Al-Quds University

Deanship of Graduate Studies

Faculty of Public Health

The Power of C-Reactive Protein Biomarker in Detecting the Severity Progress of COVID-19 Patients' Illness.

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Thesis Approval

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Dedication

This research is humbly dedicated to Allah. It is in honor of my esteemed teacher, Prophet Mohammed, and in tribute to my homeland, Palestine, a symbol of resilience and courage embodied by the great martyrs and prisoners who stand as beacons of sacrifice.

I extend this dedication to my remarkable parents, whose endless selflessness and sacrifices have been my guiding force. To my beloved brothers and sisters, whose presence is a constant source of strength.

A special dedication is given to my cherished wife, whose hope and support illuminate my path, and to my beloved children, Zain, Yousef, and Abd Al Rahman, who drive my endeavors.

Gratitude is also extended to Al-Quds University, a magnificent abode of learning that has been like a second home to me. I sincerely appreciate my advisor, Dr. Atef Al Rimawi, for his invaluable guidance, patience, and support throughout this journey.

This work is also in honor of my entire family, the epitome of love and generosity.

In dedicating this research, I celebrate these pillars of my life.

Declaration

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

Signature:

Mohammed Yousef Hasan Awad

Date: 3/1/2024

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Abstract

Background: Identification of COVID-19 patients at high risk increases the risk of admission to intensive care units (ICUs); mechanical ventilation and advanced management (use of inotropic dialysis machines) and patient mortality can significantly improve patient management and resource allocation within hospitals. This study seeks to identify reliable biomarkers for patient outcomes, which has been critical. This study focuses on C-reactive protein (CRP) as a significant indicator and examines its relationship with patient outcomes (discharged or deceased) and patient status (severe illness or critical illness) in COVID-19 cases.

Method: A quantitative retrospective descriptive and correlation study was conducted at Istishari Arab Hospital (IAH) – in Ramallah, Palestine. A consecutive non-probability sampling method was used, SPSS, to present descriptive results, frequencies, percentages, means, and standard deviation. We also employed quantitative analysis with chi-square tests and adjusted residuals to investigate the association between CRP levels with patient outcomes (discharge or deceased) and patient status (severe illness or critical illness) in COVID-19 cases.

Results: The study found a statistically significant association between CRP levels and patient outcomes. Elevated CRP levels correlated with increased severity of illness and higher mortality rates. Adjusted residuals indicated a clear gradient in patient outcomes based on CRP levels.

Conclusion: CRP levels are a valuable prognostic biomarker in assessing the severity and outcomes of COVID-19. These findings provide actionable insights for healthcare professionals and contribute to the broader understanding of COVID-19 management and prognosis. The study recommends further research for comprehensive analysis and application in clinical practice.

دراسة **قوة المؤشر الحيوي للبروتين التفاعلي (CRP) في الكشف عن مدى تقدم و شدة المراضة للمرضى المصابين بكوفيد 19.**

اعداد: محمد يوسف حسن عواد

المشرف : الدكتور عاطف الريماوي

الملخص

المقدمة: أثناء تعرض العالم لجائحة كورونا وما تخللها من تأثيرات وبائية، كان تحديد المرضى الأكثر عرضة لتأثيرات فيروس Covid-19 من التحديات الكبيرة، نظراً لما بنطوي عليه هذا الأمر من عامل حاسم لتحسين أولويات التعامل مع المرضى وتخصيص الموارد الطبية والدوائية بشكل فعال في المستشفيات. تركز هذه الدراسة على الفحص المخبري للدم (CRP) باعتباره مؤشراً رئيسياً لربط العلاقة بين نتائج تحليل المرضى المصابين بفيروس Covid-19 وطبيعة شدة تأثير المرض عليهم (درجة شديدة، درجة حرجة) إضافة للوفيات الناجمة عن الإصابة بالفيروس.

المنهجية: تم تنفيذ الدراسة من عدة جوانب؛ كمية ووصفية واسترجاعية وبحث العلاقة، وفقاً لبيانات المستشفى الاستشاري العربي خلال الفترة ابريل 2020 وابريل 2022 للمرضى الذين تعامل معهم المشتفى، وقد تم تحليل كافة البيانات ضمن الدراسة باستخدام برنامج (SPSS) لعرض وتحليل البيانات، كما تم استخدام نموذج اختبار الاحصائي Chi Square Test لاختبار النتائج الوصفية والتحليل الكمي لفحص العلاقة بين مستويات CRP وحدة تأثير الفيروس على المرضى.

النتائج:وجدت الدراسة أن هناك علاقة إحصائية بين مستويات CRP وحدة تأثير الفيروس على المرضى من خلال، حيث ارتبط ارتفاع مستويات نتائج الفحوص المخبري CRP مع سوء حالة المرضى وارتبط أيضاً ارتفاع مستوى النتائج المخبرية مع زيادة معدلات الوفاة.

