة 60.2٪. كما بلغ معدل معدلات الأيام التي سجلت أول نتيجة غير طبيعية لجميع الفحوصات المخبرية نهاية اليوم الرابع من الدخول إلى المشفى. وفيما يتعلق

بالأدوية، فقد تلقى 82.7٪ من المرضى "ديكساميثازون" وتلقى 83.5٪ "إينوكسابارين"، وتلقى 97.1٪ مضادات حيوية المرضى رغم أن نسبة المرضى المصابين بالعدوى المصاحبة بلغت 19% فقط.

وأظهرت النتائج تأثير كل من العمر والجنس على المتغيرات، كما أشارت إلى أن الفئة العمرية الواقعة بين 61–80 عامًا أدّت إلى التقليل من أيام البقاء على قيد الحياة بـ 1.27 ضعف، وكذلك مرض السكري بـ 1.202 ضعف، ومرض السرطان بـ 1.320 ضعف، وتطور الصدمة الإنتانية بـ 1.309 ضعف، من ناحية أخرى، أدى العيش في جنوب الضفة الغربية إلى زيادة أيام البقاء على قيد الحياة أي تأخير الوفاة بـ 0.799 ضعف، وكذلك التنبيب بـ 0.74 ضعف، وقصور الغدة الدرقية بـ 0.46 ضعف، وتلقي "توسيليزوماب" بـ 0.74 ضعف.

الخلاصة: هذه الدراسة هي الأولى في فلسطين التي تسلط الضوء على وفيات كوفيد–19 من جميع محافظات الضفة الغربية وتحدد خصائصها السريرية وتحقق في عوامل الخطر المحتملة في المشافي. كما اتفقت معظم النتائج التي توصلنا إليها مع الدراسات العالمية الأخرى. وأظهرت دراستنا ارتباطًا بين كل من كبار السن، الذكور، ذوي فصيلة الدم +A، ذوي الأمراض المصاحبة، ذوي المضاعفات وحدوث الوفاة، وكان لكل من العمر والجنس تأثير على بعض متغيرات الدراسة مثل مدة الإقامة في المشفى، الأمراض المصاحبة، احتمالية ظهور الأعراض والمضاعفات، واحتمالية الحاجة إلى الأكسجين الغازي أو غير الغازي. فيما أظهرت المؤشرات كالتصوير الإشعاعي والفحوصات المخبرية نتائجًا غير طبيعية تنبأت بمراحل متقدمة من كوفيد–19. إضافة إلى ذلك، برز عامل الزمن بوضوح مثل أيام البقاء على قيد الحياة، أيام المكوث في المشافي، وتوقيت إمداد الحالات بالأكسجين بأنواعه، حيث أثرت بعض المتغيرات بشكل كبير على أيام البقاء على قيد الحياة منذ تاريخ تشخيص كوفيد–19. لذلك، فإن تحديد شدة المرض في الوقت المناسب عبر المؤشرات الحيوية سيساعد على توفير التدخل المناسب في الوقت المناسب. وفيما يتعلق بالتدخل، فقد اتبعت معظم المشافي المشمولة في دراستنا بروتوكولًا متشابهًا بإعطاء "كورتيكوستيرويد"، مضادات التخثر، مضادات الفيروسات، المضادات الحيوية، مكملات المعادن والفيتامينات كخيارات علاجية لها دون تأثير كبير على أيام البقاء على قيد الحياة باستثناء دواء " توسيليزوماب".

List of abbreviations

MOH	Ministry of Health	CI	Confidence Intervals
WHO	World Health Organization	UNRWA	The United Nations Relief and Works Agency for Palestine Refugees
CDC	Center of Disease Control and Prevention	BMI	Body mass index
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2	PCBS	Palestinian Central Bureau of Statistics
ARDS	Acute Respiratory Distress Syndrome	OCHA	United Nations Office for the Coordination of Humanitarian Affairs
SD	Standard deviation	CT	Computerized Tomography
SPSS	Statistic Package for Social Science	ICU	Intensive Care Units
ACE	Angiotensin Converting Enzyme	PCR	Polymerase Chain Reaction
WBC	White Blood Cells	CRP	C-Reactive Protein
CPAP	Continuous Positive Airway Pressure	RAS	Renin-Angiotensin System
LDH	Lactate Dehydrogenase	CK	Creatine Kinase
BIPAP	Bilevel Positive Airway Pressure	ECDC	European Center of Disease Control and Prevention

Chapter One: Introduction

1.1. Background

COVID-19 is an infectious disease caused by a new coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The World Health Organization (WHO) declared a new virus on 31st of December 2019, following a report of a cluster of cases of 'viral pneumonia' in Wuhan, People's Republic of China. (WHO, 2021). This disease acquired global concern due to its zoonotic transmission and rapidly human-to-human spreading from Wuhan to other areas in different countries (Panthee, et al., 2020). So, after 118,000 cases and 4,291 deaths were reported in 114 countries, on 11 March 2020, WHO declared COVID-19 as a pandemic (Williamson, et al., 2020).

Prior to the emergence of the COVID-19 pandemic, the world suffered from two β-coronaviruses outbreaks; severe acute respiratory syndrome coronavirus (SARS-CoV-1) in 2003 and middle east respiratory syndrome coronavirus (MERS-CoV) in 2012 (Hassan, et al., 2020).

Both SARS-CoV-2 and SARS-CoV enter the host cell via the same receptor, angiotensin-converting enzyme 2 (ACE2) (Ni, et al., 2020). ACE2, a homolog of angiotensin-converting enzyme (ACE) that is expressed in human tissues and organs, has wide biological activities, and therefore can affect the renin-angiotensin system (RAS) in several diseases (Ni, et al., 2020).

Considering that the spike protein of SARS-CoV-2 interacts with ACE2, as does that of SARS-CoV, COVID-19 may have a pathogenic mechanism similar to that of SARS (Ni, et al., 2020). However, SARS-CoV-2 is more infectious than SARS-CoV and MERS-CoV (Ping, et al., 2020), the clinical picture of SARS-CoV-2 includes asymptomatic infection, mild upper respiratory tract infection, and severe respiratory failure even death. (Wang, et al., 2020)

The Incidence of COVID-19 varies around the world, in the general population was 36,556 per 1000,000. While the mortality rate worldwide was 6.8 per 1000 until the 31st of December 2021(WHO, 2021).

Numerous risk factors have been associated with severe cases and deaths from COVID-19; age, gender, and comorbidities (Bhaskaran, et al., 2021) that lead to organ dysfunction such as acute

respiratory distress syndrome (ARDS), acute hepatic failure, acute cardiac failure, and acute kidney failure (Ni, et al., 2020).

As for the SARS, age above 60 and the presence of diabetes mellitus and/or cardiac diseases were related to a higher mortality rate and severe cases (chan, et al., 2003).

1.2. Study Justification

The global death numbers due to COVID-19 exceed 5.44 million until December 2021 (WHO, 2022). Many studies highlighted age and chronic diseases as risk factors for deaths due to COVID-19 such as the increasing number of deaths among patients having ischemic heart disease, diabetes, and hypertension in some regions of the United States during the initial phase of the COVID-19 pandemic (Wadhera, et al., 2021). In Wuhan, China, a study of 85 fatal cases of COVID-19 showed that most cases were males aged over 50 years with noncommunicable chronic diseases (Du, et al., 2020). Also, preliminary reports on COVID-19 have some clinical and laboratory finding correlation including thrombocytopenia, elevated D-dimer, prolonged prothrombin time, and disseminated intravascular coagulation (Giannis, et al., 2020). However, there is not yet sufficient evidence to confirm the association between hypertension and death (Leung, 2020).

There were many fatal cases among young patients with no chronic diseases, especially after the occurrence of the COVID-19 new mutations.

In Palestine, the incidence of COVID-19 was 8.96%, the COVID-19 mortality rate was 0. 1%, and deaths due to COVID-19 which showed a case fatality ratio of 1.04% until the 31st of December 2021. (See Figure 1 to Figure 4) (MOH, 2021).

According to Figure1&2, over time, the disease is spreading and the number of reported cases and deaths is wavily increasing, especially after the occurrence of gatherings (social events) with no prevention measures.

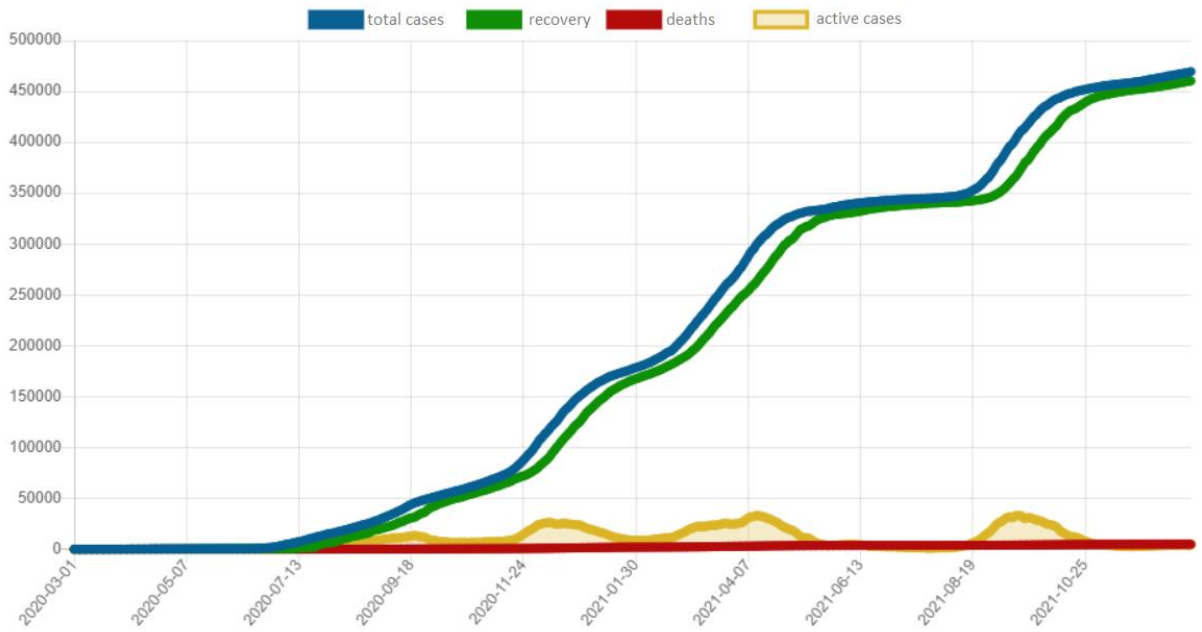

Figure 1: Distribution of COVID-19 cases, Palestine 2020-2021 (MOH, 2021).

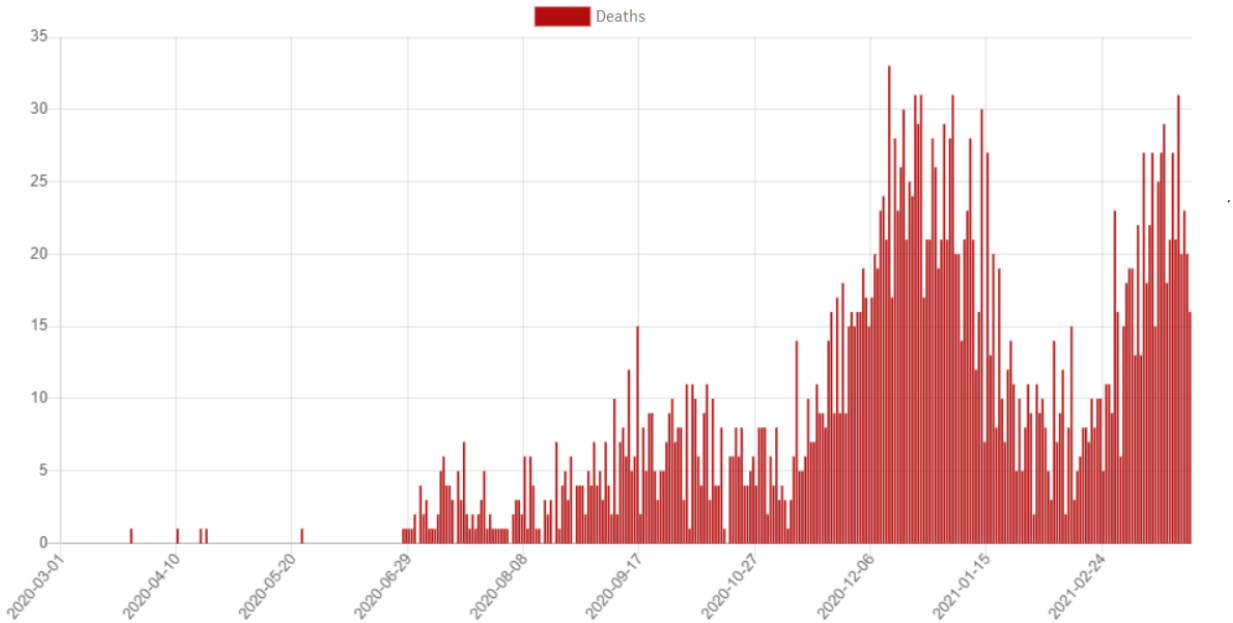

Figure 2: Distribution of COVID-19 deaths, Palestine 2020-2021 (MOH, 2021).

The following figure shows that the percentage of infected males and females is approximately equal.

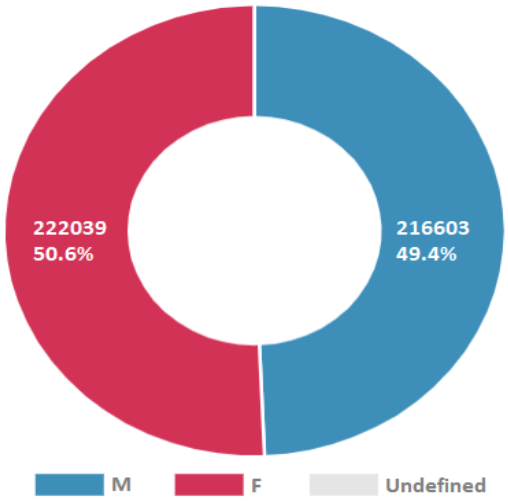

Figure 3: Distribution of COVID-19 cases by gender, Palestine 2020-2021 (MOH, 2021).

The following figure shows that the percentage of infected cases differed among the age groups, the lowest percentage was observed in the age group 0-9 years and over the age of 70, while the highest percentage was in the group 18-29 years. Taking into consideration that young generation is the predominant among Palestinian community.

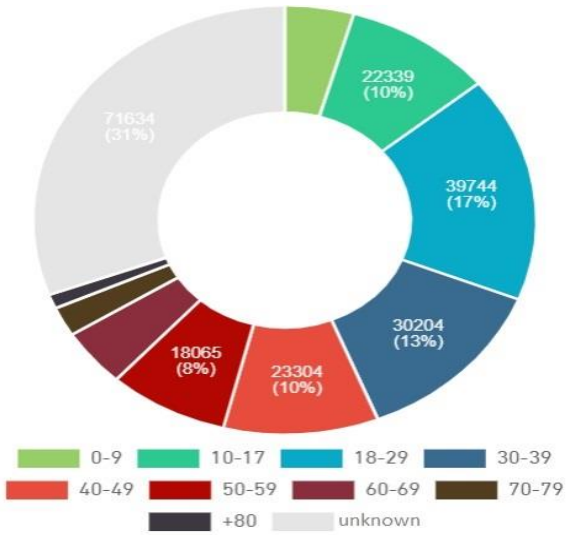

Figure 4: Distribution of COVID-19 cases by age, Palestine 2020-2021 (MOH, 2021).

Seen the clear variation among the number of patients and fatal cases, further studies on the severity and risk factors for death are demanded to have a valid and valuable recommendation to highlight the severity and mortality related to similar infections and situations.

1.3. Problem Statement

The mortality rate among the population in West Bank related to COVID-19 is increasing and attributed to some risk factors such as advanced age and chronic diseases. On the other hand, many fatal cases were recorded among young infected individuals without comorbidities, while many cases with advanced age and\or comorbidities were still surviving. So that requires accurate analysis and interpretation of the risk factors to understand the magnitude of this problem. The Palestinian Ministry of Health reports is statistics on the active, recovered, and fatal cases, but without any analysis of the exposures or causes. Therefore, we would like to conduct a study in Palestine that will highlight clinical characteristics and different epidemiological risk factors.

1.4. Study Expected Outcome

The results of this research will contribute to understanding better the clinical characteristics and risk factors for COVID-19 deaths in Palestine which will give opportunities for better planning of prevention and control measures and policies in the future.

1.5. Aim of Study

To highlight the risk factors and clinical characteristics (severity) for COVID-19 deaths in West Bank**.**

1.6. Study Objectives

1. To highlight the risk factors related to COVID-19 among deaths in different hospitals.
2. To highlight the demographic characteristics of COVID-19 deaths.
3. To highlight the clinical characteristics of COVID-19 deaths and
4. To analyze indicators of COVID-19 progression.
5. To evaluate the correlation between medical intervention and deaths in different hospitals.

1.7. Context of the study

After the Palestinian National Council announced in its session held in Algeria in 1988, the establishment of the Palestine State on the 1967 borders, and the establishment of the National Authority, the Authority divided the territories of the Palestinian state administratively to 16 governorates, including 11 in the West Bank and 5 in Gaza Strip (WAFA, 2021). The Jordanian authorities called those governorates "West Bank" due to it being located at the west of the Jordan River, while most of the territory of the Jordan lies at the east of the river (PRB, 2002). Its climate is affected by location and surface factors. Generally, Palestine lies within the Mediterranean climate region, which is characterized by moderation (UNRWA, 2021). The area of West Bank constitutes approximately 21% of the historical Palestine area, or approximately 5660 km2 (PCBS, 2017), and has a 3.1 million population (PCBS, 2021). These populations have special characteristics as shown in the lower table according to PCBS.

Table 1.1: Population characteristics in the West Bank in 2020 (PCBS, 2021).

Population in by selected age group		
0-14 years	15-29 years	60 years and over
35.8%	28.6%	6%
Population by gender		
Male	Female	
51%	49%	
Population with difficulty/disability by gender		
Male	Female	
5.2%	4.8%	
Average housing density (average number of persons in one room)		
1.3		
Percent of households with 3 persons or more per room		
4.9%		
Population by health insurance coverage		
65.7%		

Unemployed population (15 years and over)		
2.5%		
Poverty		
Poverty Rate	Extreme Poverty rate	
13.9	5.8%	
Health facilities		
Number of hospitals (governmental and private)	Number of doctors/1000 people	Number of beds/1000 People
87	3.03	1.3

Regarding COVID-19, above 250 Israeli settlements were established across the occupied West Bank since 1967 which robs the lands of Palestinian citizens and impedes their access to humanitarian and health services (OCHA, 2017).

The global COVID-19 crisis hit the occupied Palestinian territory in March 2020, when the first cases having the virus were confirmed. This triggered the declaration of an emergency state and the imposition of restrictions to contain the spread (OCHA, 2021).

The Palestinian Authority benefited relatively from the suspension of airports and tourist movement in the world, to control the numbers of arrivals through the al-Karama and Rafah crossings, but the movement of the workers inside Israel remained a loophole that impedes preventive measures, that was synchronous with all critical indicators such as poor human and material capabilities, the financial crisis, the political administration of Jerusalem, and Area C by the Israeli occupation.

The screening of disease by nasopharyngeal swab investigated by PCR or rapid COVID-19 in the laboratory is still the main screening and diagnostic method in Palestine, and it is free for all populations regardless of the insurance state of clients. Patients with COVID-19 disease were treated for free also regardless of the insurance state, but there was overcrowding of hospitals and a lack of some essential specialists such as intensive care and anesthesia as well as a small number of ICU beds.

1.8. Operational definitions

- COVID-19 deaths: Patients who died while he was under treatment in the hospital as an active case of COVID-19 and never announced or counted as a recovery one.
- Clinical characteristics: Features of the disease and the ways in which it can be presented.
- Risk factors**:** Variables that could increase morbidity and severity.