الخلاصة:خلصت الدراسة إلى ارتباط ارتفاع مستويات CRP مع حدة تأثير الفيروس على المرضى، وهذا يعتبر مؤشراً قيماً يفتح آفاق عملية لأولويات تعامل المنشآت والطواقم الصحية مع الحالات المصابة بفيروس COVID-19، كما تسهم في إدراك أوسع لإدارة وتشخصي المرضى المصابين بالفيروس، وعليه فإن الدراسة توصي بإجراء مزيد من البحوث التحليلية الشاملة بشكل أوسع وتطبيقها في الممارسات السريرية اللاحقة

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List of Abbreviations

CRP	C-Reactive Protein: A biomarker of inflammation, often elevated in COVID-19 patients
CRP1	C-Reactive Protein level on the day of admission
CRP2	C-Reactive Protein level second day of admission
CRP3	C-Reactive Protein level two days before discharge or deceased the day of admission
CRP4	C-Reactive Protein level day of discharge or deceased the day of admission
ICU	Intensive Care Unit: A specialized hospital department for critically ill patients
PCR (RT-PCR)	Polymerase Chain Reaction (Reverse Transcription-PCR): A technique for amplifying and detecting DNA/RNA sequences, used in COVID-19 diagnosis
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2: The virus causing COVID-19
SUH	Stanford University Hospital: One of the hospitals involved in the study
COVID-19	Coronavirus Disease 2019: The disease caused by SARS-CoV-2
ANOVA	Analysis of Variance: A statistical method to compare means of different groups
SPSS	Statistical Package for the Social Sciences: Software for statistical analysis
LOS	Length of Stay: Duration of hospitalization
JCI	Joint Commission International: Organization for healthcare accreditation
EMR	Electronic Medical Records: Digital records of patient health information
CDC	Centers for Disease Control and Prevention: U.S. national public health institute
WHO	World Health Organization: UN agency for international public health
NIH	National Institutes of Health: U.S. agency for biomedical and public health research
SARS	Severe Acute Respiratory Syndrome: A respiratory illness caused by a coronavirus
MERS	Middle East Respiratory Syndrome: A respiratory illness caused by a coronavirus

Definitions

- COVID-19: short for Coronavirus Disease 2019, is the infectious disease caused by the most recently discovered coronavirus, SARS-CoV-2. This novel virus and disease were unknown before the outbreak began in Wuhan, China, in December 2019. COVID-19 quickly spread globally, leading to an ongoing pandemic. The disease manifests primarily with respiratory symptoms, ranging from mild to severe, and can lead to death in severe cases.(World Health Organization., 2023)
- Severe COVID-19 Illness: This condition involves significant symptoms that generally necessitate hospitalization. Key characteristics include difficulty in breathing, oxygen saturation below 94% on room air at sea level, a ratio of arterial oxygen partial pressure to fractional inspired oxygen below 300, and lung infiltrates greater than 50%. Patients often require supplemental oxygen.
- Critical COVID-19 Illness: This is the most severe form of COVID-19. Patients typically exhibit complications such as respiratory failure, septic shock, and multiple organ dysfunction or failure. Management often requires mechanical ventilation and intensive care support.(National Institutes of Health (NIH), 2023)

Chapter One

1.0.Introduction

Knowing that Coronavirus Disease 2019 it's not the first outbreak occurring from this family of viruses, the first coronavirus disease is a severe acute respiratory syndrome (SARS) and the Middle East Respiratory Syndrome (MERS) which has appeared in the past two decades. The third outbreak was in December 2019. Coronavirus disease (COVID-19) first appeared in China and has spread worldwide, forcing the World Health Organization (WHO) to decline COVID-19 as a pandemic in March 2020. (World Health Organization, 2020)

The mode of transition of this virus is droplets. While the patient is sneezing and coughing, the virus spreads everywhere through the infected person, resulting in its fast spread among people. According to the WHO COVID-19 dashboard, the statistics of the infected cases from the first moment of the primary cases to 8 April 2022, more than 490,000,000 million people were confirmed with the virus worldwide, and more than 6,170,000 deaths have occurred due to the disease. Accordingly, to reduce the mortality of the disease, the patient severity and the effectiveness of the early intervention for COVID-19 patients should be monitored (World Health Organization, 2021).

A recent study shows the majority of patients with COVID-19 signs and symptoms develop mild to moderate symptoms, with quick recovery, and patients who develop severe forms have a high mortality rate, which can reach up to 60% in patients admitted to Intensive Care Unit (ICU) and treated with mechanical ventilation (Yang et al., 2020)

The Centers for Disease Control and Prevention (CDC) mentioned in the Interim Clinical Guidance for Management of Patients with confirmed COVID-19 that patients can range from mild to critical ill symptoms in the mild to moderate category; mild symptoms up to mild pneumonia present 81%, Severe symptoms; dyspnea, hypoxia or more than 50 % lung involvement on imaging present around 14% and critical ill symptoms; range from respiratory failure, shock and multiorgan failure present 5% of total patients. (CDC, 2020). The involvement of human body systems such as Neurologic, Cardiovascular, and coagulation Cascade. Rise the urge to identify biomarkers for the disease severity, which could help to determine the patients who are at risk of developing severe symptoms or death after prolonged admission to intensive care.

The inflammation response which occurs in the body can be detected using multiple blood tests and biomarkers, such as markers of the inflammatory response, to identify the chemical severity and complication. (Auld et al., 2020; Sharifpour et al., 2020; Wu & McGoogan, 2020).No specific biomarker has been identified as a defiant (Placeholder1) indicator; however, the CRP is one of them, as several studies reported that CRP levels are elevated in patients with COVID-19 and may correlate with the severity of the disease and disease progression.(Vasileva & Badawi, 2019; J. T. Wang et al., 2004; Zeng et al., 2020). During the pandemic, the lack of ICU beds and the increase in the demand for Mechanical ventilation led to the use of simple, easy, inexpensive, fast, and reliable biomarkers to assess the prognosis of those patients. (Auld et al., 2020; Sharifpour et al., 2020; Wu & McGoogan, 2020).