1.9. Study Hypothesis

- Old age and comorbidities are significantly correlated with covid 19 mortality.
- Male gender is correlated with COVID-19 mortality.
- Smoking is negatively correlated with infection and positively correlated with death due to COVID-19.
- The risk of death is more after the 7th day of COVID-19 admission.
- Complications are positively associated with disease progression in COVID-19 patients.
- Mechanical ventilation is related to worse prognosis in COVID-19 patients.
- Comorbidities are significantly correlated with COVID-19 mortality.
- Co-infections are positively associated with death due to COVID-19.
- Antiviral drugs have a low effect on COVID-19 mortality.
- Supplements are negatively correlated with COVID-19 progression.
- Abnormal lab findings are positively correlated with COVID-19 mortality.
- Pregnancy is correlated with COVID-19 mortality.
- Blood group A+ is related to COVID-19 mortality.

Chapter Two: Literature review

2.1. Conceptual framework

The world health organization (WHO), the center of disease control and prevention (CDC), and many worldwide studies; i.e. (Bhaskaran, et al., 2021; Ni, et al., 2020; Drefahl, et al., 2020; Williamson, et al., 2020; Wang, et al., 2020; Nadim, et al., 2020), showed similar models of clinical characteristics and risk factors for COVID-19 deaths and found that the multisystemic nature of COVID-19 does not affect the respiratory system only, but also kidneys, the cardiovascular system, and nervous system. The risk of these complications increases with comorbidities such as diabetes, hypertension, cancer, heart disease, and pulmonary disease (Lv, et al., 2021). Moreover, there was a positive correlation between the number of co-existing symptoms and disease progression in the patients (Lv, et al., 2021). Accordingly, abnormal laboratory findings and radiological findings (X-ray & CT) were regarded as risk factors for death due to COVID-19 (Ooi, et al., 2021).

There is an association between mistakes in clinical management protocols such as drugs, mechanical ventilation, and mortality due to COVID-19 (WHO, 2020). Consequently, the authors observed a trend toward a higher mortality rate among cases that had multidrug-resistant bacterial infection (Nori et al., 2021).

The study will highlight the dependent variables of death related to covid 19 and the independent variables related to different risk factors that lead to death, which are affected by the clinical characteristics of patients who died, in addition to tests and clinical management. So, the conceptual model is built upon the above theoretical models as follows:

- Risk factors and Clinical Characteristics:
  1- Demographic characteristics: Age, Gender, Pregnancy, Blood Group, Residency
  2- Lifestyle: Smoking
  3- Clinical history
     a. Signs and Symptoms
     b. Comorbidities
     c. Survival and hospital days

d. Complications
e. Other infectious diseases

4- Treatment and Clinical management
   a. Respiratory support: Invasive O2 \ Non-invasive O2
   b. Drugs: Corticosteroids, Interleukin-6 blockers, Anticoagulants, Antivirals, Antibiotics
   c. Supplements

- Indicators:

5- Investigations: Laboratory results, X-Ray, and CT results

The presence of some factors, the clinical characteristics of the patients at the time of diagnosis or admission, and abnormal lab values may carry a high probability of death in COVID-19 patients.

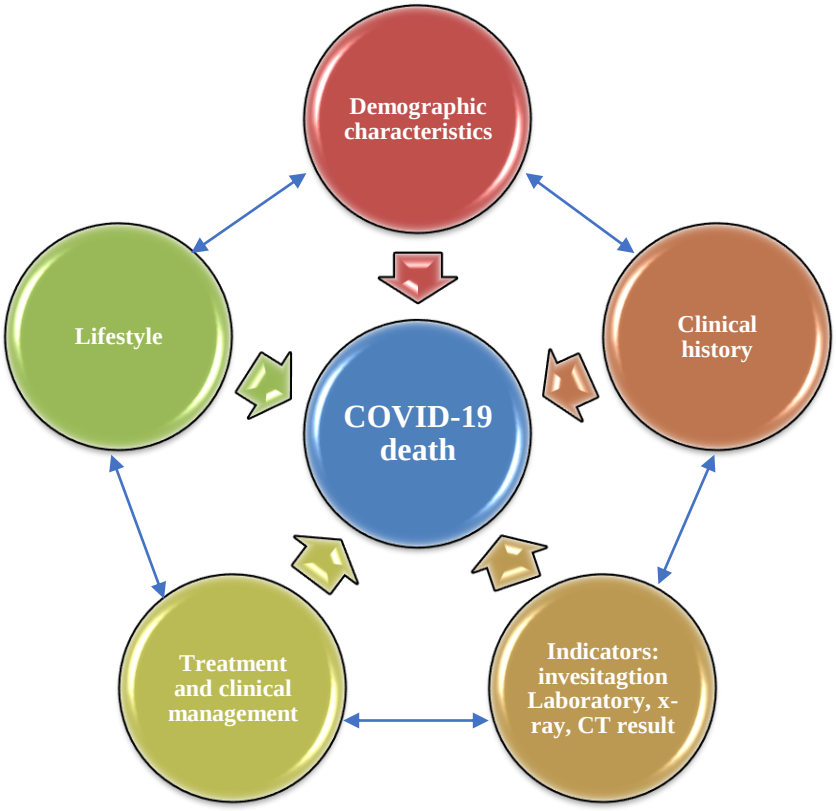

Figure 5: Study conceptual frame work

2.2. Definition of variable

The variables that used in the study are defined as follow:

Table 2.1: Definition of variables

Variables	Definition
COVID-19	The presence of documented positive PCR or rapid test by M.O.H.
Older patients	Patients who are above 60 years according to UN and PCBS.
Co-Infection	The presence of any other communicable disease with covid19 infection.
Signs and symptoms	Presence the evidence of disease such as; fever, fatigue, myalgia, cough, shortness of breath, chest discomfort, sore throat, rash, headache, seizure, abdominal pain, diarrhea, constipation, nausea, vomiting, sweating, neurological abnormalities, joint pain, chills.
Comorbidity	The presence of disease simultaneously with the presence of covid 19 infection such as; diabetes, hypertension, ischemic heart disease, heart failure, cerebrovascular accident (CVA), valvular heart disease, cancer, respiratory disease, obesity (BMI>40), kidney disease, hypothyroidism or any other disease.
Complication	Any medical conditions that developed as a consequence of covid 19 disease itself or the treatment regimen such as; cardiogenic shock, sepsis, septic shock, hepatic dysfunction, hyper coagulopathy status, heart failure, arrhythmia, myocardial infarction, pneumonia, acute kidney injury, cerebrovascular accident (CVA).
Survival days	The days' number between the diagnosis (first positive PCR for last COVID-19 infection) and death.
Ct scan	A computed tomographic imaging study used to investigate covid 19 patients, it is considered to be positive if there is a documented report of findings that are related or could be related as a direct effect or as a complication of covid 19 disease.
Drugs	Authorized and registered medication by M.O.H in Palestine that is recommended in the treatment of hospitalized covid 19 patients.
Supplement	Vitamins and minerals which indicated to support the general condition of covid 19 patients.

Invasive respiratory support	The delivery of oxygen to the patient by insertion of the endotracheal tube and attaching it to a machine called a ventilator.
Noninvasive respiratory support	The delivery of oxygen to the patient by face mask or nasal cannula include continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BiPAP).

The following table defines the ranges of laboratory results in the study.

Table 2.2: Definition of laboratory results ranges

Test	Ranges	Reference
Hemoglobin	Normal range: Male: 12-15 g/dL, Female: 13-17 g/dL, Mild anemia: 11-11.9 g/dL for f, 11-12.9 g/dL for m	(WHO, 2011)
White blood cells	Normal range: 4-11 x 10^9/L, Leukocytosis: >11 x 10^9/L, Leukopenia: <4 x 10^9/L	(Riley, et al., 2015)
Platelets count	Normal: 150-400 K/uL, Thrombocytopenia: <150 K/uL, Thrombocytosis: >400 K/uL	(Farinde., 2019), (Vitiritti., 2010), (Jinna, et al., 2022)
Ferritin	Normal range: M: 15-200 ng/mL, F: 15-150 ng/mL, Iron deficiency: <15, Iron overload: >180	(WHO, 2020)
CRP	Normal range: < 5 mg/L or <10 mg/L	(Farinde., 2019)
D-Dimer	Normal range: < 500 ng/mL	(Farinde., 2019)
Creatinine	Normal range: 0.8-1.3 mg/dL	(Farinde., 2019)
LDH	Normal range: < 180 U/L	(Farhana, et al., 2022)

CK	Normal range: 25-200 U/L	(Farinde., 2019)
Troponin	Normal range: 0.04 ng/mL	(Farinde., 2019)
Blood Ph	Normal range: 7.35-7.45, Acidosis: < 7.35, Alkalosis: > 7.45	(Hopkins, et al., 2022)
Sodium	Normal range: 135-145 mmol/l, Hypernatremia: >145 mmol/l, Hyponatremia: < 135 mmol/l	(Sonani, et al., 2022), (Rondon, et al., 2022)
Potassium	Normal range: 3.5-5.5 mmol/l, Hyperkalemia: >5.5 mmol/l, Hypokalemia: <3.5 mmol/l	(Simon, et al., 2022), (Castro, et al., 2022)

2.3. Literature review

2.3.1. Age

Preliminary data from Chinese studies indicated that COVID-19 was more lethal in the elderly than younger people (Wu, et al., 2020), and its severity was rare in children (Dong, et al., 2020). So, studies showed that older age was one of the most important independent risk factors for death (Wu, et al., 2020) as in SARS and Middle East respiratory syndrome (Choi, et al., 2003).

The median age of Italian patients was 61 years which was similar to that reported in a case series from New York city (63 years) (Richardson, et al., 2020) as opposite the Chinese cases that was 47 years according to hospitals data, this difference may represent the demographic differences between Italy and China (Guan, et al., 2020).

On the one hand, elderly patients have weak immune functions, limited organ function, more comorbidities before infection and more complications after infection (Sheng, et al., 2021). On the other hand, previous studies in macaques inoculated with SARS-CoV found that older macaques

had stronger host innate responses to virus infection than younger adults, along with the excessive differential expression of genes related with inflammation, while type I interferon beta expression was reduced" (Smits, et al., 2010).

The age-dependent defects in B-cells and T-cells function and the increasing production of type 2 cytokines may contribute in decreasing the control of viral replication and led to prolonged pro-inflammatory responses that could lead to worse outcome. (Opal, et al., 2005).

These may be the reasons for the high proportion of deaths in elderly COVID-19 patients (Sheng, et al., 2021). So, it wasn't complicated to understand that old age was one of the risk factors for death (Lv, et al., 2021).

An interesting observation from prospective systematic postmortem surveillance study in Lusaka, Zambia that deaths from COVID-19 were equal across the age spectrum, not among older people only. Most deaths occurred among 20-59 years, and 10% of COVID-19 deaths were in children (Mwananyanda, et al., 2021). According to data from Nigeria, the age category that most influenced by COVID-19, since June 2020 were 21-50 years with an infection apex among 31-40 years (NCDC).

These results are different from that described in the United States, the European Union, (Giacomelli, et al., 2020), and China that recorded 87% of cases among age 30-79 years old with a median age of 48-58 years (Abd El-Aziz, et al., 2020). So, the differences in death age also depended on common distributions and population age structures in countries (Giacomelli, et al., 2020).

In the United Kingdom, United States of America, Germany, Italy, France, Spain and South Korea, deaths from COVID-19 among children were rare until February, 2021, at 0.17 per 100,000 population, include 0.48% of the estimated total mortality due to all causes in a normal year (Bhopal, et al., 2021). However, the additional deaths occurred clearly among children and young people through periods of highly community transmission (Bhopal, et al., 2021).

The evidence indicates that most of children have still spared the worst outcome of the COVID-19 (Olabi, et al., 2021). But interestingly that among younger children who affected by COVID-19, gastrointestinal rather than respiratory complaints predominated (Mansourian, et al., 2021).

Among the younger children, gastrointestinal rather than respiratory complaints predominated, which may be a factor explaining why only one had been tested for COVID-19 before death (Mansourian, et al., 2021). The preponderance of gastrointestinal symptoms among children with COVID-19 has been described previously (Mansourian, et al., 2021), they could be a part of the multisystem inflammatory disorder that has identified as a rare complication of COVID-19 among children (Chiappini, et al., 2020).

2.3.2. Gender

Many studies found that male more susceptible to worse outcome due to COVID-19, and Europe data shows that male-to-female death ratio of 2.1 and increases to 3.9 in cases aged 50–65 years (ECDC). Also, a retrospective cohort study from U.S hospitals found that males were independently associated with 30% higher mortality risk for Covid-19 (Goodman, et al., 2021). Furthermore, a study concluded that the gender-based immunological differences contribute to differences at susceptibility to infections (Klein, et al., 2016).

2.3.3. Pregnancy

Physiological and immunologic changes through pregnancy increase the concern for outcome from viral infection similar to that from MERS-CoV and SARS-CoV-1 (Overton, et al., 2022). Consequently, many studies have estimated COVID-19 risk during pregnancy.

Meta analysis found that pregnant women who infected by COVID-19 have a significantly higher probability of need the ICU and get ventilation than non-pregnant women who infected by COVID-19, but the pregnancy wasn't correlated with a significant increase in mortality (Wang, et al., 2022). In the same line, after analyzing 8207 cases of COVID-19, (CDC) found that pregnant women have higher risk of ICU admission and mechanical ventilation compared to non-pregnant women but have not high risk of mortality (Nakamura-Pereira, et al., 2020). Another study found that severe COVID-19 was strongly associated with preeclampsia and gestational diabetes (Wei, et al., 2021).

Conversely, retrospective cohort study about mortality among pregnant women in Mexico found that pregnant who got COVID-19 don't have higher risk for complications or death compared with

non-pregnant but the risk will increase by presence of chronic diseases like diabetes at childbearing age and not specifically in pregnant (Ríos-Silva, et al., 2020).

2.3.4. Blood Groups

Based on genetic similarity between SARS-CoV and SARS-CoV2, many studies tried to find association between COVID-19 and ABO blood groups (Bhattacharjee, et al., 2022). In addition to that, the SARS-CoV experience showed a link with ABO blood groups via blocking the adhesion of SARS-CoV S-protein to ACE2 expressing cell lines by anti-A antibodies (Bhattacharjee, et al., 2022).

A genome wide association study of severe COVID-19 cases showed that cases with blood group A had a higher risk for severity while cases with blood group O had a protective effect (Ellinghaus, et al., 2020). That is supported by other study that found that O group would be correlated to low risk of COVID-19 infection (OR 0.88) but would not affect the disease prognosis while A group would be a risk factor for COVID-19 infection (OR 1.08) and death (OR 1.13), whereas B group would not alter the risk of COVID-19 infection but would have a lower risk of death (OR 0.88) (Gutiérrez-Valencia, et al., 2022).

In contrast, a meta-analysis study negated the possible significant correlation between the lack of anti-A antibodies and bad COVID-19 outcomes (Bhattacharjee, et al., 2022). So, the discrepancy in the results of the studies warrants more research.

2.3.5. Smoking

Smoking was suggested to decrease the risk of infection but increase the risk of severe or fatal COVID-19 post infection (Simons, et al., 2020). In a study, smoking on enrolment was positively associated with risk of COVID-19 death. (Elliott, et al., 2021).

Another study found that 40% of deaths by COVID-19 were smokers, and indicated that smoking was related with a higher risk for COVID-19 severity including mechanical ventilation or death (Poudel, et al., 2022). While a study from Japan found that COVID-19 severity was not associated with smoking but with the comorbidities which were caused by smoking (Matsushita, et al., 2021).

However, the studies found that increasing of ACE-2 expression which is upregulated in lung tissue significantly associated with smoking history (Smith, et al., 2020), that explains the increasing of SARS-CoV-2 loads which led to increase the risk of sever diseases and death (Reddy, et al., 2021).

2.3.6. Survival and hospital days

A study showed that mortality was more notable and statistically significant after Day 7 from admission (Bordon, et al., 2021). In addition to that, in a cross-section study of hospitalized COVID-19 Patients in Saudi Arabia, the median duration of deaths stay at the hospital was 6.0 days (IQR: 300– 10:00) and the duration of stay in the hospital ranged from one day to 55 days (Alwafi, et al., 2021)

However, a study included 4806 cases with COVID-19 found that median (IQR) of days from symptom to discharge or death equal 23.00 (16.00, 31.00) (Liu, et al., 2022). where another study showed that mean of hospital days for critical cases was 14.5 (Kelesoglu, et al., 2021). Also, (Wang, et al., 2020) showed that the mean of survival days (from onset of disease to death) was 17 days.

2.3.7. Oxygen requirement

COVID-19 led to an increase in patients' number who need of mechanical ventilation that is regarded as a risk of ventilator-associated pneumonia (Garcia, et al., 2020). Invasive ventilation was even related to worse prognosis, corresponding to previous studies (Singer, et al., 2020).

According to (Bordon, et al., 2021) study, more than 41.9% of patients admitted with COVID-19 pneumonia became in critical case, and more than 52% of them developed acute respiratory distress syndrome. Among the 25% of patients who were weaned off invasive mechanical ventilation, those with severe acute respiratory distress syndrome need approximately 2 weeks on invasive mechanical ventilation, compared to about 1 week for patients with non-severe acute respiratory distress syndrome (Bordon, et al., 2021).

A retrospective observational study from India found that cases who intubated within 48 hours of ICU admission (early group) had a mortality of 60% while cases who intubated after 48 hours of

ICU admission (delayed group) had a mortality of 77.7% with statistically significant (p = 0.02), and the median time for death after intubation was 6 days (Zirpe, et al., 2021).

Among 469 cases, 179 (38%) died, 13 (6.4 %) of them didn't require ventilation while 62 (40.8%) required non-invasive ventilation, and 104 (92.0%) required invasive ventilation (Hua, et al., 2020). Another study showed an unusually high incidence of ventilator associated pneumonia in severe cases mechanically ventilated for COVID-19 (Blonz, et al., 2021).

(Luo, et al., 2020) showed that approximately half of critical cases with Covid-19 needed intubation and the time of intubation initiation was associated with high risk of death due to Covid-19. Therefore, the findings of (Rehman, et al., 2022) study indicated that intubating patients very early may be risky. In contrast, (Riera, et al., 2023) found that delayed intubation has been associated with a higher risk of COVID-19 mortality.

In (Singer, et al., 2020) study, the median time of suppling mechanical ventilation was 4.7 days (IQR 2.6 to 8.5 days) for patients who died and 7.1 days (IQR 3.4 to 9.8) for survivors. Also, (Mohammadi, et al., 2021) study concluded that the cases who received non-invasive O2 had lower mortality than cases who were intubated. Furthermore, (Ogbuka, et al., 2022) study showed that the mean age of intubated COVID-19 patients who underwent CPR was 54 years.

2.3.8. Sign and Symptoms

In a study of clinical characteristics, imaging and laboratory findings and outcomes for 2,054 hospitalized COVID-19 patients in 25 Brazilian hospitals, the fever, cough, headaches, shortness of breath, ageusia, anosmia, rhinorrhea, sore throat, myalgia, nausea, vomiting, and diarrhea neurological abnormalities dyspnea at admission were more common among COVID-19 cases (Marcolino, et al., 2021).

A retrospective cohort study about clinical characteristics of 409 COVID-19 patients found that the main symptoms were fever (95.6%), cough (74.3%), sputum (18.1%), tiredness (21.5%), diarrhea (7.8%) and body aches (15.6%) (Lv, et al., 2021).

In addition, the study found a positive correlation between number of co-existing symptoms and disease progression in patients (Lv, et al., 2021). So, many symptoms' kinds means that the load

of virus in patients was large that led to seriously affected multiple body systems, not only respiratory system (Lv, et al., 2021).

Among 430 COVID-19 deaths, the signs and symptoms were arthralgia (0.7%), Headache (9.8%), Diarrhea (8.9%), Dyspnea (69%), Sore throat (7.1%), Fever (50,3%), Neurological manifestations (3.6%), Myalgia (15.7%), Nausea/vomiting (12.9%), Skin rash (0%), Productive cough (13.9%), Dry cough (41.7%) (Marcolino, et al., 2021). Moreover, other study of 660 patients with COVID-19, 18% was died, 30% of deaths had abdominal pain, 4.2% had chills, 0% had seizures (Alizadehsani, et al., 2022).

Regard to effects of age and gender on developing the signs and symptoms, (Penfold, et al., 2022) study found that that increasing age among covid 19 cases correlated with lower temperature (Raimondi, et al., 2021). Furthermore, (Penfold, et al., 2022) study showed that females were significantly more prone to gastrointestinal symptoms such as diarrhea, nausea and vomiting.

2.3.9. Comorbidities

Many previous studies showed that patients with comorbidities have a higher risk for death due to COVID-19 (Marcolino, et al., 2021). Among these comorbidities, Diabetes mellitus, cardiovascular diseases, obesity, respiratory diseases (Marcolino, et al., 2021), chronic kidney disease (He, et al., 2020) and cancer (Zhang, et al., 2021) while the hypothyroidism was not associated with increased risk of death due to COVID-19 (van Gerwen, et al., 2020). Furthermore, (Henkens, et al., 2022) showed that that all comorbidities were more common in the elderly.

Patients with diabetes have high morbidity and mortality to infectious diseases. It may be due to chronic immune system imbalances, excess nutrition caused by obesity or metabolic syndrome. On the other hand, some viruses were diabetogenic themselves (Jaeckel, et al., 2002). Interestingly, a study about SARS showed that even non-severe cases who had not taken glucocorticoid had high fasting blood glucose levels. (Yang, et al., 2006).

According to meta-analysis that examined 3019 patients with cancer and COVID-19, with a broad geographical distribution. the patients with cancer have high risk of severe illness and fatality due to COVID-19 and that may be accentuated by age, sex, and comorbidities (Zhang, et al., 2021).

These comorbidities are featured by low-grade inflammation and high immune senescence (Nadim, et al., 2020). Recent studies have found that a renin-angiotensin system imbalance due to COVID-19 can increase the inflammatory state and lead to more serious clinical course of the disease (Lanza, et al., 2020). As MERS-CoV (Badawi, et al., 2016) and SARS-CoV-1(Kuba, et al., 2005), angiotensin converting enzyme 2 (ACE2) was the gateway to SARS-CoV-2 (Lv, et al., 2021). The association between ACE2 expression and Angio cardiopathy was confirmed in previous studies (Li, et al., 2017). This partly showed why hypertension and heart disease could affect COVID-19 progression (Lv, et al., 2021).

Many previous studies showed that patients with comorbidities have a higher risk for death due to COVID-19 (Marcolino, et al., 2021). A cohort study in 25 Brazilian hospitals found that 439 COVID-19 deaths were having hypertension (70.6%), coronary artery disease (8.4%), heart failure (12.3%), atrial fibrillation/flutter (5.2%), stroke (6.4%), rheumatic valve disease (0%), respiratory diseases (17.5%), diabetes mellitus (39.4%), obesity (15.3%), chronic kidney disease (10.7%), cancer (8.9%) (Marcolino, et al., 2021). Moreover, among analysis of 1000 COVID-19 deaths in India, 96% were having comorbidities such as diabetes (66%), hypertension (54%), hypothyroidism (4%), coronary artery disease (18%) and chronic kidney disease (15%) (Koya, et al., 2021). In other study, among 430 COVID-19 deaths, kidney disease (51.1%), lung diseases (17.9%), cancer (25%), diabetes (16.9%), hypertension (17.4%), (Alizadehsani, et al., 2022).

2.3.10. Complications

Many studies showed that COVID-19 patients with complications such as shock, hepatic dysfunction, acute respiratory distress syndrome, acute kidney failure, and myocardial injury (Chen, et al., 2021) and comorbidities such as hypertension, diabetes, heart disease, pulmonary disease were difficult to treat, and their illness more likely to be worse which led to death. (Lv, et al., 2021).

Among 3011 patients with COVID-19, cardiac complications found in 349 (11.6%) patients such as atrial fibrillation (n=142, 4.7%), heart failure (n=55,1.8%), ventricular arrhythmia (n=14, 0.5%) and acute coronary syndrome (n=15, 0.5%) (Linschoten, et al., 2020). Moreover, literature showed that myocardial infraction may occur in 7–17% of hospitalized cases and more than 20% of ICU cases with COVID-19 (Avila, et al., 2021). Furthermore, in a study of 108 COVID-19 cases, acute

cardiac injury was common of cardiovascular complication in 28 (25.9%) cases followed by heart failure, cardiogenic shock, and acute cardiogenic shock in 4 (3.7%) cases each (Kunal, et al., 2020).

Among 219 cases of COVID-19, 10 (4.6%) developed stroke (Li, et al., 2020), while in review of 181 studies about COVID-19 complications, 14.13% of cases developed liver injury (Xie, et al., 2022). While in other study, 191 patients with COVID-19 developed complications such as sepsis (59%), respiratory failure (54%), ARDS (31%), heart failure (23%), septic shock (20%), coagulopathy (19%), acute cardiac injury (17%), acute kidney injury (15%), secondary infection (15%), hypoproteinemia (12%), acidosis (9%). Among those cases, 54 died and had sepsis (100%), respiratory failure (98%), ARDS (93%), heart failure (52%), septic shock (70%), coagulopathy (50%), acute cardiac injury (59%), acute kidney injury (50%), secondary infection (50%), hypoproteinemia (37%), acidosis (30%) (Zhou, et al., 2020).

Therefore, there is a suspicion that activation of renin-angiotensin (RAS) in hypertension and heart disease patients due to COVID-19 leaded to exacerbated injury for lung (Lv, et al., 2021), while cardiac complications including heart failure, arrhythmia, or myocardial infarction are common in patients with pneumonia (Marrie, et al., 2007). The factors that contribute to get cardiac disorders after pneumonia are old age, pre-existing cardiovascular illness and increased pneumonia severity at presentation (Corrales-Medina, et al., 2013). That is supported by studies that found that coronary heart disease is associated with acute cardiac illnesses and the serious outcomes in influenza and the rest of respiratory viral infections (Blackburn, et al., 2018).

On the one hand, contributory mechanisms contain responses of systemic pro-inflammatory cytokine that are regarded as mediators of atherosclerosis directly lead to rupture of plaque rupture through local inflammation, hemodynamic changes, induction of procoagulant factors which predispose to ischemia and thrombosis (Corrales-Medina, et al., 2012). On the other hand, the receptor for SARS-CoV-2, angiotensin converting enzyme 2 (Gallagher, et al., 2008) is expressed on vascular endothelial cells and myocytes (Torres, et al., 2015). So, there is a potential of direct cardiac involvement by SARS-CoV-2 (Xu, et al., 2020). However, (Dherange, et al., 2020) concluded that arrhythmia may not occur only by viral effect that affect cardiac system by hypoxia, inflammatory stress or infection-related myocarditis but also by drug interactions and systemic illness.

Although infections of bacteria are usually regarded as a cause of sepsis, infection of viruses can also lead to sepsis syndrome (Zhou, et al., 2020). Previously, sepsis was occurred in approximately 40% of adults with community acquired pneumonia due to viral infection (Zhou, et al., 2020). This nearly consistent with a result of study that found that over half of COVID-19 patients developed sepsis, who have not bacterial pathogens on admission. So, sepsis was a common complication that might be directly caused by COVID-19 (Zhou, et al., 2020). Moreover, (Chen, et al., 2022) showed that the onset of shock and time of death were very closely correlated chronologically, and many cases appear to have septic shock signs shortly before death.

Other study indicated to the correlation between higher creatine kinase levels at admission and the risk of death (Giacomelli, et al., 2020). So, acute kidney failure was prevalent in approximately third of the cases and in above 68% of cases who died (Nadim, et al., 2020). There are some possibilities for the impact of Covid-19 on the kidneys, including, the virus may target the cells of kidneys, low levels of oxygen may lead to malfunction of kidney, cytokine storms may damage the kidney tissue, and the small clots in the bloodstream may close the blood vessels in the kidney (Sperati, 2022).

2.3.11. Radiology

Radiological severity of lung involvement with COVID-19 pneumonia was prognostic factor determined to be correlated with mortality (Cecchini, et al., 2020). CXR scans are accurate in diagnosing of COVID-19 pneumonia while chest CT scans have a higher sensitivity in detecting of lung involvement at early stage of the disease (Cecchini, et al., 2020).

In many studies, bilateral lung involvements were predominant in cases with COVID-19 and abnormal chest CT images, mainly manifested as subpleural lesions and multiple ground-glass opacities (Zhang, et al., 2021). One of these studies analyzed 54 COVID-19 deaths and found Consolidation (74%), Ground-glass opacity (81%), Bilateral pulmonary infiltration 45 (83%) (Zhou, et al., 2020). Another study showed that 48 COVID-19 deaths had monoliteral consolidation (50%), bilateral consolidation (29.2%), pleural effusion (12.5%) (Giacomelli, et al., 2020). Moreover, CT features of 42 cases in a study showed consolidation (55%), pleural effusion (12%) (Xiong, et al., 2020).

2.3.12. Laboratory results

Laboratory results are considered an indicator of disease levels and outcome. A study about COVID-19 found that 23 (5.4%) participants were anemic, 69 (16.1%) had leukocytosis and 61 (14.2%) had leukopenia (Leulseged, et al., 2021). So, among cases with COVID-19, leukocytosis, leukopenia, decreased platelet count and anemia are found to be related with disease severity and worse outcome in cases (Leulseged, et al., 2021). However, the lower white blood cells increase the potential to develop severe infection and rises the effect of an existing pathogen which is lead to the progress of disease stage at any infection. Likewise, despite the high white cells is an indication of an immune system responses, it also indicates to that the body is under great stress from the pathogen (Leulseged, et al., 2021).

According to studies, the decrease of platelet count in deaths could be related to sepsis or might be attributed to consumption that may be linked to widespread thrombosis or disseminated intravascular coagulation (DIC), or because the inhibition of development and maturation of megakaryocytes in bone marrow by the inflammatory response (Sheng, et al., 2021). On the other hand, the thrombocytosis is attributed to the increased number of released cytokine and disease severity (Kenya, et al., 2022).

In other study, COVID-19 deaths had higher levels of CRP (Girija, et al., 2020). Furthermore, (Mukhi, et al., 2022) showed that the inflammatory response leads to iron dysmetabolism, resulting in increased levels of hepcidin, decreased iron utilization, increased ferritin level, and anemia.

A study found that lactate dehydrogenase (LDH) and creatine kinase (CK) are an independent predictor of heart failure until death in COVID-19 critical cases, both were significantly high at admission then increased rapidly (Chen, et al., 2021). Furthermore, (Liu, et al., 2022) showed that the double elevated CK/LDH increases the risk of death.

An analysis showed that severe cases had higher levels of d-dimer than moderate cases. Furthermore, deaths had higher level of d-dimer than survival cases. The interpretation of these difference is that fibrinolysis was inhibited in serious COVID-19 cases (Sheng, et al., 2021) and formation of extensive thrombus was found at autopsy in COVID-19 deaths (Barnes, et al., 2029).

Moreover, (Zhou, et al., 2020) study found that more than half COVID-19 deaths had elevated high-sensitivity cardiac troponin.

In addition, elevated creatinine increases the mortality risk specifically for elderly (Bertsimas, et al., 2020) by acute kidney injury which is common among COVID-19 cases due to renal hypoperfusion, cytokine storm and multi-organ failure (Oto, et al., 2021).

According to blood PH, a study showed that high incidence of metabolic alkalosis among critically COVID-19 cases and it is related with high mortality (Jiang, et al., 2022). In contrast, another study for 54 COVID-19 deaths recorded that 16 (30%) had acidosis (Zhou, et al., 2020).

Moreover, a study found that 59 (73.8%) sever cases with COVID-19 had an abnormal level of sodium, and 79 (54.9%) sever cases with COVID-19 had an abnormal level of potassium (Leulseged, et al., 2021). Moreover, 127 (29.6%) had hyperkalemia and 63 (14.7%) had hyponatremia (Leulseged, et al., 2021) which might be considered a prognosis factor among cases with COVID-19 (Gheorghe, et al., 2021). In another study, high incidence of hypokalemia was found among hospitalized cases with pneumonia due to COVID-19, with percentage of 37% and median of 2,9 (2,7-3,3). So, hypokalemia was considered positively related to higher levels of lung tissue damage and acute phase proteins (Tsiberkin, et al., 2020).

However, the electrolyte which can result from the losing of fluid from the body via various routes, medications effect, renal damage was strong associated with severe disease due to COVID-19 (Leulseged, et al., 2021).

2.3.13. Management

Among prospective meta-analysis of seven randomized clinical trials which included 1703 critical cases with COVID-19 recruited from countries on five continents, corticosteroids administration was associated with low all-cause mortality in 28 days after randomization (WHO, 2020). The use of steroids was increased in the second phase in Italy after it has been proven effective in reducing the complications of COVID-19 (Sterne, et al., 2020). The odds ratios for the association between corticosteroids and mortality were similar for hydrocortisone and dexamethasone (WHO, 2020). This association was stronger in patients who did not receive vasoactive medication at randomization than in those who received vasoactive medication at randomization (WHO, 2020) .

In a study, the Dexamethasone was used for 7.7% of 81 Covid 19 deaths (Chen, et al., 2021), while in another study, Dexamethasone was used for 43.2% of 431 COVID-19 deaths (Marcolino, et al., 2021).

Many patients were treated with antivirals, which researches has shown to be less effective than hoped (WHO, 2020). One of these, study indicated that using of antiviral treatment for 54 COVID-19 deaths was 22% (Zhou, et al., 2020).

Other drugs were used to treat COVID-19 as anticoagulant that was given to 88.2% of 431 COVID-19 deaths in in 25 hospitals in Brazil (Marcolino, et al., 2021), and Tocilizumab that contributed to decrease mortality in cases with severe COVID-19 according to studies (Berardicurti, et al., 2020).

Because of heavy burden of the pandemic on health care systems, there was an increased risk of neglecting the implementation of good practices, and poor monitoring the excessive use of antimicrobials and following the nosocomial infections (WHO, 2020).

In a study, antimicrobials were administered to approximately 90% of the patients (Rawson, et al., 2020). In the same context, A study in a hospital in New York City showed that 71% of patients with COVID-19 antibiotics, while only 4% had a true bacterial coinfection (Nori, et al., 2021).

Another study of 181 Covid 19 deaths showed that antibiotics were used as by 92.3% (Chen, et al., 2021). And many types of antibiotics were used such as Azithromycin which was given to 69.8% of 431 COVID-19 deaths (Marcolino, et al., 2021), and was the most frequently prescribed by 44.3%, followed by levofloxacin (41.8%), and ceftriaxone (16.8%) but the rare frequently prescribed was Meropenem (1%), Vancomycin (3%) (Suranadi, et al., 2022).

Overuse of antimicrobials was prevalent in therapy of COVID-19 patients (Rawson, et al., 2020), That's probably because the resemblance in clinical presentation of bacterial or fungal sepsis and severe COVID-19 (Marcolino, et al., 2021). Additionally, overuse of antibiotics could have contributed to the increase in candidemia, and increase in the resistance of E. cloacae, K. pneumoniae, and P. aeruginosa for several classes of antibiotics, that was found by comparing the results of 2020 with 2019 results in the same institution (Nori, et al., 2021).

The authors observed a trend towards a higher mortality rate among cases who had multidrug-resistant infection (Nori et al., 2021). So, the worrying potential consequence of the pandemic is the increasing of antimicrobial resistance (Mahoney, et al., 2021).

Regard to supplements, a large population-based study observed that cholecalciferol or calcifediol supplements are likely to be beneficial for resist SARS-CoV2 infection, COVID-19 severity and mortality in cases have serum 25-hydroxy vitamin d levels ≥ 30 ng/ml (Oristrell, et al., 2022). Also, because of zinc has several antiviral effects that are realized via generating both innate and acquired (humoral) immune responses, multiple antiviral effects of zinc have been shown in many viral species, including nidoviruses, for which SARS-CoV-2 belongs (Kumar, et al., 2020).

Chapter Three: Methodology

3.1. Study design

Retrospective Cohort Study.

3.2. Study population

COVID-19 deaths in West Bank.

3.3. Sample frame

COVID-19 deaths in the hospitals.

3.4. Study setting

The study was conducted in all hospitals in West Bank which treated COVID-19 patients as follow:

1. **Martyr Abu Al-Hassan Al-Qassim Governmental Hospital**, it built in Yatta, south of Hebron Governorate. it provides services to more than 100,000 citizens through its various departments: emergency, general surgery, gynecology and obstetrics, pediatrics, hemodialysis, outpatient clinics, Radiology, pharmacy, laboratory, and blood bank.
2. **Martyr Thabet Thabet Hospital** is the only governmental hospital in Tulkarm Governorate. It has been operating since the Ottoman era when it was called Al-Jihad Hospital. It provides services to more than 250 thousand citizens through its various departments: emergency, general surgery, intensive care, hemodialysis, internal and cardiac departments, orthopedics, gynecology and obstetrics, children and nursery, the otolaryngology department, in addition to the department of thalassemia, and oncology, physiotherapy, outpatient, laboratory, blood bank, pharmacy, and radiology, including tomography.
3. **The new Jericho Governmental Hospital** is one of the Palestinian governmental hospitals, built in 1998. it is the only one to perform endoscopic sinus surgeries, and it is the only government hospital in which this type of operation is performed, in addition to the use of endoscopes in the removal of the gallbladder and part of the urinary tract surgery, and lithotomy in the ureters. It is accredited as a training center in laparoscopic surgery,

and is also accredited as a safe surgery center. In addition to general hospital with different department.

4. **Alia Governmental Hospital**, it was built in Hebron in 1957 and considered one of the largest health institutions in the south of West Bank, it provides services to more than 800 thousand citizens during 2017 through its various departments: emergency, surgery, and specialized surgeries in the urinary tract. And orthopedics surgery and neuro surgery, (ENT), internal medicine, intensive care and cardiac intensive care, intermediate care, hemodialysis, ophthalmology, pediatric services, gynecology, obstetrics and nursery, hematology, hemophilia and thalassemia, laboratory and blood bank, radiology, outpatient clinics, burn unit, and physiotherapy. Hospital occupancy rate in the same year was about 155%, which is the highest among government hospitals.
5. **Hugo Chavez Hospital** is a government specialized hospital in ophthalmology and ophthalmic surgery, built in the town of Thormasia with funding from the Venezuelan government in 2011, in 2020, the Palestinian Ministry of Health decided to use it temporarily to treat COVID-2019 cases.
6. **Palestine Medical Complex**, the largest Palestinian governmental hospital, was built in Ramallah in 1963, to provides medical services by its departments: emergency, pediatric emergency, outpatient, hemodialysis, general surgery, internal diseases, cardiology, orthopedics, cardio surgeries, kidney transplant, and pediatric cardiology, intensive care, critical care, gynecology and obstetrics, physiotherapy, Radiology, pharmacy.
7. **Al Mutlaa Hospital** or the Augusta Victoria Complex is a church and hospital located on the Mount of Olives in Jerusalem, it was built in 1907. Today, the hospital provides specialized care to Palestinians from all over the West Bank and Gaza Strip in areas such as pediatric, kidney dialysis, oncology, nuclear medicine, radiotherapy and a specialized care unit.
8. **Al-Ahli Hospital** was built in Hebronin1988, and contains all the auxiliary medical departments. Medical facilities and departments are also available and other devices such as the unit for treating electrical heart problems, cerebral catheters, and the only unit licensed in Palestine for nuclear medicine. The hospital includes several departments: ambulance and emergency, outpatient clinics, surgery, obstetrics and gynecology,

newborn, pediatric, internal medicine, intensive care, daily cases, lithotripsy departments, radiology, pharmacy, laboratory, blood bank, and Physiotherapy.