1.1.The Problem of the Study

In 2003, the world woke up to the news of an outbreak of severe acute respiratory syndrome (SARS), which spread quickly between countries, resulting in more than 8,000 infected patients, with approximately 10% mortality. (LeDuc & Barry, 2004). In 2012, another coronavirus relative, the Middle East Respiratory Syndrome Coronavirus (MRSA), appeared in Saudi Arabia, and according to the World Health Organization report, in September 2019, more than 2000 confirmed cases were identified. (Al-Tawfiq et al., 2021). In December 2019, an outbreak of coronavirus (COVID-19) showed up in China, and then the pandemic spread to become a worldwide health challenge and problem due to the highly contagious characteristics of the virus and infected more than 490,000,000 million.

The patients with COVID-19 mortality are higher than regular patients, as mentioned in a systematic review study, which presents more than 10% for adult patients and 345 for critically ill patients (Potere et al., 2020). The world's countries found themselves facing a pandemic disease that must be dealt with without any delay, and the healthcare systems have to respond to the dramatic spread of infection. The cases become more dependent on intensive care services. This increase in ICU care increased rapidly and suddenly. Efforts were exerted to face these challenges and attempts to reduce the need for intensive care by providing treatment before the patient's health condition deteriorated. Blood tests monitor and assess the progress of the patient's condition. The risk of COVID-19 patients who present with mild symptoms of worsening and becoming severely ill was high and significant among admitted COVID-19 patients. The biggest challenge that treating physicians face is identifying and predicting those patients' early stages of the disease. This study will try to study the ability of the CRP test, one of the biomarkers, to predict the prognosis of COVID-19 patients. However, no single biomarker or test was identified as the cornerstone to rely on the progress of the disease.

1.2. Justification of the Study

Severely ill COVID-19 patients may need Intensive Care Units (ICUs) and become more dependent on oxygen and ventilation therapy by mechanical ventilation (Herold et al., 2020). Without knowing the progression of COVID-19 patients, the risk of late intervention or procedure increases the mortality or prolonged rehabilitation therapy ((Yuki et al., 2020). The result adds challenges to the healthcare systems, from the increased demand for ICU beds, qualified staff, oxygen therapy, and mechanical ventilation. The prediction of the prognosis of COVID-19 will result in quick and inexpensive recovery with available resources (Sharifpour et al., 2020). State of Palestine, the capacity and resources of the health care system which is considered under-resourced, mainly the ICU beds and ICU specialists. This shortage and insufficiency complicated the increased demand, primarily the severe cases, which yields more pressure on the Palestinian health care system. No available studies were found in Palestine about any reliable method for predicting COVID-19 progress. (Palestine ministry of health, 2021)

1.3.Purpose of the study

The study aims to assess the reliability of CRP in predicting the severity prognosis of COVID-19 patients.

1.4.Objectives

1.4.1. To assess the correlation between CRP levels and the severity of COVID-19 prognoses.

1.4.2. To examine the relationship between CRP levels and other biomarkers for COVID-19 patients.

1.4.3. To predict the ability of CRP to measure the severity of COVID-19 patients' prognosis.

1.5.Research Question

1.5.1. What is the relationship between the CRP test and the severity prognosis (severe and critically ill) of COVID-19 patients?

1.5.2. Does the CRP test predict the prognosis of COVID-19?

Chapter Two

Literature Review

2.0.Introduction

An overview of the available literature explores the severity of COVID-19 and patient characteristics, in addition to outcomes after the infection, and similar studies suggest the prediction of CRP in severely and critically ill COVID-19 patients. Intensive research in electronic resources was conducted using different databases, including PUBMED, EBSCO, HINIRI, and Google Scholar search. The researcher found a few similar studies conducted in China, the United States of America, and the European Union, which examined the prediction of biomarkers of the severity and the outcomes of COVID-19. There are no studies in the Arab world.

2.1.Coronavirus disease 2019 (COVID-19).

A new viral infection spread in Wuhan City, China, in December 2019, then quickly discovered that a novel coronavirus(2019-nCoV) was responsible for this disease. On January 3, 2020 (2019-nCoV), using samples of bronchoalveolar lavage fluid from a patient in Wuhan and using full-genome sequencing and phylogenic analysis showed that viral is beta coronaviruses associated with human severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) (Zhu et al., 2020). The new viral was named the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2, 2019-nCoV), which caused acute respiratory distress syndrome (ARDS) and high mortality from (2002- 2003) viral.(Ksiazek et al., 2003; Maciej Serda, 2013)

The virus affects the respiratory system as the main organ, and the involvement of other systems may occur during the infection. The primary symptoms of the lower respiratory tract that appears in patients in China were fever (84 %), dry cough (83%), and dyspnea (33%) (H. Huang et al., 2021; D. Wang et al., 2020). Also, other symptoms may appear, such as generalized weakness, dizziness, and headache in addition to Gastrointestinal (GI) symptoms, abdominal pain, nausea, vomiting, and diarrhea (2-8) % (Chen et al., 2020; Shi et al., 2020).In summary, the symptoms may start from mild to severe with hypoxia and ARDS presentation, which develop within a few days (H. Huang et al., 2021).

At the outbreak's start in Wuhan, epidemiological investigations identified an initial link to a seafood market that sold live animals. Many affected individuals had either worked at or visited this market, which was subsequently closed for disinfection(Jaakkola, 2020). However, as the outbreak progressed, person-to-person transmission became the primary mode of spreading the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Person-to-person transmission of the virus is believed to occur mainly through respiratory droplets, like how influenza spreads. When the sick person sneezes, coughs, or talks, the virus is released in respiratory secretions, which can infect another person if they come into direct contact with the mucous membranes. If the person touches a contaminated surface and then touches their eyes, nose, or mouth, infections can also happen. Generally, droplets do not travel more than six feet (about two meters) and do not stay suspended in the air. However, due to the current uncertainties surrounding transmission mechanisms, some countries recommend airborne precautions as a routine measure, while others suggest implementing them during specific high-risk procedures. (CDC, 2020).