9. **The Arab Istishari Hospital** is a private hospital in the suburb of Al-Rayhan in the city of Ramallah, was built in 2016, and it is the largest private hospital in Palestine, it includes many departments: general surgery, endoscopic surgery, emergency, oral and maxillofacial surgery, molecular genetics laboratory, ENT, head and neck surgery, neurosurgery, bones and joints, anesthesiology, internal medicine, endocrinology and diabetes, urology, interventional radiology, diagnostic radiology, tissue examination and clinical laboratories, cardiothoracic surgery, pediatric cardiology, cardiology, gynecology and obstetrics, vascular surgery hematology, chest diseases for adults and children, outpatient clinics.
10. **Al-Makassed Islamic Charitable Society Hospital** is a charitable hospital and Islamic teaching hospital founded by Makassed Islamic Charitable Society, it is located on Mount of Olives in Jerusalem. The hospital has 250 beds and many departments such as emergency, general surgery, internal medicine, specialized surgeries, genetic diseases, endocrinology, metabolism and rheumatism, radiology, physiotherapy, sterilization, specialized laboratories, pharmacy, etc.
11. **The National Rehabilitation Center** is a governmental center established in 2019 in Bethlehem, with a capacity of 56 beds. It provides free treatment and services as detoxification, medical follow-up, treatment program for opioid addiction, health education and psychological counseling and rehabilitation, in addition to following the cases discharged after rehabilitation.
12. **AL-Watani Hospital** is a government hospital established in 1888 in Nablus, with a capacity of 55 beds. It provides many services to about 2 million citizens in the northern governorates of the West Bank, by its departments such as emergency, internal medicine for men and women, oncology, day care, hematology, intensive care, radiology, outpatient clinics, pharmacy, laboratory catering and housekeeping.
13. **Nablus Military Hospital** is a government hospital established in 2015 in Nablus. It is affiliated with the Palestinian military medical services. It provides services to military and civilian citizens. The hospital has 48 beds. It includes several departments such as emergency, radiology, internal medicine, pediatric, intensive care, and laboratory.

14. **Najah National University Hospital** was built in 2013 in partnership with the Medicine and Health Sciences Faculty at An-Najah National University in Nablus. The hospital has 120 beds and includes many departments such as an intensive care unit, a dialysis department, an emergency room, radiology department. It provides services for complex cases requiring ophthalmic surgery and cardiac care in addition to neurosurgery and pediatric diseases.
15. **Ibn Sina Specialized Hospital** was built in Jenin in 2021, It began operating with a capacity of 41 beds, then kept working gradually to increase the number of beds in order to reach 205 beds. The hospital provides its services through the specialists such as internal medicine and emergency.

3.5. Sampling method

All deaths' files or excel sheets of previously collected data for the years 2020, 2021 were included in the study.

3.6. Inclusion and exclusion criteria

Inclusion: Deaths who had COVID-19 positive tests (Rapid or PCR) and documented death inside the hospital with death certificate include that COVID-19 was a cause of death.

Exclusion: Cases who hadn't documented positive tests of COVID-19 or died outside the hospital or death certificate didn't include that COVID-19 was a cause of death.

3.7. Sample size

All COVID-19 patients who died in the targeted hospitals in West Bank from March 1, 2020 to December 31, 2021 that equal 1001 deaths.

3.8. Study tools

The medical files of deaths were collected to extract and analyze the data of COVID-19 deaths.

3.9. Pilot study

A pilot study was implemented using 5% of the expected sample; to detect of the suitability of the research tool and troubleshoot problems and deficiencies to modify them before collecting the data. This helps for testing the feasibility of combination techniques.

3.10. Data Collection

In every hospital, files content was checked by the researcher to be sure that data is consistent in all targeted hospitals, or if available, an excel sheets of previously collected data from the hospital were used. Accordingly, data collection sheet was prepared. The data was collected from hospitals' files related to COVID-19 patients which included demographic characteristics, clinical history, laboratory results, treatment management. Also, to ensure the privacy and safety of data, the data was collected under supervision of hospital administration.

3.11. Statistical analysis

The data was collected from patient's electronic medical records in hospitals, then manually coded, cleaned and analyzed using the Statistical Package for Social Sciences (SPSS version 26.0). Descriptive statistics were represented to show frequencies and percentages for categorical variables, means, and standard deviation for continuous variables. Chi-square test was used as needed to measure associations between study variables and age and gender. A P-value <0.05 was considered statistically significant. Cox proportional hazard ratio was used to measure the variables associated with the mortality rate and survival of COVID-19 with 95% confidence intervals (95% CI).

3.12. Ethical consideration

In order to launch this research, the approval from Al Quds University-Research Ethical Committee of public health college was taken after submitting the research proposal for discussion. then permission to conduct the study was obtained from the MOH for the government hospitals and from the general manager of each private hospital. Ethical considerations were taken through data collection from the patients' files. Also, the names of the deaths were coded during the analysis through a serial number which was given to each patient without any identities or names. The excel sheet was secure with a password till the end of research or publication, after then it can be provided to the Al-Quds University and MOH if requested then it will be destroyed or can be used for additional research after taking legal permission.

Chapter Four: Study Results

4.1 Introduction

In this chapter, study results will be presented. Study sample characteristics will be shown in a descriptive analysis alongside the laboratory results and the imaging finding. Univariate and multivariate analyses will also be presented in the chapter.

4.2 Descriptive analysis

4.2.1 Sample distribution by hospitals and residency

Our study was composed of 1001 COVID-19 deaths from 15 different private and governmental hospitals all over West Bank as Table 4.1 shows. The highest percentage of deaths in our sample was in Ramallah governmental hospital with (21.0%) of the study sample, followed by Hebron governmental hospital with (17.8%) whereas the lowest percentage deaths was at Al-Askari hospital with (0.8%).

The area of residency showed the same pattern as the largest percentage of the sample was from middle West Bank cities with a percentage of (41.4%) such as Ramallah Governorate (30.1%), followed by the south of the West Bank (34.8%) such as Hebron Governorate (31.9%), then the north of the West Bank (23.9%) such as Nablus (15.0%).

Table 4.1: Sample distribution by hospitals and residency

Variable		Count	Percentage
Hospital name	Ibn Sina Hospital	18	1.8%
	Jericho Gov. Hospital	28	2.8%
	Istishari Arab Hospital	53	5.3%
	AL-Ahli Hospital	106	10.6%
	AL- Askari Hospital	8	0.8%
	Ramallah Gov. Hospital	210	21.0%

	AL-Watani Hospital	106	10.6%
	Palestine National Rehabilitation Center	15	1.5%
	Thabit Thabit Hospital	27	2.7%
	Hebron Gov. Hospital	178	17.8%
	Augusta Victoria Hospital	28	2.8%
	AL-Makassed Hospital	34	3.4%
	Hugo Chavez Hospital	146	14.6%
	Yatta Gov. Hospital	14	1.4%
	AL- Najah Hospital	30	3.0%
Governorate	Jenin	27	2.7%
	Jericho	39	3.9%
	Jerusalem	74	7.4%
	Hebron	320	31.9%
	Ramallah	301	30.1%
	Nablus	150	15.0%
	Tulkarm	49	4.9%
	Salfit	8	0.8%
	Bethlehem	28	2.8%
	Qalqilya	3	0.3%
	Tubas	2	0.2%
Area of residency	Northern West Bank	239	23.9%
	Middle West Bank	414	41.4%
	Southern West Bank	348	34.8%

4.2.2 Sample distribution by demographic characteristics

Table 4.2 shows that males compromise (57.5%) of the study sample compared to females (42.5%). The mean age of deaths was 68.21 years. Starting from 17 years old to 100 years old, and half of the sample was between 61-80 years old, and most of the deaths were above 61 years old. In addition to that, among 59 females in childbearing age, 12 (22.6%) were pregnant, and five of them had comorbidities. Smoking status was only reported for 288 deaths, among them, non-smokers were (59.7%) while smokers were (40.3%). In the same context, the blood group was reported for 247 deaths only and showed that the dominant blood group was A-positive (33.6%) followed by O-positive (31.2%) while uncommon blood group among reported deaths was AB-negative (0.8%), and it's clear that positive blood groups were more than negative.

Table 4.2: Sample distribution by demographic characteristics

Variable		**Count**	**Percentage**
Gender	Male	576	57.5%
	Female	425	42.5%
Age	Mean (SD) Min-Max	68.21 (14.03) 17-100	
Age category	≤40 years old	49	4.9%
	41-60 years old	203	20.3%
	61-80 years old	575	57.4%
	>81 years old	174	17.4%
Pregnancy*	No	429	77.4%
	Yes	12	22.6%
Smoking Status	No	172	59.7%
	Yes	116	40.3%
Blood group	A-Positive	83	33.6%
	A-Negative	12	4.9%

	B-Positive	44	17.8%
	B-Negative	7	2.8%
	O-Positive	77	31.2%
	O-Negative	7	2.8%
	AB-Positive	15	6.1%
	AB-Negative	2	0.8%

*. Pregnancy among 59 women in reproductive age (16-49 years) according to WHO

4.2.3 Sample distribution by survival days and stay duration in the hospital

Table 4.3 shows that the stay duration in the hospital ranged from one day to 53 days with a mean of 12.98 and a standard deviation of 9.09. Moreover, the patients who survived up to 14 days from admission to hospital were twice the patients who died after 14 days from admission.

While the survival days indicated by the number of days between diagnosis (first positive result) and death and ranged from one day to 62 days with a mean of 15.91 and a standard deviation of 10, and the patients who survived up to 14 days from diagnosis were more than the patients who died after 14 days from diagnosis.

Table 4.3: Sample distribution by survival days and stay duration in the hospital

Variable		**Count**	**Percentage**
No. of days between admission and death		Mean (SD) Min-Max	12.98 (9.09) 1-53
Hospital days	≤14* days	663	66.2%
	> 14 days	338	33.8%
No. of days between diagnosis and death		Mean (SD) Min-Max	15.91(10) 1-62
No. of days between diagnosis and death	≤14 days	536	53.5%
	> 14 days	465	46.5%

*. Comparison by 14 days according to mean and previous studies

4.2.4 Sample distribution by oxygen needs

Table 4.4 and Figure 6 show that almost all patients required O2 management (99.1%), most of them received non-invasive O2 (94.6%) while half of them were intubated (56.3%). In addition to that, the initiation of giving the non-invasive O2 was early with a mean of one day from admission while the initiation of giving the invasive O2 was late with a mean of 7 days from admission.

However, the mean of survival days after receiving non-invasive O2 only (12.4) was more than the mean of survival days after intubation (7), and the patients who died on the twelfth day from receiving non-invasive O2 or after were more than the patients who died before the twelfth day. On the other hand, the patients who died on the seventh day from intubation or before were double the patients who died after the seventh day.

Table 4.4: Sample distribution by oxygen needs

Variable		Count	Percentage
Receiving O2 support	No	9	0.9%
	Yes	992	99.1%
Non-Invasive O2	No	54	5.4%
	Yes	947	94.6%
Invasive O2 (Tube)	No	437	43.7%
	Yes	564	56.3%
No. of days between admission and need of non-invasive O2		Mean (SD) Min-Max	1.9 (3.15) 1-48
No. of days between admission and need of invasive O2		Mean (SD) Min-Max	7.8 (7.4) 1-48
No. of days between need non-invasive O2 only and death		Mean (SD) Min-Max	12.4(8.79) 1-52
No. of days between need non-invasive O2 only and death	≤ 12 days	568	59.9%
	>12 days	380	40.1%

No. of days between need invasive and death		Mean (SD) Min-Max	7.3 (7.06) 1-45
No. of days between need invasive and death	≤ 7 days	352	62.6%
	> 7 days	210	37.4%

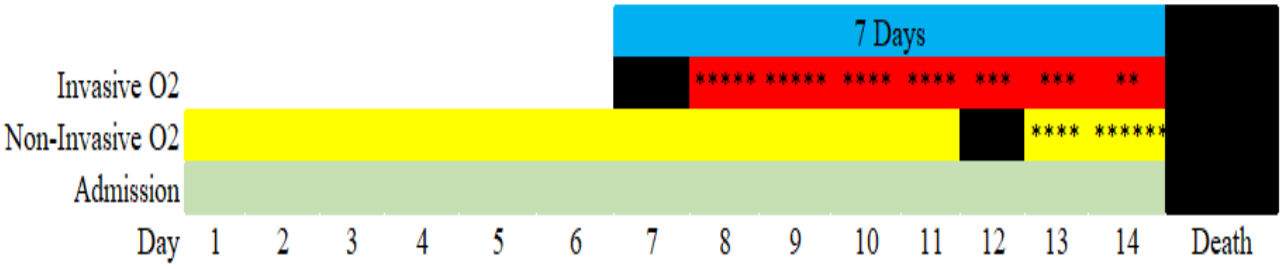

Figure (6): Means of sample distribution by O2 needs. Green color refers to admission to hospital, yellow color refers to patients who received non-invasive O2 only, red color refers to patients who received invasive O2 and black color refer to death occurrence.

4.2.5 Sample distribution by signs and symptoms

Table 4.5 shows the signs and symptoms that were seen among the patients as fatigue (84.4%) was common, and the majority of patients had respiratory symptoms such as shortness of breath (89.6%), chest discomfort (80.5%), and cough (70.2%). In addition to that, more than half of patients developed a fever (65.6%), and abdominal pain, myalgia, headache, sweating, and chills didn't exceed (18%).

Gastrointestinal symptoms were less common but with different variations as the percentage of patients with nausea (11.7%) was close to the percentage of patients with vomiting (9.0%), while the patients with diarrhea (11.2%) were higher than the patients with constipation (3.1%). However, less common symptoms were rash (0.4%), seizure (1.7%), sore throat (3.4%), and neurological abnormalities (3.6%).

Table 4.5: Sample distribution by signs and symptoms

Variable		N	%	Variable		N	%
Fever	No	344	34.4%	**Seizure**	No	984	98.3%
	Yes	657	65.6%		Yes	17	1.7%
Fatigue	No	156	15.6%	**Abdominal pain**	No	929	92.8%
	Yes	845	84.4%		Yes	72	7.2%
Myalgia	No	825	82.4%	**Diarrhea**	No	889	88.8%
	Yes	176	17.6%		Yes	112	11.2%
Cough	No	298	29.8%	**Constipation**	No	970	96.9%
	Yes	703	70.2%		Yes	31	3.1%
Shortness of breath	No	104	10.4%	**Nausea**	No	884	88.3%
	Yes	897	89.6%		Yes	117	11.7%
Chest discomfort	No	195	19.5%	**Vomiting**	No	911	91.0%
	Yes	806	80.5%		Yes	90	9.0%
Sore throat	No	967	96.6%	**Sweating**	No	941	94.0%
	Yes	34	3.4%		Yes	60	6.0%
Rash	No	997	99.6%	**Neurological abnormalities**	No	965	96.4%
	Yes	4	0.4%		Yes	36	3.6%
Headache	No	887	88.6%	**Chills**	No	862	86.1%
	Yes	114	11.4%		Yes	139	13.9%

4.2.6 Sample distribution by comorbidities

Table 4.6 shows that most of the patients (82.9%) had comorbidities, the majority of them had hypertension (62.0%), followed by diabetes (52.0%) and ischemic heart disease (23.2%) while the

lowest patients had valvular heart disease (1.2%), hypothyroidism (3.6%), obesity (7.4%). However, the patients who had heart failure (14.7%) were more than patients who had CVA (10.7%) and cancer (8.2%), while the patients who had respiratory diseases were 7.8% only.

Table 4.6: Sample distribution by comorbidities

Variable		N	%	Variable		N	%
Had comorbidities?	No	171	17.1%	**Valvular heart disease**	No	989	98.8%
	Yes	830	82.9%		Yes	12	1.2%
Diabetes	No	480	48.0%	**Cancer**	No	919	91.8%
	Yes	521	52.0%		Yes	82	8.2%
Hypertension	No	380	38.0%	**Respiratory diseases**	No	923	92.2%
	Yes	621	62.0%		Yes	78	7.8%
Ischemic heart disease	No	769	76.8%	**Obesity (BMI>40)**	No	927	92.6%
	Yes	232	23.2%		Yes	74	7.4%
Heart failure	No	854	85.3%	**kidney diseases**	No	808	80.7%
	Yes	147	14.7%		Yes	193	19.3%
Cerebrovascular accident (CVA)	No	894	89.3%	**Hypothyroidism**	No	965	96.4%
	Yes	107	10.7%		Yes	36	3.6%

4.2.7 Sample distribution by complications

Table 4.7 shows the complications that reported among our study sample as pneumonia was dominant (88.9%) while half of patients (51.7%) developed acute kidney injury. In addition to that, sepsis was reported in 39.7% of patients which was similar approximately to septic shock (33.7%), and cardiac diseases were also reported as heart failure (10.0%), arrhythmia (14.0%) and myocardial infarction (13.4%). In contrast, along with CVA (3.2%), cardiogenic shock (5.7%) and hyper Coagulopathy status (3.8%) occurred with the lowest percentage of patients.

Table 4.7: Sample distribution by complications

Variable		Count	Percentage
Cardiogenic shock	No	944	94.3%
	Yes	57	5.7%
Sepsis	No	604	60.3%
	Yes	397	39.7%
Septic shock	No	664	66.3%
	Yes	337	33.7%
Hepatic dysfunction	No	918	91.7%
	Yes	83	8.3%
Hyper Coagulopathy status	No	963	96.2%
	Yes	38	3.8%
Heart failure	No	901	90.0%
	Yes	100	10.0%
Arrhythmia	No	861	86.0%
	Yes	140	14.0%
Myocardial infarction (MI)	No	867	86.6%
	Yes	134	13.4%
Pneumonia	No	111	11.1%
	Yes	890	88.9%
Acute kidney injury (AKI)	No	483	48.3%
	Yes	518	51.7%
Cerebrovascular accident (CVA)	No	969	96.8%
	Yes	32	3.2%

4.2.8 Sample distribution by imaging findings

Table 4.8 shows the imaging finding that reported for only 504 deaths from total with a chest x-ray investigation, while high-resolution CT was reported only in 27% of documented deaths and Angio CT was reported only in 1.8%.

In Figure 4.7, It's clear that more than half of these patients had pulmonary infiltrates (60.2%), and the patients with bilateral pneumonia (12.9%) were more than patients with unilateral pneumonia (4.4%), and the patients with ground-glass lung opacities (15.1%) were more than patients with pleural effusion (6.3%) while the percentage of patients with ARDS picture and lobar consolidation were low (5.0%), (4.6%).

Table 4.8: Sample distribution by imaging findings

		Count	Percentage
Chest x-ray with report	No	0	0.0%
	Yes	504	100.0%
High-resolution CT with report	No	368	73.0%
	Yes	136	27.0%
Angio CT with report	No	494	98.2%
	Yes	9	1.8%

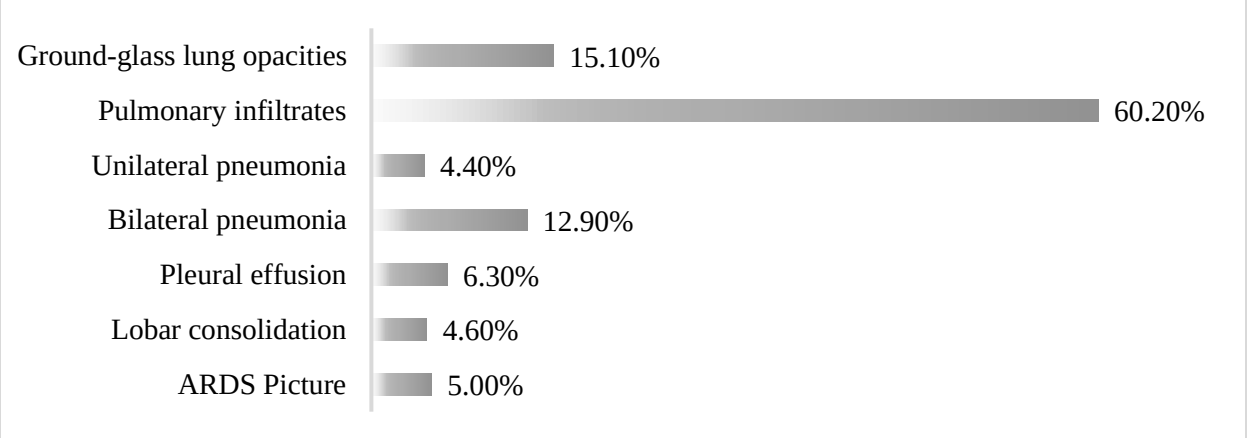

Figure (7): Sample distribution by imaging findings

4.2.9 Sample distribution by laboratory findings

The following table (4.9) presents the results of available laboratory tests for patients, as were shown by mean and SD at admission and death, in addition to the percentage of patients who had abnormal results with mean and SD for the first day that recorded abnormal results. It is clear a wide range among results and a considerable difference between the mean of results at admission and at death for all following laboratory tests and the mean of means of the first day of abnormal results among all laboratory tests was 4.7.

Regarding the blood components, among 845 patients, 70.1% recorded a low level of hemoglobin at the mean of 10 days from admission. Moreover, among 845 patients, 17.2% recorded a low level of WBC at the mean of 6 days from admission. While 86% recorded a high level of WBC at the mean of 3 days from admission. However, among 854 patients, 54.9% recorded a low level of platelets at the mean of 5 days from admission, while 25.4% recorded a high level of platelets at the mean of 5 days after admission.

Regarding the inflammatory biomarker, among 666 patients, 0.6% recorded a low level of ferritin at the mean of 3 days from admission while 84.5% recorded a high level of ferritin at the mean of 2 days from admission. On the other hand, among 804 patients, 98.8% recorded a high level of CRP at the mean of 1 day from admission.

Moreover, among 711 patients, 94.6% recorded a high level of d-dimer at the mean of 3 days from admission, and among 845 patients, 74.5% recorded a high level of creatinine at the mean of 3 days from admission. In addition to that, among 723 patients, 94% recorded a high level of LDH at the mean of 2 days from admission. As is the case with CK, among 615 patients, 56.4% recorded a high level at the mean of 4 days from admission. However, among 684 patients, 60.9% recorded a high level of troponin at the mean of 4 days from admission.

Regarding the blood PH, among 400 patients, 66.5% recorded a low level of blood PH at the mean of 6 days from admission, while 52.2% recorded a high level of blood PH at the mean of 5 days from admission.

In relation to the electrolytes, among 755 patients, 66.7% recorded a low level of sodium at the mean of 3 days from admission, while 58% recorded a high level of sodium at the mean of 7 days

from admission. On the other hand, among 773 patients, 38% recorded a low level of potassium at the mean of 6 days from admission, while 42.6% recorded a high level of potassium at the mean of 7 days from admission.

Table 4.9: Sample distribution by laboratory findings

Hemoglobin (g/dL)	**Number**	**845**
At admission	Mean (SD)	12.3 (2.8)
At death	Mean (SD)	11.1 (2.3)
<11.5	N (%)	593 (70.1%)
First day of hemoglobin <11.5	Mean (SD)	10.3 (1.09)
WBC (x10^9/L)	**Number**	**845**
At admission	Mean (SD)	10.6 (10.6)
At death	Mean (SD)	16 (11.2)
< 4	N (%)	146 (17.2%)
First day of WBC < 4	Mean (SD)	6.7 (8.7)
> 11	N (%)	727 (86%)
First day of WBC > 11	Mean (SD)	3.4 (3.3)
Platelets count (K/uL)	**Number**	**845**
At admission	Mean (SD)	212.6 (90.6)
At death	Mean (SD)	209.3 (122.8)
< 150	N (%)	464 (54.9%)
First day of Platelets < 150	Mean (SD)	5.1 (5.8)
> 400	N (%)	215 (25.4%)
First day of platelets > 400	Mean (SD)	5.5 (4.7)
Ferritin (ng/mL)	**Number**	**666**

At admission	Mean (SD)	1224.80 (3980.0)
At death	Mean (SD)	2617.11 (11834.8)
<15	N (%)	4 (0.6%)
First day of ferritin < 15	Mean (SD)	3.75 (2.7)
>180	N (%)	563 (84.5%)
First day of ferritin > 180	Mean (SD)	2.36 (3.061)
CRP (mg/L)	**Number**	**804**
At admission	Mean (SD)	131.7 (108.6)
At death	Mean (SD)	136.9 (131.7)
> 6	N (%)	793 (98.8%)
First day of CRP > 6	Mean (SD)	1.65 (1.5)
D-Dimer (ng/mL)	**Number**	**711**
At admission	Mean (SD)	3262.7 (8473.3)
At death	Mean (SD)	5724.7 (10896.9)
> 500	N (%)	673 (94.6%)
First day of d-dimer > 500	Mean (SD)	3 (2.3)
Creatinine (mg/dl)	**Number**	**845**
At admission*	Mean (SD)	1.35 (1.02)
At death	Mean (SD)	2.8 (2.6)
>1.3	N (%)	630 (74.5%)
First day of creatinine > 1.3	Mean (SD)	3.8 (5.2)
LDH (U/L)	**Number**	**723**
At admission	Mean (SD)	518 (335)
At death	Mean (SD)	730.3 (913.5)

> 180	N (%)	680 (94%)
First day of LDH > 180	Mean (SD)	2.4 (2.9)
CK (U/L)	**Number**	**615**
At admission	Mean (SD)	301.4 (691.9)
At death	Mean (SD)	508.2 (1300.8)
> 200	N (%)	347 (56.4%)
First day of CK > 200	Mean (SD)	3.9 (4.8)
Troponin (ng/mL)	**Number**	**684**
At admission	Mean (SD)	0.6 (2.1)
At death	Mean (SD)	130.4 (2430)
> 0.04	N (%)	417 (60.9%)
First day of troponin > 0.04	Mean (SD)	4.1 (4.8)
Blood PH	**Number**	**400**
At admission	Mean (SD)	7.37 (0.18)
At death	Mean (SD)	7.29 (0.16)
< 7.35	N (%)	266 (66.5%)
First day of PH > 7.35	Mean (SD)	5.9 (5.2)
> 7.45	N (%)	205 (52.2%)
First day of PH > 7.45	Mean (SD)	4.8 (5)
Sodium (mmol/l)	**Number**	**775**
At admission	Mean (SD)	135.3 (8.1)
At death	Mean (SD)	143 (11.1)
< 135	N (%)	517 (66.7%)
First day of sodium < 135	Mean (SD)	2.8 (4.1)

> 145	N (%)	450 (58%)
First day of sodium > 145	Mean (SD)	6.8 (5.3)
Potassium (mmol/l)	**Number**	**773**
At admission	Mean (SD)	4.38 (0.81)
At death	Mean (SD)	4.86 (1.14)
< 3.5	N (%)	294 (38%)
First day of potassium < 3.5	Mean (SD)	5.9 (5.8)
> 5.5	N (%)	330 (42.6%)
First day of potassium > 5.5	Mean (SD)	7.2 (12)

*. Patients who had chronic kidney disease were excluded from the mean.

4.2.9 Sample distribution by drugs and supplements

Table 4.10 shows the protocol of management applied in our hospitals that regarded corticosteroids, anticoagulants, antiviral drugs, supplements, and antibiotics. Most patients received Dexamethasone (82.7%) and Enoxaparin (83.5%) while Remdesivir was given for only 7.8% of patients and Tocilizumab was given for only 9.3% of patients. Almost one-third of the patients received zinc (36.3%) while vitamin D was slightly less than zinc (22.9%). On the other hand, the majority of patients received antibiotics (97.1%) in spite of the patients who had co-infection 19.1% only.

Moreover, the patients who received antibiotics without co-infection were 78%, and patients who received antibiotics without co-infection and intubation were (37%). However, patients received antibiotics as following, more than half of patients received Ceftriaxone (66.7%) and Azithromycin (64.7%), and less slightly than half of the patients received Meropenem (40.8%) and Vancomycin (38.8%) while one-third of patients received Ampicillin-Tazobactam (34.2%), In contrast, the least of patients received Ciprofloxacin (2.0%) and colistin (7.7%).

Table 4.10: Sample distribution by drugs and supplements

Variable		Count	Percentage
Dexamethasone	No	173	17.3%
	Yes	828	82.7%
Enoxaparin	No	165	16.5%
	Yes	836	83.5%
Remdesivir	No	923	92.2%
	Yes	78	7.8%
Zinc	No	638	63.7%
	Yes	363	36.3%
Vitamin D	No	772	77.1%
	Yes	229	22.9%
Tocilizumab	No	908	90.7%
	Yes	93	9.3%
Had co-infection?	No	810	80.9%
	Yes	191	19.1%
Received antibiotics?	No	29	2.9%
	Yes	972	97.1%
Meropenem	No	593	59.2%
	Yes	408	40.8%
Ceftriaxone	No	333	33.3%
	Yes	668	66.7%
Ceftazidime	No	813	81.2%
	Yes	188	18.8%

Ciprofloxacin	No	981	98.0%
	Yes	20	2.0%
Azithromycin	No	353	35.3%
	Yes	648	64.7%
Ampicillin-Tazobactam	No	659	65.8%
	Yes	342	34.2%
Vancomycin	No	613	61.2%
	Yes	388	38.8%
Levofloxacin	No	758	75.7%
	Yes	243	24.3%
Colistin	No	924	92.3%
	Yes	77	7.7%

4.3 Univariate analysis

4.3.1 The relationship between each of gender, age and O2 needs, hospital and survival days

Table 4.11 shows that the males who were older than 60 were more than females (58.3% vs 41.6%), and males were more slightly for O2 needs than females (98.4% vs 99.7%), moreover, the females who had survival days above 14 days were less than males (45.4%vs 47.2%). On the other hand, patients who were older than 60 years were more likely to need non-invasive O2 (96.0% vs 90.5%) while patients who were younger than 60 years were more likely to need intubation (65.1% vs 53.4%), and older patients were less likely to survive >14 days (31.9%% vs 39.3%) and less likely to stay >14 days in the hospital (45.3%% vs 50.0%).

Study sample comparison by age with variables, hospital days, non-invasive O2, and invasive O2 showed a significant relationship at p-value < 0.05, and Study sample comparison by gender with variables, O2 needs showed a significant relationship at p-value < 0.05.

Table 4.11: The relationship between each of gender, age and O2 needs, hospital and survival days

		Gender				P value of Chi Square	Age				P value of Chi Square
		Male		Female			≤ 60 years		> 60 years		
		N	%	N	%		N	%	N	%	
Gender	Male	576	100.0 %	0	0.0%		139	55.2%	437	58.3%	0.376
	Female	0	0.0%	425	100.0%		113	44.8%	312	41.7%	
Age cat	≤ 60 years	139	24.1%	113	26.6%	0.376	252	100.0 %	0	0.0%	
	> 60 years	437	75.9%	312	73.4%		0	0.0%	749	100.0%	
O2	No	2	0.3%	7	1.6%	.031*	2	0.8%	7	0.9%	.838[c]
	Yes	574	99.7%	418	98.4%		250	99.2%	742	99.1%	
Non-Invasive O2	No	37	6.4%	17	4.0%	0.093	24	9.5%	30	4.0%	.001*
	Yes	539	93.6%	408	96.0%		228	90.5%	719	96.0%	
Invasive (Tube)	No	260	45.1%	177	41.6%	0.271	88	34.9%	349	46.6%	.001*
	Yes	316	54.9%	248	58.4%		164	65.1%	400	53.4%	
Hospital days	≤14 days	386	67.0%	277	65.2%	0.543	153	60.7%	510	68.1%	.032*
	> 14 days	190	33.0%	148	34.8%		99	39.3%	239	31.9%	
No. days between diagnosis and death	≤14 days	304	52.8%	232	54.6%	0.570	126	50.0%	410	54.7%	0.192
	> 14 days	272	47.2%	193	45.4%		126	50.0%	339	45.3%	

**. By using the Chi-square test. *. Statistically significant result

4.3.2 The relationship between each of gender, age, and signs and symptoms

Table 4.12 shows that percentages of signs and symptoms between males and females were similar, but females were more prone to diarrhea (13.4% vs 9.5%), nausea (14.6% vs 9.5%), and

vomiting (11.1 vs 7.5). On the other hand, percentages of signs and symptoms between older and younger than 60 years were also similar but patients who were younger than 60 years were more prone to fever (71.8% vs 63.6%), shortness of breath (92.1% vs 88.8), chest discomfort (84.1% vs 79.3%) while the patients who older than 60 years were more prone to fatigue (85.6% vs 81.0%). However, study sample comparison by age with the variables, fever showed a significant relationship at p-value < 0.05 while study sample comparison by gender with the variables, fever showed a significant relationship at p-value < 0.05.

Table 4.12: The relationship between each of gender, age, and signs and symptoms

		Gender				P value of Chi Square	Age cat				P value of Chi Square
		Male		Female			≤ 60 years		> 60 years		
		N	%	N	%		N	%	N	%	
Fever	No	195	33.9%	149	35.1%	0.692	71	28.2%	273	36.4%	.017*
	Yes	381	66.1%	276	64.9%		181	71.8%	476	63.6%	
Fatigue	No	100	17.4%	56	13.2%	0.071	48	19.0%	108	14.4%	0.080
	Yes	476	82.6%	369	86.8%		204	81.0%	641	85.6%	
Myalgia	No	484	84.0%	341	80.2%	0.119	206	81.7%	619	82.6%	0.746
	Yes	92	16.0%	84	19.8%		46	18.3%	130	17.4%	
Cough	No	173	30.0%	125	29.4%	0.831	69	27.4%	229	30.6%	0.338
	Yes	403	70.0%	300	70.6%		183	72.6%	520	69.4%	
Shortness of breath	No	54	9.4%	50	11.8%	0.221	20	7.9%	84	11.2%	0.140
	Yes	522	90.6%	375	88.2%		232	92.1%	665	88.8%	
Chest discomfort	No	108	18.8%	87	20.5%	0.497	40	15.9%	155	20.7%	0.095
	Yes	468	81.3%	338	79.5%		212	84.1%	594	79.3%	
Sore throat	No	556	96.5%	411	96.7%	0.878	244	96.8%	723	96.5%	0.822
	Yes	20	3.5%	14	3.3%		8	3.2%	26	3.5%	

Rash	No	572	99.3%	425	100.0 %	.085[c]	251	99.6%	746	99.6%	.994[c]
	Yes	4	0.7%	0	0.0%		1	0.4%	3	0.4%	
Headache	No	510	88.5%	377	88.7%	0.936	220	87.3%	667	89.1%	0.449
	Yes	66	11.5%	48	11.3%		32	12.7%	82	10.9%	
Seizure	No	570	99.0%	414	97.4%	0.061	248	98.4%	736	98.3%	.875[c]
	Yes	6	1.0%	11	2.6%		4	1.6%	13	1.7%	
Abdominal pain	No	536	93.1%	393	92.5%	0.723	230	91.3%	699	93.3%	0.275
	Yes	40	6.9%	32	7.5%		22	8.7%	50	6.7%	
Diarrhea	No	521	90.5%	368	86.6%	0.055	223	88.5%	666	88.9%	0.853
	Yes	55	9.5%	57	13.4%		29	11.5%	83	11.1%	
Constipation	No	558	96.9%	412	96.9%	0.952	248	98.4%	722	96.4%	0.110
	Yes	18	3.1%	13	3.1%		4	1.6%	27	3.6%	
Nausea	No	521	90.5%	363	85.4%	.014[*]	217	86.1%	667	89.1%	0.209
	Yes	55	9.5%	62	14.6%		35	13.9%	82	10.9%	
Vomiting	No	533	92.5%	378	88.9%	.049[*]	225	89.3%	686	91.6%	0.269
	Yes	43	7.5%	47	11.1%		27	10.7%	63	8.4%	
Sweating	No	547	95.0%	394	92.7%	0.137	238	94.4%	703	93.9%	0.735
	Yes	29	5.0%	31	7.3%		14	5.6%	46	6.1%	
Neurological abnormalities	No	553	96.0%	412	96.9%	0.433	239	94.8%	726	96.9%	0.124
	Yes	23	4.0%	13	3.1%		13	5.2%	23	3.1%	
Chills	No	493	85.6%	369	86.8%	0.577	219	86.9%	643	85.8%	0.675
	Yes	83	14.4%	56	13.2%		33	13.1%	106	14.2%	

**. By using the Chi-square test. *. Statistically significant result

4.3.3 The relationship between each of gender, age, and comorbidities

Table 4.13 shows that the females who had heart failure (17.6% vs 12.5%), obesity (5.0% vs 10.6%), and hypothyroidism (2.4% vs 5.2) were more than males while the males who had ischemic heart disease were more than females (28.1%vs 16.5%).

On the other hand, the patients who were older than 60 years with comorbidities were more than patients who were younger than 60 years (85.3% vs 75.8%) and those old patients were more likely to have diabetes (55.3% vs 42.5%), hypertension (68.4% vs 43.3%), ischemic heart disease (27.2% vs 11.1%), heart failure (17.4% vs 6.7%), CVA (12.8% vs 4.4%) and less likely to have obesity than patients who were younger than 60 years (5.3% vs 13.5%).

However, sample comparison by age with the variables, diabetes, hypertension, ischemic heart disease, heart failure, CVA, and obesity showed a significant relationship at p-value < 0.05, while sample comparison by gender with the variables, heart failure, obesity, hypothyroidism, and ischemic heart disease showed a significant relationship at p-value < 0.05.

Table 4.13: The relationship between each of gender, age, and comorbidities

		Gender				P value of Chi Square	Age cat				P value of Chi Square
		Male		Female			≤ 60 years		> 60 years		
		N	%	N	%		N	%	N	%	
Had comorbidities?	No	93	16.1%	78	18.4%	0.359	61	24.2%	110	14.7%	.001*
	Yes	483	83.9%	347	81.6%		191	75.8%	639	85.3%	
Diabetes	No	270	46.9%	210	49.4%	0.427	145	57.5%	335	44.7%	.000*
	Yes	306	53.1%	215	50.6%		107	42.5%	414	55.3%	
Hypertension	No	225	39.1%	155	36.5%	0.404	143	56.7%	237	31.6%	.000*
	Yes	351	60.9%	270	63.5%		109	43.3%	512	68.4%	
Ischemic heart disease	No	414	71.9%	355	83.5%	.000*	224	88.9%	545	72.8%	.000*
	Yes	162	28.1%	70	16.5%		28	11.1%	204	27.2%	

Heart failure	No	504	87.5%	350	82.4%	.023*	235	93.3%	619	82.6%	.000*
	Yes	72	12.5%	75	17.6%		17	6.7%	130	17.4%	
Cerebrovascular accident (CVA)	No	511	88.7%	383	90.1%	0.478	241	95.6%	653	87.2%	.000*
	Yes	65	11.3%	42	9.9%		11	4.4%	96	12.8%	
Valvular heart disease	No	568	98.6%	421	99.1%	0.520	250	99.2%	739	98.7%	.494c
	Yes	8	1.4%	4	0.9%		2	0.8%	10	1.3%	
Cancer	No	531	92.2%	388	91.3%	0.610	225	89.3%	694	92.7%	0.091
	Yes	45	7.8%	37	8.7%		27	10.7%	55	7.3%	
Respiratory diseases	No	533	92.5%	390	91.8%	0.653	229	90.9%	694	92.7%	0.361
	Yes	43	7.5%	35	8.2%		23	9.1%	55	7.3%	
Obesity (BMI>40)	No	547	95.0%	380	89.4%	.001*	218	86.5%	709	94.7%	.000*
	Yes	29	5.0%	45	10.6%		34	13.5%	40	5.3%	
kidney diseases	No	458	79.5%	350	82.4%	0.260	207	82.1%	601	80.2%	0.508
	Yes	118	20.5%	75	17.6%		45	17.9%	148	19.8%	
Hypothyroidism	No	562	97.6%	403	94.8%	.021*	239	94.8%	726	96.9%	0.124
	Yes	14	2.4%	22	5.2%		13	5.2%	23	3.1%	

**. By using the Chi-square test. *. Statistically significant result

4.3.4 The relationship between each of gender, age, and complications

Table 4.14 shows that arrhythmia (16.5% vs 10.6%) and acute kidney injury (54.2% vs 48.5%) were more common among males while sepsis (63.1% vs 58.3%) and pneumonia (91.1% vs 87.3%) were more common among females. On the other hand, patients older than 60 years were more likely to develop cardiogenic shock (6.5% vs 3.2), myocardial infarction (14.7% vs 9.5%), acute kidney injury (55.1% vs 41.7%) while patients younger than 60 years were more likely to develop hyper coagulopathy (6.0% vs 3.1%) and sepsis (42.5% vs 38.7%).