According to scientific research involving full-genome sequencing and phylogenetic analysis, it has been established that the coronavirus responsible for the COVID-19 pandemic

belongs to the beta coronavirus subgenus. This subgenus shares similarities with the severe acute respiratory syndrome (SARS) virus and various bat coronaviruses. However, it is categorized into a distinct clade within this subgenus. The receptor-binding gene region of this coronavirus shows a significant resemblance to that of the SARS coronavirus, and it has been scientifically confirmed that it utilizes the angiotensin-converting enzyme 2 (ACE2) receptor for cell entry(McIntosh et al., 2020). In recognition of these findings, the Coronavirus Study Group of the International Committee on Taxonomy of Viruses has proposed naming this virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). (Gorbalenya, Baker, Baric, de Groot, et al., 2020).

The Middle East respiratory syndrome (MERS) virus, belonging to the beta coronavirus family, shows a more distant relationship to the COVID-19 virus(Gorbalenya, Baker, Baric, Groot, et al., 2020), (Baloch et al., 2020). Two bat coronaviruses exhibit the closest RNA sequence similarity, suggesting that bats are likely the primary source. However, it remains unclear whether the COVID-19 virus is transmitted directly from bats or through an intermediate host(Fehr & Perlman, 2015).

2.2.COVID-19 Patients' characteristics, severity, and outcomes.

A retrospective cohort study aimed to find the Coronavirus Disease 2019 Severity and Risk of Subsequent Cardiovascular Events. The study included a total of 1,357,518 adults diagnosed with COVID-19. This was a retrospective cohort study conducted using nationwide health insurance claims data from the US Health Verity Real-Time Insights and Evidence database. The study included adults aged 18 years and older diagnosed with COVID-19 between April 1, 2020, and May 31, 2021. The severity of COVID-19 was categorized based on the level of care required: intensive care unit (ICU) admission, non-ICU hospitalization, or outpatient

care only. The association between COVID-19 severity and the risk of cardiovascular events (CVEs) >30 days after COVID-19 diagnosis was evaluated using inverse probability of treatment–weighted competing risks regression. Various demographic and clinical characteristics were considered as covariates in the analysis. The study found that COVID-19 patients who were hospitalized or required critical care had a significantly higher risk of experiencing and being hospitalized for post–COVID–19 cardiovascular events compared to patients with milder COVID-19 managed in the outpatient setting. Also, the risk of any cardiovascular event was increased for patients requiring ICU admission or non-ICU hospitalization. The risk of subsequent hospitalization for cardiovascular events was even higher for ICU patients and non-ICU hospitalized patients compared to outpatients. The findings of this study emphasize the importance of preventing severe COVID-19 illness by reducing the risk of long-term cardiovascular complications. (Wiemken et al., 2023)

A large observational cohort was used to study the patient characteristics and outcomes of 11721 patients with coronavirus disease 2019 (COVID-19) hospitalized in the United States of America. Hospital chargemaster data on adult patients with COVID-19 admitted to 245 hospitals in 38 states between February 15 and April 20, 2020, assessed. The clinical course from admission through hospitalization to discharge or death was analyzed. However, the research focused on examining patients' clinical progression from admission throughout their hospital stay until discharge or death. Most patients were over 60 (59.9%) and male (53.4%). Common comorbidities observed among the patients included hypertension (46.7%), diabetes (27.8%), cardiovascular disease (18.6%), obesity (16.1%), and chronic kidney disease (12.2%). Mechanical ventilation is required for 1,967 patients (16.8%). The mortality rate among hospitalized patients was 21.4%, which increased to 70.5% among those who needed mechanical ventilation. Several risk factors, including male sex, older age, obesity, geographic

region, and chronic kidney disease or preexisting cardiovascular disease, were associated with higher odds of mechanical ventilation and death. ((Fried et al., 2021)).

A retrospective study (Lobo-Valbuena et al., 2021) in Spain's secondary care hospitals was conducted to identify the Characteristics of critical patients with COVID-19. The sample size of 48 patients was included in the study researchers between March 5th and May 7th, 2020. The findings of the study show that the median age was 65 years. 65.3% were men, and 73.5% of the patients had associated comorbidity (cardiovascular, COPD, asthma or interstitial lung disease, chronic kidney disease, malignancy, endocrine diseases, chronic liver disease, and neurologic diseases).