However, patients comparison by age with the variables, cardiogenic shock, MI, acute kidney injury, and hyper coagulopathy showed a significant relationship at p-value < 0.05. while patients comparison by gender with the variables, arrhythmia showed a significant relationship at p-value < 0.05.

Table 4.14: The relationship between each of gender, age and complications

		Gender				P value of Chi Square	Age categories				P value of Chi Square
		Male		Female			≤ 60 years		> 60 years		
		N	%	N	%		N	%	N	%	
Cardiogenic shock	No	539	93.6%	405	95.3%	0.246	244	96.8%	700	93.5%	.046*
	Yes	37	6.4%	20	4.7%		8	3.2%	49	6.5%	
Sepsis	No	336	58.3%	268	63.1%	0.131	145	57.5%	459	61.3%	0.294
	Yes	240	41.7%	157	36.9%		107	42.5%	290	38.7%	
Septic shock	No	375	65.1%	289	68.0%	0.338	165	65.5%	499	66.6%	0.739
	Yes	201	34.9%	136	32.0%		87	34.5%	250	33.4%	
Hepatic dysfunction	No	524	91.0%	394	92.7%	0.326	232	92.1%	686	91.6%	0.813
	Yes	52	9.0%	31	7.3%		20	7.9%	63	8.4%	
Hyper Coagulopathy status	No	553	96.0%	410	96.5%	0.704	237	94.0%	726	96.9%	.038*
	Yes	23	4.0%	15	3.5%		15	6.0%	23	3.1%	
Heart failure	No	515	89.4%	386	90.8%	0.461	233	92.5%	668	89.2%	0.134
	Yes	61	10.6%	39	9.2%		19	7.5%	81	10.8%	
Arrhythmia	No	481	83.5%	380	89.4%	.008*	225	89.3%	636	84.9%	0.083
	Yes	95	16.5%	45	10.6%		27	10.7%	113	15.1%	
Myocardial infarction (MI)	No	494	85.8%	373	87.8%	0.358	228	90.5%	639	85.3%	.037*
	Yes	82	14.2%	52	12.2%		24	9.5%	110	14.7%	

Pneumonia	No	73	12.7%	38	8.9%	0.063	27	10.7%	84	11.2%	0.827
	Yes	503	87.3%	387	91.1%		225	89.3%	665	88.8%	
Acute kidney injury	No	264	45.8%	219	51.5%	0.075	147	58.3%	336	44.9%	.000*
	Yes	312	54.2%	206	48.5%		105	41.7%	413	55.1%	
(CVA)	No	559	97.0%	410	96.5%	0.607	245	97.2%	724	96.7%	0.662
	Yes	17	3.0%	15	3.5%		7	2.8%	25	3.3%	

**. By using Chi-square test. *. Statistically significant result

4.4 Multivariate analysis

Table 4.15 summarizes the Cox proportional Hazard model which is investigating the effect of several variables upon the timing of death due to COVID-19.

Regarding the sociodemographic characteristics, aged from 61-80 years decreased the survival days and increased the mortality rate of COVID-19 by 1.27 folds (127%) compared to other age groups. In contrast, the southern west bank increased the survival days and decreased the mortality rate of COVID-19 by 0.799 folds (79.9%) compared to other areas of residency.

Regard to comorbidities, diabetes decreased the survival days and increased the mortality rate of COVID-19 by 1.202 folds (120%), and cancer decreased the survival days and increased the mortality rate of COVID-19 by 1.320 folds (132%) while hypothyroidism increased the survival days and decreased the mortality rate of COVID-19 by 0.46 folds (46%).

In relation to complications, the septic shock decreased the survival days and increased the mortality rate of COVID-19 by 1.309 folds (130%) while the arrhythmia increased the survival days and decreased the mortality rate of COVID-19 by 0.78 folds (78%).

In regard to management, invasive O2 support increased the survival days and decreased the mortality rate of COVID-19 by 0.74 folds (74%). Moreover, Tocilizumab increased the survival days and decreased the mortality rate of COVID-19 by 0.74 folds (74%).

Table 4.16: Cox proportional Hazard model for survival of COVID 19 patients

Variables		P-value	HR	95.0% CI	
				Lower	Upper
Gender	Female	.299	1.077	.937	1.237
Age category	≤20-40 years old				
	41-60 years old	.322	1.198	.838	1.714
	61-80 years old*	.039	1.272	1.012	1.599
	>80 years old	.719	.966	.800	1.167
Area of residency	Northern West Bank	.086			
	Middle West Bank	.312	.905	.745	1.099
	Southern West Bank*	.028	.799	.655	.976
Non-Invasive O2	Yes	.820	1.037	.759	1.416
Invasive (Tube)	Yes	.000	.740	.633	.866
Diabetes	Yes*	.021	1.202	1.028	1.407
Hypertension	Yes	.397	.925	.772	1.108
Ischemic heart disease	Yes	.690	1.035	.873	1.227
Heart failure	Yes	.988	1.002	.814	1.232
Cerebrovascular accident	Yes	.368	.832	.556	1.243
Valvular heart disease	Yes	.092	.575	.302	1.095
Cancer	Yes*	.043	1.320	1.009	1.726
Respiratory diseases	Yes	.201	1.185	.914	1.536
Obesity (BMI>40)	Yes	.762	.960	.739	1.248
kidney diseases	Yes	.068	1.186	.988	1.423
Hypothyroidism	Yes*	.000	.469	.324	.680

Cardiogenic shock	Yes	.120	1.277	.938	1.739
Septic shock	Yes*	.027	1.309	1.032	1.661
Hepatic dysfunction	Yes	.280	.853	.638	1.139
Hyper Coagulopathy status	Yes	.387	.845	.578	1.237
Heart failure	Yes	.073	1.274	.977	1.660
Arrhythmia	Yes*	.021	.784	.638	.964
Myocardial Infarction	Yes	.855	1.019	.836	1.241
Pneumonia	Yes	.552	1.078	.842	1.381
Acute kidney injury	Yes	.973	1.003	.867	1.159
Dexamethasone	Yes	.432	1.082	.889	1.317
Enoxaparin	Yes	.564	.941	.766	1.156
Remdesivir	Yes	.089	.789	.600	1.037
Zinc	Yes	.749	1.027	.873	1.207
Vitamin D	Yes	.991	.999	.833	1.198
Tocilizumab	Yes*	.017	.741	.579	.948

*. Statistically significant result

Chapter Five: Discussion

5.1 Introduction

In this chapter, the research results are discussed and compared to similar studies worldwide. As well as, conclusions, limitations, and recommendations are included at the final of the chapter.

5.2 Socio-demographic variables and COVID-19 by survival days

Hospitals: The distribution of 1001 COVID-19 deaths obtained from the 15 hospitals showed that the highest percentage of the sample was in Ramallah governmental hospital (21.0%) followed by Hebron governmental hospital (17.8%) while the lowest percentage of deaths was in AL-Askari hospital (0.8%). The differences were depending on several factors such as population density, place of residency, size, and facilities of central hospitals to receive COVID-19 cases during the state of emergency for the first period of the pandemic, referral hospitals, and the availability of data and information computerized system.

Residency: The area of residency showed the same pattern as all governorates of the West Bank were present but at different rates, less than half of the sample was coming from the middle of the West Bank (41.4%), more than one-third of the sample were from the south of the West Bank (34.8%) while the north of the West Bank included (23.9%) of deaths.

Furthermore, our study showed a statistical significance in the residency places as the living in southern west bank increased the survival days and decreased the mortality rate of COVID-19 by 0.799 folds (79.9%) compared to living in other areas of residency. However, no study indicated the reason for this statistical indication but there are several factors that could interpret our results such as lifestyle, the level of care provided at the hospitals of southern West Bank, and early case detection.

Age: The mean age of the study sample was 68.21 years with 17 years old being the youngest patient and 100 years old being the oldest patient, half of the patients were between 61-80 years old and most of the deaths were above 61 years. Moreover, our study showed that aged from 61-80 years decreased the survival days and increased the mortality rate of COVID-19 by 1.27 folds (127%) compared to other age groups. So, old age is related to COVID-19 mortality and that is consistent with the international studies that found that COVID-19 was more lethal in the elderly

than younger people (Lv, et al., 2021; Wu, et al., 2020), and its severity was rare in children (Dong, et al., 2020).

Many factors were suggested in the literature for the high rate of deaths in elderly COVID-19 patients as the elderly patients have weak immune functions, limited organ function, and more comorbidities before infection and more complications after infection (Sheng, et al., 2021). In addition to that, according to (Opal, et al., 2005), the defects in B-cell and T-cell related to age and increasing production of type 2 cytokines may contribute to decreasing the control of viral replication that led to prolonged pro-inflammatory responses that could lead to a worse outcome. Moreover, our study found a significant relationship between age and some variables that will be discussed in the following sections.

Gender: Our study showed that the males (57.5%) were higher than the females (42.5%) among COVID-19 deaths, and the males who were older than 60 years were more than females (58.3%), (41.6%). It is compatible with many previous studies showed that males were more susceptible to worse outcome due to COVID-19, and Europe data showed that male-to-female death ratio of 2.1, which increased to 3.9 in cases aged 50–65 years (ECDC). However, a study concluded that gender-based immunological differences contribute to differences in susceptibility to infections (Klein, et al., 2016). Moreover, our study showed a significant relationship between gender and some variables that will be discussed in the following sections.

Pregnancy: The world health organization defined the women's reproductive age that starts from 16 to 49 years (WHO, 2023), and in our study, among 59 females in childbearing age, 12 (22.6%) were pregnant, the percentage seems small but it is considerable, as many studies indicated to the risk of exposure to infection as SARS-CoV-2 during pregnancy that increase the requiring of ICU and mechanical ventilation compared to non-pregnant women (Wang, et al., 2022; Wei, et al., 2021; Nakamura-Pereira, et al., 2020).

Our study showed that only 5 (41.6%) of pregnant had comorbidities, it contradicts (Ríos-Silva, et al., 2020), who found that pregnant with COVID-19 don't have a higher risk for complications or death compared with non-pregnant but the risk will increase by the presence of chronic diseases like diabetes at childbearing age and not specifically in pregnant (Ríos-Silva, et al., 2020). However, Physiological and immunologic changes through pregnancy increase the concern for an

outcome from viral infection similar to that from MERS-CoV and SARS-CoV-1 (Overton, et al., 2022).

Blood Group: Among hospitals, the blood group was reported for only 247 deaths, and showed that the dominant blood group was A-positive (33.6%) followed by O-positive (31.2%) while uncommon blood groups were B-negative (2.8%) and AB-negative (0.8%), Moreover, positive blood groups were more than negative.

Our results were similar to other studies that showed that blood group A had a higher risk for severity (Ellinghaus, et al., 2020) and blood group B had a lower risk of death due to COVID-19 (Gutiérrez-Valencia, et al., 2022). While for blood group O, it was similar to blood group A in our study despite another study concluded that blood group O had a protective effect (Ellinghaus, et al., 2020) while another study showed that it would not affect the progression of the disease (Gutiérrez-Valencia, et al., 2022).

In contrast, a meta-analysis study negated the possible significant correlation between the lack of anti-A antibodies and bad COVID-19 outcomes (Bhattacharjee, et al., 2022).

Many studies tried to find an association between COVID-19 and ABO blood groups based on the genetic similarity between SARS-CoV and SARS-CoV2, as the SARS-CoV experience showed a link with ABO blood groups via blocking the adhesion of SARS-CoV S-protein to ACE2 expressing cell lines by anti-A antibodies (Bhattacharjee, et al., 2022).

However, the differences in the results of the previous studies warrant more research that considers the variation in the prevalence of blood groups among the population of each region.

5.3 Lifestyle variables (Smoking) and COVID-19

Smoking status was only reported for 288 deaths. Among them, non-smokers (59.7%) were more than smokers (40.3%). Although the smokers were less than non-smokers, the percentage of smokers is considerable. Moreover, among smokers, 81.8% had comorbidities, this result is consistent with a study found that 40% of deaths by COVID-19 were smokers and indicated that smoking was related to a higher risk for COVID-19 severity including mechanical ventilation or death (Poudel, et al., 2022) and with a study from Japan that found the severity of COVID-19 was

not associated with smoking but with the comorbidities which were caused by smoking (Matsushita, et al., 2021).

However, the studies showed that increasing in ACE-2 expression which is upregulated in lung tissue significantly associated with a smoking history (Smith, et al., 2020), this explains the increase of SARS-CoV-2 loads which led to an increase in the risk of severe diseases and death (Reddy, et al., 2021)

5.4 Survival days, hospital stay duration, and COVID-19 by age and gender

Hospital days: The duration of stay in the hospitals ranged from one day to 53 days with a mean of 12.9 days, and the patients who survived up to 14 days from the admission were twice more than the patients who died after 14 days from the admission. Our results are close to a study that showed the mean of hospital stay duration for critical cases was 14.5 (Kelesoglu, et al., 2021) and to the study that showed mortality was more notable and statistically significant after day 7 from admission (Bordon, et al., 2021), and to range of stay duration in the hospital (1-55) in a study from Saudi Arabia (Alwafi, et al., 2021).

However, there is convergence and divergence between the results of the studies, but the difference was not large, and this depends on many factors for each study, such as the quality and timing of services provided in the hospitals, demographic characteristics, and health condition of cases by comorbidities, complications, and intubation requirement.

Therefore, our study showed that the patients who were younger than 60 years and stayed above 14 days in the hospital were more than patients who were older than 60 years. However, patients' comparison by age with hospital days showed a significant relationship.

On the other hand, the females who stayed in the hospitals more than 14 days were less slightly than males, but we found no significant relationship between gender and hospital days.

Survival days: Our study showed that the survival days since the diagnosis (first positive result) ranged from one day to 62 days with a mean of 15.91 which is similar to what was shown by (Wang, et al., 2020). Furthermore, our patients who survived up to 14 days from diagnosis were more than patients who died after 14 days from diagnosis. However, multivariate cox proportional regression of survival of COVID-19 patients will be discussed in the following sections.

5.5 O2 needs and COVID-19 by age, gender and survival days

Almost all our patients required respiratory support and received supplemental oxygen (99.1%), most of them received non-invasive O2 (94.6%) while half of them received invasive O2 (56.3%) and that is consistent with (Luo, et al., 2020) study that also concluded that the time of intubation initiation was associated with a high risk of death due to Covid-19. So, the findings of (Rehman, et al., 2022) investigation indicate that intubating patients very early may be risky. In contrast, (Riera, et al., 2023) found that delayed intubation has been associated with a higher risk of COVID-19 mortality. In the same context, our study showed that the initiation of giving the non-invasive O2 was early with a mean of one day from admission while the initiation of giving the invasive O2 was late with a mean of 7 days from admission.

Similar to (Singer, et al., 2020), the mean of survival days after receiving only non-invasive O2 (12.4) was more than the mean of survival days after intubation (7), and the patients who died on the twelfth day from receiving non-invasive O2 or after were more than the patients who died before the twelfth day. On the other hand, the patients who died on the seventh day from intubation or before were double the patients who died after the seventh day.

Despite (Mohammadi, et al., 2021) study indicated that cases who received non-invasive O2 had lower mortality than cases who were intubated, we found that intubation increased the survival days and decreased the mortality rate of COVID-19 by 0.740 folds (74%).

However, the respiratory support including non-invasive O2 and invasive O2 did not improve the outcome for our patients, and the survival days without intubation were longer, but it was used to save a life in the status of severe respiratory failure or cardiac arrest due to increasing in survival days, furthermore, the timely mean of death from intubation was early. So, we can't confirm that reason was the delayed intubation because of the variation between studies despite their agreement on linking the intubation timing to the risk, on the other hand, we can suggest the possibility of developing complications such as ventilator-acquired infections, but when we consider the incubation period, most our intubated patients died before the seventh day from intubation, so we can indicate to other complications as aspiration and tension pneumothorax or due to the worse deterioration before intubation.

Moreover, we noted that the males were more likely to require oxygen support. However, study sample comparison by gender, O2 support showed a significant relationship. In addition to that, the patients who were older than 60 years were more likely to need non-invasive O2 while the patients who were younger than 60 years were more likely to need intubation. However, study sample comparison by age, non-invasive O2 and invasive O2 showed a significant relationship which is compatible with (Ogbuka, et al., 2022).

5.6 Signs and Symptoms and COVID-19 by age, gender & survival days

There was a positive correlation between the number of co-existing symptoms and disease progression in patients (Lv, et al., 2021), our study showed that all patients had more than one symptom, and fatigue was dominant among the patients (84.4%). Also, similar to (Alizadehsani, et al., 2022; Lv, et al., 2021), most of the patients had respiratory symptoms such as shortness of breath (89.6%), chest discomfort (80.5%), cough (70.2%), and more than half of patients developed fever (65.6%). However, each of abdominal pain, myalgia, headache, sweating, and chills didn't exceed (18%) but were more common than each of rash (0.4%), seizure (1.7%), sore throat (3.4%), neurological abnormalities (3.6%).

In spite of the gastrointestinal symptoms were less common but with different variations, the percentage of patients with nausea (11.7%) was close to the percentage of patients with vomiting (9.0%), while the patients who had diarrhea (11.2%) were higher than the patients who had constipation (3.1%). So, according to (Lv, et al., 2021), many symptoms' kinds mean that the load of the virus in patients was large which led to seriously affected multiple body systems, not only the respiratory system.

Furthermore, our study showed that the percentages of signs and symptoms between males and females were similar, but females were more affected with diarrhea (13.4% vs 9.5%), nausea (14.6% vs 9.5%), and vomiting (11.1 vs 7.5). Also, we found a statistically significant difference between males and females in nausea and vomiting which is consistent with a study that found females were significantly more affected with gastrointestinal symptoms such as diarrhea, nausea, and vomiting (Raimondi, et al., 2021).

On the other hand, percentages of signs and symptoms between older and younger than 60 years were also similar but patients who were younger than 60 years were more affected with fever

(71.8% vs 63.6%), shortness of breath (92.1% vs 88.8), and chest discomfort (84.1% vs 79.3%) while the patients who older than 60 years were more affected with fatigue (85.6% vs 81.0%). However, sample comparison by age with the signs and symptoms, only fever showed a significant relationship, this agrees with a study that found increasing age among covid 19 cases correlated with lower temperature (Penfold, et al., 2022). However, multivariate cox proportional hazard regression showed that no significant effect of signs and symptoms on the survival days.

5.7 Comorbidities and COVID-19 by age, gender & survival days

Many previous studies showed that patients with comorbidities have a higher risk for death due to COVID-19 (Marcolino, et al., 2021), most patients (82.9%) had comorbidities, that is similar to a study analyzed 1000 COVID-19 deaths in India and found 96% with comorbidities (Koya, et al., 2021).

In line with (Marcolino, et al., 2021) study, the majority of our patients had hypertension (62.0%), followed by diabetes (52.0%) and ischemic heart disease (23.2%) while the lowest patients had valvular heart disease (1.2%), hypothyroidism (3.6%) and obesity (7.4%). However, the patients who had kidney disease (19.3%) were more than patients who had heart failure (14.7%), CVA (10.7%), and cancer (8.2%). Interestingly, patients who had respiratory diseases were only 7.8% and that is consistent with (Henkens, et al., 2022) study.

Moreover, our study showed that females who had heart failure (17.6% vs 12.5%), obesity (5.0% vs 10.6%), and hypothyroidism (2.4% vs 5.2) were more than males while males who had ischemic heart disease were more than females (28.1%vs 16.5%). Also, study sample comparison by gender with the variables, obesity, hypothyroidism, and ischemic heart disease showed a significant relationship.

On the other hand, in line with (Henkens, et al., 2022) study, the patients who were older than 60 years with comorbidities were more than patients who were younger than 60 years (85.3% vs 75.8%) and those old patients were more likely to have diabetes (55.3% vs 42.5%), hypertension (68.4% vs 43.3%), ischemic heart disease (27.2% vs 11.1%), heart failure (17.4% vs 6.7%), and CVA (12.8% vs 4.4%) and less likely to have obesity than patients who were younger than 60 years (5.3% vs 13.5%). So, study sample comparison by age with the variables, diabetes, hypertension, ischemic heart disease, heart failure, CVA, and obesity showed a significant relationship.

The association between ACE2 expression and Angio cardiopathy was confirmed in previous studies (Li, et al., 2017). So, this showed that hypertension and heart disease could affect COVID-19 progression (Lv, et al., 2021).

Furthermore, in our study, multivariate cox proportional hazard regression showed that diabetes decreased the survival days and increased the mortality rate of COVID-19 by 1.20 folds (120%). In addition to that, cancer decreased the survival days and increased the mortality rate of COVID-19 by 1.32 folds (132%). However, patients with diabetes have high morbidity and mortality from infectious diseases, it may be due to chronic immune system imbalances, excess nutrition caused by obesity, or metabolic syndrome. Moreover, some viruses were diabetogenic themselves (Jaeckel, et al., 2002). Interestingly, a study about SARS showed that even non-severe cases who had not taken glucocorticoid had high fasting blood glucose levels (Yang, et al., 2006). On the other hand, according to a meta-analysis that examined 3019 patients with cancer and COVID-19 with a broad geographical distribution, the patients with cancer have a high risk of severe illness and fatality due to COVID-19 and that may be accentuated by age, gender, and comorbidities (Zhang, et al., 2021).

According to annual reports of the Palestinian Ministry of Health, the reported number of diabetic patients in PHC clinics in the West Bank was 4,420 with an incidence rate of 160.4 per 100,000 populations, in addition to that, diabetes and cancer were the most common cause of death in West Bank (MOH, 2020).

On the other hand, in our study, hypothyroidism increased the survival days and decreased the mortality rate of COVID-19 by 0.54 folds (54%), which is compatible with the study that showed hypothyroidism was not associated with an increased risk of death due to COVID-19 (van Gerwen, et al., 2020).

5.8 Complications and COVID-19 by age, gender & survival days

In our study, the patients developed complications such as pneumonia which was dominant (88.9%) while half of the patients (51.7%) developed acute kidney injury, and sepsis (39.7%) was similar to septic shock (33.7%). Cardiac diseases were also developed in similar percentages such as heart failure (10.0%), arrhythmia (14.0%), and myocardial infarction (13.4%). While CVA (3.2%), cardiogenic shock (5.7%), and hyper Coagulopathy status (3.8%) appeared with the lowest

percentage of patients, these findings were similar to the literature (Avila, et al., 2021; Chen, et al., 2021; Linschoten, et al., 2020; Zhou, et al., 2020).

Moreover, arrhythmia (16.5% vs 10.6%) and acute kidney injury (54.2% vs 48.5%) were more common among males while sepsis (63.1% vs 58.3%) and pneumonia (91.1% vs 87.3%) were more common among females. However, sample comparison by gender with the complications, arrhythmia showed a significant relationship.

On the other hand, the patients who were older than 60 years were more likely to develop cardiogenic shock (6.5% vs 3.2), myocardial infarction (14.7% vs 9.5%), and acute kidney injury (55.1% vs 41.7%) while the patients who were younger than 60 years were more likely to develop hyper coagulopathy (6.0% vs 3.1%) and sepsis (42.5% vs 38.7%). However, sample comparison by age with the complications, cardiogenic shock, MI, acute kidney injury, and hyper coagulopathy showed a significant relationship.

Many previous studies justify our results as there is a suspicion that activation of renin-angiotensin (RAS) in hypertension and heart disease patients due to COVID-19 led to exacerbated injury for lung (Lv, et al., 2021), moreover, the cardiac complications including heart failure, arrhythmia, or myocardial infarction are common in patients with pneumonia (Marrie, et al., 2007). And the factors that contribute to getting cardiac disorders after pneumonia are old age, pre-existing cardiovascular illness, and increased pneumonia severity at presentation (Medina, et al., 2013). That is supported by studies that found coronary heart disease is associated with acute cardiac illnesses and serious outcomes in influenza and the rest of respiratory viral infections (Blackburn, et al., 2018). On the other hand, the receptor for SARS-CoV-2, angiotensin-converting enzyme 2 (Gallagher, et al., 2008) is expressed on vascular endothelial cells and myocytes (Torres, et al., 2015). So, there is a potential for direct cardiac involvement by SARS-CoV-2 (Xu, et al., 2020).

In relation to acute kidney injury, there are some possibilities for the effect of Covid-19 on the kidneys, including, the virus may target the cells of the kidneys, low levels of oxygen may lead to malfunction of the kidney, cytokine storms may damage the kidney tissue, and the small clots in the bloodstream may close the blood vessels in the kidney (Sperati, 2022).

Furthermore, in our study, multivariate cox proportional hazard regression showed that the septic shock decreased the survival days and increased the mortality rate of COVID-19 by 1.309 folds

(130%) while the arrhythmia increased the survival days and decreased the mortality rate of COVID-19 by 0.78 folds (78%).

Our result is consistent with the study that focused on the cases with septic shock due to COVID-19 and found the onset of shock and time of death were very closely correlated chronologically, and many cases appear to have septic shock signs shortly before death (Chen, et al., 2022). Furthermore, septic shock can be caused by inflammation imbalance, viral or bacterial infection, and the complicated interaction with an immune system that sometimes triggers an excessive inflammatory response (Chen, et al., 2020; Liao, et al., 2020).

However, arrhythmia may not occur only by the viral effect that affects the cardiac system through hypoxia, inflammatory stress, or infection-related myocarditis but also by drug interactions and systemic illness (Dherange, et al., 2020).

5.9 Indicators of COVID-19

Radiology:

One of the essential steps in the management of COVID-19 pneumonia is to determine lung involvement that is seen by radiological investigation since its correlation with mortality has been proven (Cecchini, et al., 2020). COVID-19 can be detected accurately either with chest x-ray imaging or a CT scan. However, in the early stages of the disease, a CT scan has a bigger advantage in disease detection since it has a higher sensitivity (Cecchini, et al., 2020).

Our study showed that 504 deaths of the total had a reported imaging investigation with a chest x-ray investigation, while high-resolution CT was reported only in 27% of documented deaths and Angio CT was reported only in 1.8%.

Our study showed that pulmonary infiltrates were the most reported finding with a percentage of 60.2, followed by ground-glass lung opacities (15.1%), bilateral pneumonia (12.9%) that more than unilateral pneumonia (4.4%) and pleural effusion (6.3%). While ARDS picture and lobar consolidation were one of the least reported findings with a percentage of (5.0%) and (4.6%) respectively. In comparison, the study of (Giacomelli, et al., 2020) confirmed our findings since they found that the most reported finding is pulmonary infiltration with a percentage of (83%),

followed by ground-glass opacity (81%). Whereas pleural effusion was found to be the least reported findings in contrast to our result (Giacomelli, et al., 2020; Xiong, et al., 2020).

Laboratory results

Laboratory test findings are considered an indicator of disease levels and outcomes. In our study, laboratory findings were available for different numbers of deaths, and it is notable a wide range among results and a considerable difference between the mean of results at admission and at death for all laboratory tests. In addition to that, the mean of each of ferritin, CRP, D-Dimer, LDH, CK, and troponin at admission was abnormal which predicts to worse prognosis while the mean of means of first relapse day (abnormal result) from admission among all laboratory tests was 4.7.

Regarding blood components, 70.1% of our patients developed anemia at the mean of 10 days from admission, while 17.2% developed leukopenia at the mean of 6 days, and 86% developed leukocytosis at the mean of 3 days. In addition to that, 54.9% developed thrombocytopenia at the mean of 5 days while 25.4% developed thrombocytosis at the mean of 5 days. That is similar to (Leulseged, et al., 2021) study that found that leukocytosis, leukopenia, decreased platelet count, and anemia are found to be related to disease severity and worse outcome in COVID-19 cases (Leulseged, et al., 2021).

However, having lower white blood cells increases the potential to develop severe infection and rises the effect of an existing pathogen which is lead to the progress of the disease stage at any infection. Likewise, despite the high white cells being an indication of immune system responses, it also indicates that the body is under great stress from the pathogen (Leulseged, et al., 2021).

Moreover, COVID-19 deaths had lower platelet counts than survival cases (Sheng, et al., 2021). According to studies, the decrease of platelet count in deaths could be related to sepsis or might be attributed to consumption that may be linked to widespread thrombosis or disseminated intravascular coagulation (DIC), or because the inhibition of development and maturation of megakaryocytes in bone marrow by the inflammatory response (Sheng, et al., 2021). On the other hand, thrombocytosis is attributed to the increased number of released cytokines and disease severity (Kenya, et al., 2022).

Regrade to inflammatory biomarker as ferritin and CRP, in our study, 0.6% only of patients had iron deficiency at the mean of 3 days from admission while 84.5% had elevated iron at the mean of 2 days, which is similar to those (Bordon, et al., 2021; Mukhi, et al., 2022) who showed that the inflammatory response leads to iron dysmetabolism, resulting in increased levels of hepcidin, decreased iron utilization, increased ferritin level, and anemia (Mukhi, et al., 2022). Also, in line with (Girija, et al., 2020) that found that COVID-19 deaths had higher levels of CRP, 98.8% of our patients had elevated CRP at the mean of 1 day.

Moreover, 94.6% of patients developed elevated d-dimer at the mean of 3 days from admission. According to the literature, this result related to the worse outcome of COVID-19, and the interpretation was that fibrinolysis was inhibited in serious COVID-19 cases (Sheng, et al., 2021). Furthermore, the formation of extensive thrombus was found at autopsy in COVID-19 deaths (Barnes, et al., 2029).

In line with (Bertsimas, et al., 2020), we found that 74.5% of patients reported elevated creatinine which indicated the probability of developing acute kidney injury at the mean of 3 days. However, acute kidney injury is common among COVID-19 cases due to renal hypoperfusion, cytokine storm, and multi-organ failure (Oto, et al., 2021).

Moreover, 94% of patients recorded abnormal LDH at the mean of 2 days from admission. As is the case with CK, 56.4% of patients recorded abnormal levels at mean of 4 days. That is compatible with a study that showed double elevated CK/LDH increases the risk of death (Liu, et al., 2022). However, another study found that CK and LDH are independent predictors of heart failure until death in COVID-19 critical cases, both were significantly high at admission and then increased rapidly (Chen, et al., 2021).

In line with (Zhou, et al., 2020) study that found more than half of COVID-19 deaths had elevated high-sensitivity cardiac troponin, our study found that 60.9% of patients reported troponin at the mean of 4 days.

Regarding the blood PH, 66.5% of patients developed acidosis at the mean of 6 days from admission while 52.2% of patients developed alkalosis at the mean of 5 days. However, a study showed a high incidence of alkalosis among critically COVID-19 cases and is related to high mortality (Jiang, et al., 2022). In contrast, another study of 54 COVID-19 deaths reported that 16

(30%) had acidosis (Zhou, et al., 2020). Therefore, it's clear that the acid-base imbalance in COVID-19 cases is related to mortality.

In relation to the electrolytes such as sodium and potassium, in our study, 66.7% of patients developed hyponatremia at the mean of 3 days from admission while 58% of patients developed hypernatremia at the mean of 7 days. On the other hand, 38% of patients developed hypokalemia at the mean of 6 days from admission, while 42.6% of patients developed hyperkalemia at the mean of 7 days from admission, and that is consistent with (Leulseged, et al., 2021) study that found that electrolyte imbalances (both lower and higher values of sodium and potassium) which can result from the loss of fluid from the body via various routes, medications effect, renal damage were strongly associated with severe disease due to COVID-19.

5.10 Management of COVID-19 by survival days

In regards to COVID-19 treatment management, we found that most of the hospitals included in our study followed a similar protocol by giving corticosteroids, anticoagulants, mineral and vitamin supplements, antiviral, and antibiotics as their treatment options.

Since the use of steroids has been proven effective in decreasing COVID-19 complications, its use has increased in protocols as seen in Italy, especially in the second phase (Sterne, et al., 2020). Also, our study showed that Dexamethasone was given in 82.7% of the patients, this percentage is higher than what was reported in two studies; one study by (Chen, et al., 2021) that concluded out of 81 cases only 7.7% received Dexamethasone, while in another study, Dexamethasone was used for 43.2% of 431 COVID-19 deaths (Marcolino, et al., 2021). However, this doesn't mean that the patients who did not receive Dexamethasone ended up without steroid treatment.

Other treatment options used were anticoagulants and supplements, in our study, 83.5% of patients received Enoxaparin, this is almost similar to a study in Brazil that showed that 88.2% of cases were given anticoagulants (Marcolino, et al., 2021).

In addition, almost a third of our patients received Zinc, while 22.9% were given Vitamin-D supplements. However, both Vitamin-D and Zinc supplements have been proven beneficial in the resistance to SARS-CoV-2 (Oristrell, et al., 2022; Kumar, et al., 2020).

As published by the WHO in 2020, antiviral drugs have been used in spite of lack of effectiveness, as hoped by researchers. We found that Remdesivir was given to 7.8% of patients and only 9.3% of patients received Tocilizumab. Furthermore, multivariate cox proportional hazard regression showed that Tocilizumab increased the survival days and decreased the mortality rate of COVID-19 by 0.741 folds (74%) which is similar to (Berardicurti, et al., 2020) study. In addition to that, Tocilizumab binds competitively and selectively to soluble expressing the IL-6 receptor and then inhibits the signaling which is a key to cytokine storm (Samaee, et al., 2020).

In a time of the pandemic, it was clear that the healthcare systems were under a heavy burden so it was difficult to implement good practices, particularly seen in the excessive use of antimicrobials (WHO, 2020). In our study, 97.1% of patients were given antibiotics in spite of only 19.1% were given antibiotics for the coexisting secondary infection. In comparison to (Rawson, et al., 2020) study, the antimicrobials were administered to approximately 90% of the patients. While a hospital in New York City showed that from 71% of COVID-19 patients who were given antibiotics, only 4% had a true bacterial coinfection (Nori, et al., 2021).

Moreover, in our findings, we found that the patients who received antibiotics without co-infection 78%, and 37% of patients who received antibiotics had no co-infection and were not receiving intubation together. This excessive use in management can be attributed to the resemblance in the clinical picture of sepsis, whether bacterial or fungal, and severe COVID-19 (Marcolino, et al., 2021).

Among types of antibiotics, more than half of patients received Ceftriaxone (66.7%) and Azithromycin (64.7%) while the other half have been managed with a broad-spectrum antibiotic like Meropenem (40.8%), Vancomycin (38.8%) and Ampicillin-Tazobactam (34.2%), yet the least prescribed drugs were Ciprofloxacin (2.0%) and Colistin (7.7%).

In comparison to (Suranadi, et al., 2022) study, Azithromycin was the most frequently prescribed medication with a percentage of 44.3%, followed by Levofloxacin, while Ceftriaxone was ranked third with a percentage of 16.8%. Nonetheless, the percentage of prescribed antimicrobials is less than our study finding, particularly, Meropenem and Vancomycin were rarely seen, since they were given to 1% and 3% of the cases respectively (Suranadi, et al., 2022).

Nevertheless, this misuse and overuse of antimicrobial regimens might contribute to the emergence of antimicrobial-resistant organisms, which may complicate the treatment course, hence, by comparing the numbers between 2019 and 2020, (Nori, et al., 2021) found that there is an increase in candidemia and the resistance for antimicrobial classes among bacterial strains, such as; K. pneumoniae, E. cloacae, and P. aeruginosa, this is all in regard to overuse of antibiotics.

5.11 Conclusion

This study is the first one in Palestine that highlighted the COVID-19 deaths from all governorates of West Bank and identified their characteristics and investigated the possible risk factors related to COVID-19 deaths attending the hospitals. A retrospective cohort study design was selected to test the study hypothesis. Most of our findings were consistent with other international studies.

In our study, old age, males, comorbidities, and complications were related to covid 19 mortality, and only 12 were pregnant. Also, the dominant blood group was A-positive followed by O-positive, and non-smokers were more than smokers, and approximately all patients required respiratory support and received supplemental oxygen, most of them received non-invasive O2 while half of them received invasive O2.

We found that some variables significantly affect survival days since COVID-19 diagnosis regardless of increasing or decreasing the timing of death as the aged from 60-80 years, having diabetes, having cancer, and developing septic shock decreased the survival days and increased the rate of mortality while living in the southern West Bank, receiving intubation, having hypothyroidism, developing arrhythmia, receiving Tocilizumab increased the survival days and decreased the rate of mortality.

Furthermore, each of age and gender had an effect on some study variables, as study sample comparison by age, each of hospital days, non-invasive O2, invasive O2, fever as a symptom, diabetes, hypertension, ischemic heart disease, heart failure, cerebrovascular accident (CVA). and obesity as comorbidity, cardiogenic shock, MI, acute kidney injury, and hyper coagulopathy as a complication showed a significant relationship. While study sample comparison by gender, each of O2 support, nausea and vomiting as symptoms, obesity, hypothyroidism and ischemic heart disease as a comorbidity, and arrhythmia as a complication showed a significant relationship where is no significant relationship between gender and hospital days.

The indicators such as imaging investigation and lab tests showed abnormal findings that predicted to worse COVID-19 prognosis. On one hand, among reported imaging investigations with a chest x-ray and high-resolution CT, pulmonary infiltrates were the most reported finding followed by ground-glass lung opacities and bilateral pneumonia which was more than unilateral pneumonia. On the other hand, there was wide a variety of hematologic manifestations, including anemia, thrombocytopenia, leukocytosis, leukopenia, CRP, elevated iron, elevated d-dimer, elevated creatinine, elevated LDH, elevated CK, elevated troponin, acidosis, alkalosis, hyponatremia, hypernatremia, hypokalemia, and hyperkalemia.

The time factor clearly appeared in our study as 2 third of patients died within 2 weeks from admission, and the initiation of giving the non-invasive O2 was early with a mean of one day from admission while the decision of intubation related to severe respiratory failure, cardiac arrest, and increase the risk of death with mean of 7 days from the admission that increased the survival to less than 7 days for 2 third of patients. In the same context, the mean of means of first abnormal result from admission among all laboratory tests was 4.7. Therefore, the timely identification of COVID-19 severity by biomarkers would help to provide the appropriate intervention on time.

Regarding intervention, most of the hospitals included in our study followed a similar protocol by giving corticosteroids, anticoagulants, mineral and vitamin supplements, antivirals, and antibiotics as their treatment options without significant effect on survival days except Tocilizumab as mentioned above. Interestingly, 97.1% of patients were given antibiotics in spite of only 19.1% having given antibiotics for the coexisting secondary infection which may increase the risk of the emergence of antimicrobial resistant organisms among surviving patients.

5.12 Limitations

- Large sample size and more time needed in data collection.
- Israeli obstacles prevented accessing Jerusalem hospitals easily.
- Administrative limitations in accessing the hospitals and their database.
- Lack of national database for all variants.
- Some hospitals have still depended on paper registration rather than computerized one.
- Lack of documentation of some variables such as smoking status, blood group, and radiology reports for many deaths, thus causing missing data.

- The absence of a designated place for researchers in many hospitals.
- Lack of national standard treatment protocol.
- Lack of radiologists as no x-ray reports were found in patients files.
- Computerized health information system (HIS) has many defects regarding research issues.
- High cost of the research without the availability of funding.

5.13 Recommendations

Recommendations for people at risk for COVID-19 mortality

- Avoid exposure to COVID-19 or any infectious disease.
- Receiving vaccinations is the best way of protection.
- Early detection and early treatment.
- Following a healthy lifestyle as a healthy diet and avoiding smoking.
- Apply preventive precautions such as hand hygiene.

Recommendation for decision makers and medical team

- Giving priority to vaccinations for persons at COVID-19 risk as the elderly.
- Providing more attention for groups at risk especially people in 61-80 years.
- Giving more attention for pregnant and people with A+ blood group.
- Considering the deterioration timing at infected people through the intervention.
- Well control of comorbidities such as diabetes, hypertension, and respiratory diseases.
- Good monitoring of renal function and the causes of renal impairment inpatient with COVID-19 infection.
- Education of patients with chronic disease especially the cancer about the risk of COVID-19 infection.
- Stewardship of using antibiotics in the hospitals to avoid the emergence of antimicrobial-resistant organisms.
- Design a national unified standard protocol for treatment and follow up the implementation.
- Employment of medical specialists and subspecialist as ICU physicians, pulmonologists, radiologists, anesthesia specialists and internist in center and peripheral hospitals.