Another retrospective chart review of demographic and clinical data for patients admitted to Stanford University Hospital (SUH) and Stanford Health Care-Valley Care (ValleyCare) in northern California in the United States of America by Ferguson et al., 2020conducted to explore the Characteristics and Outcomes of Coronavirus Disease Patients under Nonsurge Conditions the sample size was 72 patient meet the researchers' inclusion criteria which include all patients >18 years of age, hospitalized for >24 hours, PCR (RT-PCR)–confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and patients who spent >1 night in the hospital. The finding shows that patients' characteristics'were divided into three subgroups. The first was Demographic Characteristics based on ethnicity and place of residency. The second subgroup was concurrent Conditions. The finding was that (59.7%) of the patients had cardiovascular disease, (26.4) % had pulmonary disease, (and 8.3%) had an immunocompromised condition; on the other hand, the only condition common in ICU and Non-ICU patients was diabetes. In the third subgroup characteristics at admission, the common symptoms were fever (73.6%), dry cough (58.3%), and Shortness of breath (56.9%). (Ferguson et al., 2020b)

An analysis Summary of the Report for 72 314 Cases from the Chinese Center for Disease Control and Prevention revealed that 44,672 were confirmed COVID-19 cases based on positive viral tests. Suspected cases (16,186) were diagnosed based on symptoms and exposures, while clinically diagnosed cases (10,567) in Hubei Province relied on symptoms and lung imaging features. Asymptomatic cases (889) had positive viral tests but lacked typical symptoms. Most cases (87%) were between 30 and 79 years old, with Hubei Province and Wuhan-related exposures being predominant. Regarding severity, 81% of cases were classified as mild, 14% as severe, and 5% as critical. The overall case-fatality rate stood at 2.3%, with higher rates among older age groups and individuals with preexisting conditions. Notably, no deaths occurred in those aged nine years and younger. Among health workers, 3.8% of confirmed cases were reported, with 14.8% of these cases being severe or critical and resulting in 5 deaths. (Wu & McGoogan, 2020).

A retrospective study aimed to analyze the clinical features and outcomes of patients hospitalized with COVID-19 in a community hospital in the United States. The study included 16 hospitalized patients, and the primary composite endpoint was admission to the intensive care unit (ICU), shock, or death. The patients had a median age of 65.5 years, with 75% male. Common presenting symptoms included fever, cough, and dyspnea. Laboratory findings revealed frequent abnormalities such as hyponatremia, elevated C-reactive protein (CRP), and lactate dehydrogenase (LDH). Acute renal failure, myocardial injury, and elevated aminotransferases were also observed. The primary composite endpoint occurred in 50% of patients, and three deaths were reported among patients aged 70 years or older. These findings highlight the significance of laboratory abnormalities and the occurrence of severe complications in hospitalized COVID-19 patients. The study contributes to understanding the

clinical characteristics and outcomes of COVID-19 in the United States, emphasizing the need for comprehensive monitoring and management of patients with severe illness. (Aggarwal et al., 2020).

A study employed a systematic review and meta-analysis to examine the relationship between hypertension and severe/fatal COVID-19. The researchers conducted a comprehensive search and included relevant studies in their analysis. The pooled analysis revealed that hypertension is associated with a nearly 2.5-fold higher risk of severe COVID-19 and a 2.42-fold higher mortality risk. These findings suggest that hypertension may be a clinical predictor of worse COVID-19 outcomes. That meta-regression analysis also indicated a significant correlation between the mean age of patients with severe COVID-19 and the likelihood of hypertension and disease severity. This implies that the association between hypertension and COVID-19 severity may be influenced by age. These results highlight the importance of considering hypertension as a potential risk factor for severe and fatal COVID-19, especially in older individuals. (Lippi et al., 2020)

A Meta-Analysis was conducted for detecting Prevalence and severity of coronavirus disease 2019 (COVID-19). The study reviewed a total of 34 full-text studies. The study was conducted using data from clinical and epidemiological studies on confirmed cases of COVID-19. The search was conducted in Medline, EMBASE, Cochrane, and SinoMed Library databases. Data extraction and quality assessment were performed, and statistical analysis was conducted using STATA 15.0. The study found that the most common symptoms of COVID-19 were fever (85.6%), cough (65.7%), fatigue (42.4%), and dyspnea (21.4%). The prevalence of comorbidities was 7.7% for diabetes, 15.6% for hypertension, 4.7% for cardiovascular disease, and 1.2% for malignancy. Complications such as acute respiratory distress syndrome (ARDS), acute cardiac injury (ACI), acute kidney injury (AKI), and shock were observed in

5.6-13.2% of cases. The risks of severity and mortality ranged from 12.6% to 23.5% and from 2.0% to 4.4%, respectively. Critical cases were more prevalent in patients with diabetes (44.5%) and hypertension (41.7%). The study concluded that fevers are the most common symptom of COVID-19, and hypertension and diabetes are associated with the severity of the disease. Complications such as ARDS and ACI pose significant challenges to patient recovery. The overall case severity rate and mortality were lower than SARS and MERS. (Hu et al., 2020).

A cohort study was conducted in 33 hospitals between the United States and southern Europe to contribute a new way of finding the clinical characteristics of COVID-19. Using a comprehensive sample, the sample size was 3062 adult patients confirmed with SARS-CoV-2 using the PCR wear. The hospitals were divided into a derivation cohort and a validation cohort. One of the patients' characteristics they included was the CRP level due to his widely available, which has been independently observed as a biomarker of COVID-19 severity. The result was that CRP values outside the reference ranges do not necessarily increase mortality risk. However, a CRP level of more than 130 mg/dl significantly increases the mortality risk. (Bertsimas et al., 2020).

Another Systematic Review and Meta-Analysis study was conducted to study the Severity of COVID-19 in Lymphopenia patients. The sample size was 3,099 patients from 24 studies. The researcher's methodology was a systematic review and meta-analysis of research articles in adult patients diagnosed with COVID-19. Lymphocyte count and outcomes such as mortality, ARDS, ICU care, and severe COVID-19 were analyzed. The study's findings were that patients with poor outcomes had lower lymphocyte counts. Subgroup analysis showed lower counts in patients who died, experienced ARDS, received ICU care, and had severe COVID-19. Lymphopenia was associated with severe COVID-19. Age influenced the association between lymphocyte count and poor outcomes. (Huang & Pranata, 2020).