- Training the medical staff for dealing with outbreaks, epidemics, or pandemics and regular updating.
- Construct an electronic national database for all inpatient characteristics.
- Strengthen the computerized HIS system and networking with all hospitals.
- Absorbing people with a master of infectious diseases to strengthen nosocomial infection control and conducting research in different hospitals.
- Inclusion of infectious diseases within the compulsory courses of all study plans in universities to increase awareness and decrease community-acquired infections.
- Supporting the local pharmaceutical companies in producing vaccines by MOH and academic people.

Recommendations for researchers

- Further similar studies are needed.
- Conducting studies about the mortality related to post-COVID-19 or COVID-19 vaccine.
- Conducting more studies about the risk of pregnancy, smoking, blood groups, and coagulation along with the effectiveness of Tocilizumab.

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Annex

Annex (1): Data Collection Sheet

Demographic data	Case serial number	#
	Hospital name	(…)
	Gender	Male\Female
	Age	#
	Pregnancy	Yes\No
	Governorate	(…)
	Smoking Status	Yes\No
	ABO	(…)
Last admission data	Date of admission	d\m\y
	Date of death	d\m\y
	Date of diagnosis (positive PCR)	d\m\y
O2 requirement	O2 need?	Yes\No
	First Date	d\m\y
	Non-Invasive	Yes\No
	First Date	d\m\y
	Invasive	Yes\No
	First Date	d\m\y
Symptoms and signs	Fever	Yes\No
	Fatigue	Yes\No
	Myalgia	Yes\No
	Cough	Yes\No
	Shortness of breath	Yes\No
	Chest discomfort	Yes\No
	Sore throat	Yes\No
	Rash	Yes\No
	Headache	Yes\No
	Seizure	Yes\No
	Abdominal pain	Yes\No
	Diarrhea	Yes\No
	Constipation	Yes\No
	Nausea	Yes\No
	Vomiting	Yes\No
	Sweating	Yes\No
	Neurological abnormalities	Yes\No
	Chills	Yes\No
Comorbidities	Had comorbidities?	Yes\No
	Diabetes mellitus	Yes\No

	Hypertension	Yes\No	
	Ischemic heart disease	Yes\No	
	Heart failure	Yes\No	
	Cerebrovascular accident	Yes\No	
	Valvular Heart disease	Yes\No	
	Cancer	Yes\No	
	Respiratory diseases	Yes\No	
	Obesity; BMI >40	Yes\No	
	Kidney disease	Yes\No	
	Hypothyroidism	Yes\No	
	Other	(…)	
Complications	Cardiogenic shock	Yes\No	
	Septic shock	Yes\No	
	Hepatic dysfunction	Yes\No	
	Hyper Coagulopathy status	Yes\No	
	Heart failure	Yes\No	
	Arrhythmia	Yes\No	
	Myocardial infarction	Yes\No	
	Sepsis	Yes\No	
	Pneumonia	Yes\No	
	Acute kidney injury	Yes\No	
	Cerebrovascular accident	Yes\No	
	Other	(…)	
Laboratory results for last admission & Dates	Hb (g/dl)	#	d\m\y
	WBC (x10^9/L)	#	d\m\y
	Platelets (K/uL)	#	d\m\y
	Ferritin (ng/mL)	#	d\m\y
	CRP (mg/L)	#	d\m\y
	D-dimer (ng/mL)	#	d\m\y
	Creatinine (mg/dl)	#	d\m\y
	lactate dehydrogenase (U/L)	#	d\m\y
	Creatine kinase (U/L)	#	d\m\y
	Troponin (ng/mL)	#	d\m\y
	Blood PH	#	d\m\y
	Sodium (mmol/l)	#	d\m\y
	Potassium (mmol/l)	#	d\m\y
	Blood culture result	Positive\Negative	d\m\y
	Urine culture result	Positive\Negative	d\m\y
	Sputum culture result	Positive\Negative	d\m\y
Imaging finding	Chest x-ray	Yes\No	
	High resolution CT	Yes\No	

	Angio CT	Yes\No
	Ground-glass lung opacities	Yes\No
	Pulmonary infiltrates	Yes\No
	Unilateral pneumonia	Yes\No
	Bilateral pneumonia	Yes\No
	Pleural effusion	Yes\No
	Lobar consolidation	Yes\No
	ARDS Picture	Yes\No
Management (Drugs & supplements)	Dexamethasone	Yes\No
	Enoxaparin	Yes\No
	Remdesivir	Yes\No
	Zinc	Yes\No
	Vitamin D	Yes\No
	Tocilizumab	Yes\No
	Had Co-infection?	Yes\No
	Received Antibiotics?	Yes\No
	Meropenem	Yes\No
	Ceftriaxone	Yes\No
	Ceftazidime	Yes\No
	Ciprofloxacin	Yes\No
	Azithromycin	Yes\No
	Ampicillin-Tazobactam	Yes\No
	Vancomycin	Yes\No
	Levofloxacin	Yes\No
	Colistin	Yes\No
	Other	(…)

Annex (2): Cox proportional Hazard model for survival of COVID 19 patients

Variables		P-value	HR	95.0% CI	
				Lower	Upper
Fever	Yes	.174	1.107	.956	1.281
Fatigue	Yes	.948	.993	.812	1.216
Myalgia	Yes	.539	.920	.706	1.200
Cough	Yes	.071	.867	.743	1.012
Shortness of breath	Yes	.196	.825	.617	1.104
Chest discomfort	Yes	.076	1.224	.979	1.531
Sore throat	Yes	.634	1.096	.752	1.598
Rash	Yes	.130	.405	.126	1.306
Headache	Yes	.697	.958	.774	1.187
Seizure	Yes	.266	1.402	.773	2.542
Abdominal pain	Yes	.471	1.107	.840	1.457
Diarrhea	Yes	.394	1.098	.885	1.363
Constipation	Yes	.120	1.361	.922	2.010
Nausea	Yes	.178	1.314	.883	1.954
Vomiting	Yes	.400	.828	.533	1.285
Sweating	Yes	.203	.815	.595	1.117
Neurological abnormalities	Yes	.255	1.246	.854	1.818
Chills	Yes	.519	.933	.756	1.152

Annex (3): Study Period

	Sep-21	Oct-21	Nov-21	Des-21	Jan-22	Feb-22	March-22	April-22	May-22	Jan-22	Julay-22	Aug-22	Sep22	Oct-22	Nov-22	Des-22	Jan-23	Feb-23	March-23	April-23
Literature review																				
Proposal writing																				
Piloting																				
Data collection																				
Data analysis																				
Thesis writing																				

Annex (4): Approval letter from research ethical committee of public health collage

Al-Quds University
Jerusalem
School of Public Health

جامعة القدس
القدس
كلية الصحة العامة

التاريخ: 2022/1/29

عزيزتي الطالبة ضحى حمامدة المحترمة
برنامج ماجستير: الوقاية وضبط الامراض المعدية

الموضوع: موافقة لجنة اخلاقيات البحث العلمي

قامت اللجنة الفرعية لأخلاقيات البحث التابعة لكلية الصحة العامة بمراجعة مشروع الرسالة
بعنوان:
" Clinical characteristics and Risk factors for COVID-19 deaths in the West Bank"
المقدم من (مشرف الرسالة/ د. اسعد رملاوي).
يعتبر مشروعك مستوفيًا لمتطلبات أخلاقيات البحث في جامعة القدس.
نتمنى لكم كل التوفيق في تسيير المشروع.

رئيسة لجنة اخلاقيات البحث
د. نهى الشريف

نسخة/ أعضاء لجنة البحث
نسخة/ الملف

Annex (5): Approval letter from the Palestinian MOH

State of Palestine
Ministry of Health
Education in Health and Scientific Research Unit

دولة فلسطين
وزارة الصحة
وحدة التعليم الصحي والبحث العلمي

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

الرقم: عبد/٤١٤/٢٠٢٠
التاريخ: ٢٠٢٠/٤/٢٠

عطوفة الوكيل المساعد المدير التنفيذي لمجمع فلسطين الطبي المحترم،،،
الأخ مدير عام الادارة العامة للمستشفيات المحترم،،،
تحية واحترام،،

الموضوع: تسهيل مهمة بحث

مرفق طلب تسهيل مهمة الطالب: ضحى حمامده– ماجستير الوقاية وضبط الامراض المعدية/ كلية الصحة العامة/ جامعة القدس، وباشراف د. أسعد رملاوي، في عمل بحث بعنوان:

Clinical Characteristics and Risk Factors COVID-19 deaths in the "West Bank"

من خلال السماح للطالب بالحصول على معلومات من ملفات المرضى والبيانات الطبية للوفيات، وذلك في:

– جميع المستشفيات الحكومية المرفقة

على ان يتم الالتزام باساليب واخلاقيات البحث العلمي.
على ان يتم الالتزام بجميع تعليمات واجراءات الوقاية والسلامة الصادرة عن وزارة الصحة بخصوص جائحة كورونا، وتحت طائلة المسؤولية. وابراز شهادة التطعيم قبل دخول مرافق وزارة الصحة.
على ان يتم تزويد الوزارة بنسخة PDF من نتائج البحث، التعهد بعدم النشر لحين الحصول على موافقة الوزارة على نتائج البحث.

مع الاحترام،،

د. عبد الله القواسمي
مدير التعليم الصحي والبحث العلمي

نسخة: عميد كلية الصحة العامة المحترم/ جامعة القدس

Telfax.:09-2333901 scientificresearch.dev@gmail.com 09-2333901 :هاتف

State of Palestine
Ministry of Health
Education in Health and Scientific
Research Unit

دولة فلسطين
وزارة الصحة
وحدة التعليم الصحي
والبحث العلمي

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

الرقم .....
التاريخ .....

الاخ علي الحلو المحترم
مدير عام الادارة العامة لتكنولوجيا المعلومات .

الموضـــوع: تسهيل مهمة بحث

مرفق طلب تسهيل مهمة الطالب: ضحى حمامده– ماجستير الوقاية وضبط الامراض المعدية/ كلية الصحة العامة/ جامعة القدس، وباشراف د. أسعد رملاوي، في عمل بحث بعنوان:

Clinical Characteristics and Risk Factors COVID-19 deaths in the "West Bank"

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مع الاحترام...

د. عبد الله القواسمي
مدير التعليم الصحي والبحث العلمي

دولة فلسطين
وزارة الصحة
وحدة التعليم الصحي والبحث العلمي
صادر رقم 193/ MESR/
التاريخ 2/ 2022

نسخة: عميد كلية الصحة العامة المحترم/ جامعة القدس

Telfax: 09-2333901 scientificresearch.dep@gmail.com تلفاكس: 09-2333901

S-HESRU / Sent: 20/02/2022 /98

State of Palestine
Ministry of Health
Education in Health and Scientific
Research Unit

دولة فلسطين
وزارة الصحة
وحدة التعليم الصحي
والبحث العلمي

التاريخ 2022/02/20

عطوفة الدكتور كمال الشخرة حفظة الله
الوكيل المساعد لشؤون الصحة العامة وصحة الاسرة
تحية واحترام...

الموضـــوع: تسهيل مهمة بحث

يرجى تسهيل مهمة الطالب: ضحى حمامده– ماجستير الوقاية وضبط الامراض المعدية/ كلية الصحة العامة/ جامعة القدس، في عمل بحث بعنوان:

Clinical Characteristics and Risk Factors COVID-19 deaths in the "West Bank"

من خلال السماح للطالبة بالحصول على معلومات وبيانات طبية للوفيات المتعلقة بموضوع البحث.

على ان يتم الالتزام باساليب واخلاقيات البحث العلمي.
على ان يتم الالتزام بجميع تعليمات واجراءات الوقاية والسلامة الصادرة عن وزارة الصحة بخصوص جائحة كورونا، وتحت طائلة المسؤولية. وابراز شهادة التطعيم قبل دخول مرافق وزارة الصحة.
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مع الاحترام...

د. عبد الله القواسمي
مدير التعليم الصحي والبحث العلمي

دولة فلسطين
وزارة الصحة
وحدة التعليم الصحي والبحث العلمي
صادر رقم 193/ MESR/
التاريخ 20/02/2022

نسخة: عميد كلية الصحة العامة المحترم/ جامعة القدس

تلفاكس: 09-2333901 scientificresearch.dep@gmail.com

Annex (5): Approval letter from the Palestinian private hospitals

بسم الله الرحمن الرحيم

Al-Quds University
Jerusalem
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جامعة القدس
القدس
كلية الصحة العامة

التاريخ: 2022/3/2

حضرة الدكتور جاني ابو جوخة المحترم
مدير مستشفى ابن سينا

الموضوع: تسهيل مهمة الطالبة ضحى حمامده

تحية طيبة وبعد،،،
تقوم الطالبة ضحى حمامدة، برنامج ماجستير الوقاية وضبط الامراض المعدية/ كلية الصحة العامة/ جامعة القدس، لاعداد بحث رسالة باشراف الدكتور أسعد رملاوي بعنوان:

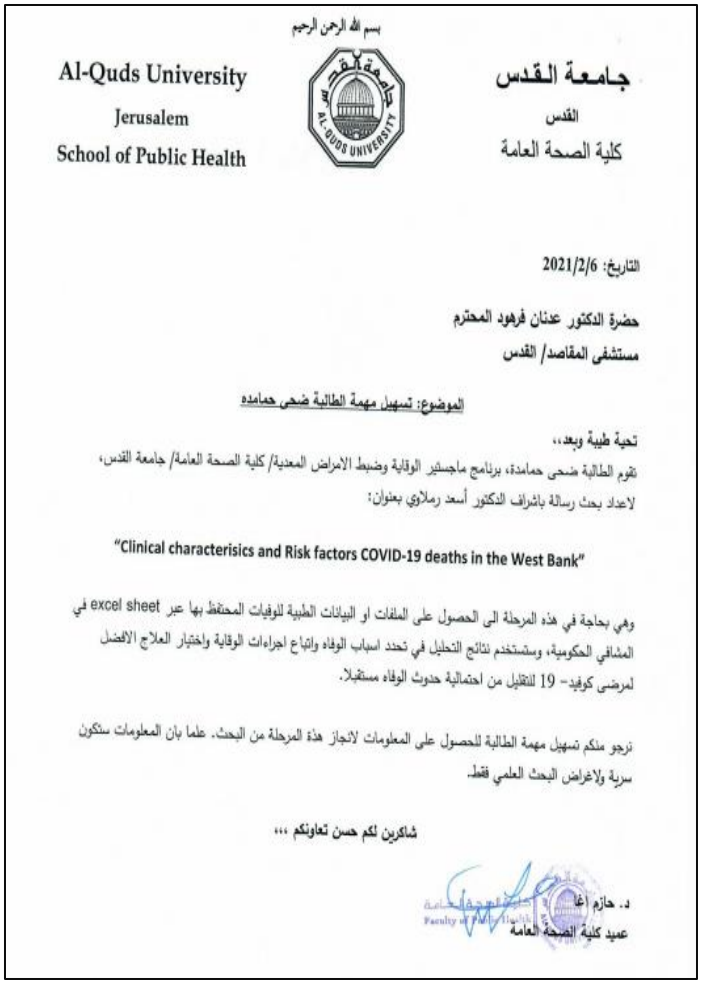
"Clinical characterisics and Risk factors COVID-19 deaths in the West Bank"

وهي بحاجة في هذه المرحلة الى الحصول على الملفات او البيانات الطبية للوفيات المحتفظ بها عبر excel sheet في مشفاكم، وستستخدم نتائج التحليل في تحدد اسباب الوفاه واتباع اجراءات الوقاية واختيار العلاج الافضل لمرضى كوفيد-19 للتقليل من احتمالية حدوث الوفاه مستقبلا.

نرجو منكم تسهيل مهمة الطالبة للحصول على المعلومات لانجاز هذة المرحلة من البحث. علما بان المعلومات ستكون سرية ولاغراض البحث العلمي فقط.

شاكرين لكم حسن تعاونكم ،،،

د. حازم اغا
عميد كلية الصحة العامة



بسم الله الرحمن الرحيم

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التاريخ: 2021/2/6

حضرة الدكتور عدنان فرهود المحترم
مستشفى المقاصد/ القدس

الموضوع: تسهيل مهمة الطالبة ضحى حمامده

تحية طيبة وبعد،،،
تقوم الطالبة ضحى حمامدة، برنامج ماجستير الوقاية وضبط الامراض المعدية/ كلية الصحة العامة/ جامعة القدس، لاعداد بحث رسالة باشراف الدكتور أسعد رملاوي بعنوان:

"Clinical characterisics and Risk factors COVID-19 deaths in the West Bank"

وهي بحاجة في هذه المرحلة الى الحصول على الملفات او البيانات الطبية للوفيات المحتفظ بها عبر excel sheet في المشافي الحكومية، وستستخدم نتائج التحليل في تحدد اسباب الوفاه واتباع اجراءات الوقاية واختيار العلاج الافضل لمرضى كوفيد-19 للتقليل من احتمالية حدوث الوفاه مستقبلا.

نرجو منكم تسهيل مهمة الطالبة للحصول على المعلومات لانجاز هذة المرحلة من البحث. علما بان المعلومات ستكون سرية ولاغراض البحث العلمي فقط.

شاكرين لكم حسن تعاونكم ،،،

د. حازم اغا
عميد كلية الصحة العامة

بسم الله الرحمن الرحيم

Al-Quds University
Jerusalem
School of Public Health

جامعة القدس
القدس
كلية الصحة العامة

التاريخ: 2021/2/6

حضرة الدكتور يوسف التكروري المحترم
مستشفى الاهلي/ الخليل

الموضوع: تسهيل مهمة الطالبة ضحى حمامده

تحية طيبة وبعد،،
تقوم الطالبة ضحى حمامدة، برنامج ماجستير الوقاية وضبط الامراض المعدية/ كلية الصحة العامة/ جامعة القدس، لاعداد بحث رسالة باشراف الدكتور أسعد رملاوي بعنوان:

"Clinical characterisics and Risk factors COVID-19 deaths in the West Bank"

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نرجو منكم تسهيل مهمة الطالبة للحصول على المعلومات لانجاز هذة المرحلة من البحث. علما بان المعلومات ستكون سرية ولاغراض البحث العلمي فقط.

شاكرين لكم حسن تعاونكم ،،،

د. حازم اغا
عميد كلية الصحة العامة

بسم الله الرحمن الرحيم

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التاريخ: 2021/2/6

حضرة الدكتور فادي الاطرش المحترم
مستشفى المطلع/ القدس

الموضوع: تسهيل مهمة الطالبة ضحى حمامده

تحية طيبة وبعد،،
تقوم الطالبة ضحى حمامدة، برنامج ماجستير الوقاية وضبط الامراض المعدية/ كلية الصحة العامة/ جامعة القدس، لاعداد بحث رسالة باشراف الدكتور أسعد رملاوي بعنوان:

"Clinical characterisics and Risk factors COVID-19 deaths in the West Bank"

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نرجو منكم تسهيل مهمة الطالبة للحصول على المعلومات لانجاز هذة المرحلة من البحث. علما بان المعلومات ستكون سرية ولاغراض البحث العلمي فقط.

شاكرين لكم حسن تعاونكم ،،،

د. حازم اغا
عميد كلية الصحة العامة

بسم الله الرحمن الرحيم

Al-Quds University
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التاريخ: 2021/2/6

حضرة الدكتور كمال حجازي المحترم
مستشفى النجاح/ نابلس

الموضوع: تسهيل مهمة الطالبة ضحى حمامده

تحية طيبة وبعد،،
تقوم الطالبة ضحى حمامدة، برنامج ماجستير الوقاية وضبط الامراض المعدية/ كلية الصحة العامة/ جامعة القدس، لاعداد بحث رسالة باشراف الدكتور أسعد رملاوي بعنوان:

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عميد كلية الصحة العامة