2.3.The Studies that Assessed the relation of CRP in discharged and deceased COVID-19 Patients.

In the study published in Scientific Reports, detailed statistical analysis was employed to elucidate the association between serum C-reactive protein (CRP) levels and COVID-19 mortality. The study involved a retrospective cohort from the Montefiore Health System, encompassing 3,545 patients with a median age of 63.7 years. Among these, 918 (25.9%) patients died during the post-admission cohort data collection period. The study revealed that when CRP levels were below 15.6 mg/L, the mortality risk increased significantly with each 10 mg/L increment in CRP, marked by an adjusted hazard ratio (HR) of 1.57 (95% CI 1.30–1.91, $P < 0.0001$). However, for CRP levels above 15.6 mg/L, the increase in mortality risk was less pronounced, indicated by an adjusted HR of 1.11 (95% CI 0.99–1.24, $P = 0.0819$) for every 10 mg/L increment. This detailed statistical analysis highlighted a nuanced relationship between CRP levels and mortality risk, emphasizing the importance of CRP as a biomarker in COVID-19 prognosis. (Li et al., 2023).

In a recent cohort study that aimed to investigate the potential value of various hemogram parameters and C-reactive protein levels in assessing mortality risk in COVID-19 patients, it was found that a number of parameters are significantly associated with mortality. The study included 148 patients with COVID-19 who were admitted to the hospital emergency department. Specifically, the parameters that were found to be statistically significant included LCRP, SII, NLR, PLR, CRP concentration, and comorbid diseases. The study also found that LCRP, NLR, PLR, and SII had high predictive capabilities for in-hospital mortality, as indicated by the ROC curve analysis. In addition, several independent predictors of in-hospital mortality were identified, namely LCRP less than 1, PLR, SII greater than or equal to 2699, white blood

cell count, CRP, age, comorbidities, and ICU stay. Taken together, these findings suggest that hemogram parameters and CRP levels could be useful in clinical practice to predict mortality risk in hospitalized COVID-19 patients. These results are highly significant, as they may help clinicians better understand and manage the disease in hospitalized patients. By identifying the key factors associated with mortality risk, medical professionals may be better equipped to provide appropriate interventions and improve outcomes for these patients. Further research is needed to confirm these findings and to develop more effective strategies for managing COVID-19.(Acar et al., 2021).

2.4.The Studies that Assessed the Prediction of CRP in Severe and Critically Ill COVID-19 Patients.

Through a retrospective study, the prognostic value of C-reactive protein (CRP) in COVID-19 was evaluated. The study, conducted between March 30 and April 30, 2020, included 429 patients diagnosed with COVID-19. The cohort was divided into severe (175 patients) and non-severe cases (254 patients), with a focus on demographic characteristics, clinical features, and laboratory findings at admission. The results indicated a significantly higher prevalence of elevated CRP levels in severe cases. CRP was identified as an independent factor in predicting COVID-19 severity, with a threshold of 64.75 mg/L for severe complications. The study underscores the importance of CRP as a predictive marker for the severity and progression of COVID-19, suggesting its utility in clinical decision-making. Further research is needed to refine the accuracy of CRP as a prognostic tool in diverse patient populations.(Sadeghi-Haddad-Zavareh et al., 2021)

A recent retrospective cohort study in Serbia found that elevated levels of D-dimer, CRP, PCT, and IL-6 at admission to the Intensive Care Unit (ICU) can predict in-hospital mortality in COVID-19 patients. The study included 318 patients and assessed their levels of biomarkers at admission and their association with in-hospital mortality. The study found that IL-6 levels above 74.98 pg/mL, CRP levels above 81 mg/L, PCT levels above 0.56 ng/mL, and D-dimer levels above 760 ng/mL were statistically significant predictors of mortality. These biomarkers may serve as essential predictors to identify patients with lower chances of survival and help guide treatment decisions. (Milenkovic et al., 2022)

Through a systematic review following the Preferred Reporting Item for Systematic Review and Meta-analysis (PRISMA) guidelines, the role of C-reactive protein (CRP) in predicting the severity of COVID-19 disease was investigated. The review included 20 articles with a total sample size of 15,434 participants, consisting of retrospective cohort studies and one case series study. A literature search was conducted using various databases and search engines, limited to English-language articles published during the COVID-19 epidemic until May 2021. Inclusion criteria involved studies reporting average CRP values and COVID-19 disease stage outcomes. The findings showed that patients with severe COVID-19 had significantly higher CRP levels than mildly infected patients, indicating CRP is a good biomarker for predicting disease severity. Further large-scale studies are needed to confirm the precision and accuracy of CRP as a predictor of COVID-19 severity. Nonetheless, investigating CRP levels can aid in detecting severe manifestations and improving prognosis, emphasizing the importance of CRP in predicting COVID-19 severity.(Yitbarek et al., 2021).

Researchers conducted a meta-analysis investigating the correlation between biomarkers of clinical laboratory tests (specifically serum C-reactive protein (CRP), serum amyloid protein (SAA), lactate dehydrogenase (LDH), and D-dimer (DD)) and poor prognosis

of COVID-19. They analyzed data from 7,739 patients with COVID-19 from 32 studies found through a comprehensive search of relevant databases, including PubMed (Medline), Web of Science, and Cochrane, up until March 1, 2021. The inclusion criteria involved original articles reporting on laboratory testing projects and outcomes of patients with COVID-19, specifically focusing on mortality, acute respiratory distress syndrome (ARDS), the need for care in an intensive care unit (ICU), and severe COVID-19. The researchers used random effects meta-analysis after synthesizing all the data and calculated mean difference (MD) and standard mean difference (SMD) at the biomarker level for different disease severities. They also calculated 95% confidence intervals (CI) and p-values. The analysis finds that elevated serum CRP, SAA, LDH, and DD levels are associated with a poor prognosis for COVID-19. Specifically, elevated serum CRP was significantly associated with a poor prognosis of COVID-19, while increased SAA levels were associated with an improved composite poor outcome in COVID-19. Elevated LDH levels were also associated with a poor composite outcome, and patients with a poor composite outcome exhibited higher DD levels. These findings suggest that monitoring these biomarkers could potentially help predict poor outcomes for COVID-19 patients. (Wang et al., 2021).

A descriptive case series study was conducted in China. The study aimed to describe the prediction of CRP Level at the Risk of COVID-19 aggravation for non-severe patients; the inclusion criteria were all patients who had laboratory-confirmed for COVID-19, adult patients (≥18 years old) who were admitted to the research hospital monitored from the period of January 17, 2021, to February 20, 2021. The total sample size was 209 patients, and the researchers were the clinical outcomes (severity and mortality). The use of Univariate and multivariate analyses using a logistic regression model to analyze the association between the progression of non-severe COVID-19 cases and related factors. The result shows that 16 patients (7.7%) wear

progressed to severe cases after admission, and the Laboratory findings for the aggravated patients on admission suggest that the CRP level (100.0%) was elevated in all 16 patients and one of the conclusions of the study that the elevation of the CRP level could be a valuable marker to predict the possibility of aggravation of no severe COVID-19 patients. (Wang et al., 2020).

A review article examines the relationship between C-reactive protein (CRP) levels and the severity of COVID-19 to find an early marker to predict risk for the severity of COVID-19 Sample Size: 3,443 patients who were involved. The study design in this review was by conducting a literature review and analyzing various clinical studies 12 studies investigating the serum concentration of CRP in patients with COVID-19. The studies included in the review were evaluated for CRP levels in both mild and severe COVID-19 cases. The findings and Conclusion consistently demonstrated that patients with severe COVID-19 exhibited significantly higher CRP levels than those with mild or non-severe symptoms. CRP concentrations were found to be, on average, 20 to 50 mg/L in COVID-19 patients, with levels reaching up to 86% in severe cases. Patients with more severe symptoms had considerably higher CRP concentrations than milder ones. In addition, patients who died from COVID-19 had approximately ten times higher CRP levels than those who recovered.in addition, patients with low oxygen saturation also showed elevated CRP levels, indicating a correlation between CRP and lung injury severity. The review suggests that elevated CRP levels may serve as an early marker to predict the risk of disease progression in non-severe COVID-19 patients. Monitoring CRP levels alongside other clinical findings could help healthcare workers identify patients who require early treatment and close monitoring.(Ali, 2020)

A study conducted a retrospective analysis of severe COVID-19 cases and identified potential biomarkers for differential diagnosis and prognosis prediction. The study included 27 COVID-19 and 75 influenza patients, with clinical data collected from electronic medical

records. The disease course was divided into four stages based on the progress of computed tomography (CT). The study measured C-reactive protein (CRP) levels, erythrocyte sedimentation rate (ESR), granulocyte/lymphocyte ratio, and lymphocyte count and correlated them with CT severity scores. The study found that in severe COVID-19 cases, lymphocyte levels decreased during the progression and peak stages but rebounded in the recovery stage. CRP levels in the severe group were higher than in the mild group at the initial and progression stages. The study also found that CRP, ESR, and granulocyte/lymphocyte ratio had positive correlations with CT severity scores, while lymphocyte count had a negative correlation. The study concluded that elevated CRP levels at the initial stage could predict subsequent disease progression and severity, with an area under the curve of 0.87 and a 20.42 mg/L cut-off value. Early identification of high CRP levels in patients could aid in allocating medical resources and providing aggressive treatment to those at risk of developing severe COVID-19. (Tan et al., 2020).

Another study utilized a systematic review and meta-analysis approach to investigate the link between inflammation markers and severe COVID-19. The meta-analysis analyzed 18 studies and 3,278 patients, searching databases such as PubMed, EMBASE, Scopus, and the Cochrane Library until April 20th, 2020. The study found that fever, leukocytosis (elevated white blood cell count), and elevated C-reactive protein (CRP) levels were associated with poor outcomes in COVID-19 patients. On the other hand, leukopenia (low white blood cell count) is linked to a better prognosis. The study concluded that leukocytosis and elevated CRP levels may serve as potential predictive markers for poor outcomes. The diagnostic accuracy of leukocytosis and CRP was also assessed, with an AUC of 0.70 and 0.89, respectively, indicating moderate to high accuracy in predicting severe outcomes. The study suggests that fever,

leukocytosis, and elevated CRP levels on admission may indicate severe COVID-19 outcomes.(Yamada et al., 2020).

A retrospective cohort analysis was conducted on 100 COVID-19 patients to investigate if inflammatory biomarker trends could predict a respiratory decline in patients initially presenting with stable disease. The study analyzed C-reactive protein (CRP) levels in the first 48 hours of hospitalization and their correlation with respiratory deterioration and intubation, as well as the relationship between CRP, interleukin-6 (IL-6), and measures of hypoxemic respiratory failure. The study also considered the patient's demographic and clinical features, treatment strategies, and mortality rates. The study found that a rapid increase in CRP levels during the first 48 hours of hospitalization better predicted respiratory decline than initial CRP levels or other respiratory function indices. CRP levels at admission correlated with disease severity measures and IL-6 levels. Therefore, the researchers concluded that rising CRP levels could predict subsequent respiratory deterioration in COVID-19 patients, providing insights for targeted immunomodulation early in hospitalization.(Mueller et al., 2020).

A recent retrospective study conducted at Cheikh Khalifa International University Hospital in Casablanca, Morocco, analyzed data from 145 COVID-19 patients between February and April 2020. The study found that C-reactive protein (CRP) levels upon admission were significantly associated with the severity of COVID-19 disease. CRP had a higher area under the curve (AUC) compared to other parameters, indicating its superior predictive value for disease severity. The odds ratios for CRP were 1.11 (95% CI: 1.01-1.22) and 1.13 (95% CI: 1.04-1.23). With a sample size of 145, the study concluded that CRP levels upon admission could serve as a simple and independent factor for early detection of COVID-19 severity. These findings suggest that CRP can be a useful biomarker for guiding primary care in managing COVID-19 patients.(Ahnach et al., 2020).

A retrospective analysis of clinical data from 443 COVID-19 patients at Wuhan Forth Hospital was conducted between January 16 and February 28, 2020. The study collected general patient information and various laboratory parameters, including leukocyte count, CRP level, and others. The severity of COVID-19 was classified into no severe and severe groups. Statistically significant differences were found between the two groups in sex distribution, presence of heart disease, age, leukocyte count, NLR, neutrophil count, lymphocyte count, platelet count, D-dimer level, CRP level, procalcitonin level, LDH level, creatinine level, and albumin level. Binary logistic regression analysis and ROC curve analysis were used to evaluate the predictive value of the significant variables in determining the severity of COVID-19. The study found that specific clinical parameters, such as leukocyte count, NLR, lymphocyte count, D-dimer level, and albumin level, can serve as indicators for predicting the severity of COVID-19.(Shang et al., 2020).

Another retrospective cohort study analyzed various biomarkers to develop a prediction model for venous thromboembolism (VTE) in critically ill COVID-19 patients. The study included 127 adult patients with confirmed COVID-19 infection admitted to the intensive care unit (ICU) of two teaching hospitals. The variables associated with VTE in both univariate and multivariate analysis were D-dimer and C-reactive protein (CRP). By using categorized values of D-dimer and CRP, the researchers computed a mean absolute risk for the combination of these variables, which showed a high positive predictive value. The predicted probability of VTE with D-dimer > 15 and CRP > 280 was 98%. Elevated CRP and D-dimer levels have a high positive predictive value for VTE in critically ill COVID-19 patients. The study developed a prediction table using these biomarkers which can assist clinicians in determining the timing of imaging in patients suspected of having VTE.(Dujardin et al., 2020).

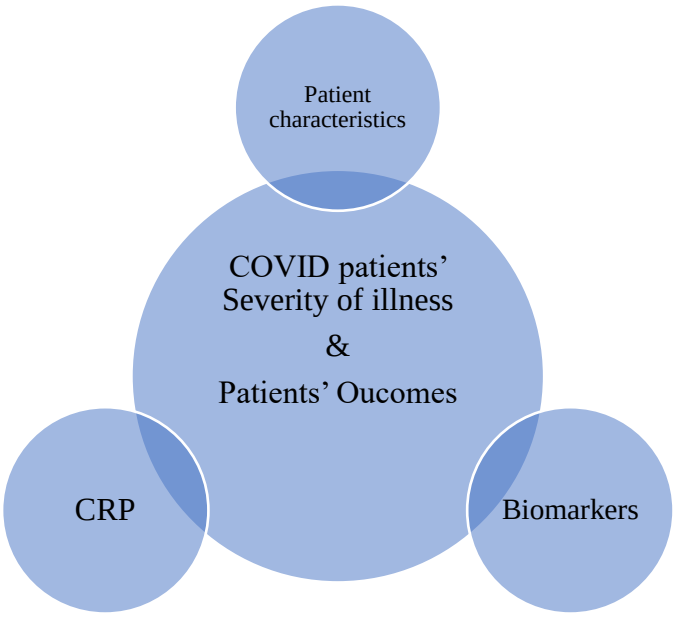
Chapter Three

Conceptual Framework

3.0. Introduction

In this chapter, we introduce a conceptual framework rooted in the guidelines and models provided by the World Health Organization (WHO). This framework examines the interrelations between C-Reactive Protein (CRP) levels, and patient outcomes, categorized as discharge or survival, within the context of severe or critical patient status. By aligning our study with WHO's established standards and insights, we aim to systematically explore these critical health variables and their impact on patient prognosis, offering a globally informed perspective on our findings and their implications in the broader field of healthcare.

Figure (3. 1) Conceptual Framework:



Since the pandemic began, healthcare organizations worldwide have started to establish protocols and guidelines to manage patients who are infected with COVID-19. The World

Health Organization (WHO) released an online platform for the clinical management of COVID-19 patients. The Centers for Disease Control and Prevention (CDC) and National Institutes of Health (NIH) circulated a conceptual and therapeutic framework that includes the WHO guideline (figure3.1) that includes clinical presentation, case definitions, triage, laboratory and radiology investigations, clinical classification, clinical early warning indicators, clinical management, and treatment of patients who were infected with COVID-19 patients. As per the conceptual framework, the cases of severe illness patients who need admission to hospitals are identified as adopted by the Palestine Ministry of Health (PMOH).

The PMOH protocol to diagnose COVID-19 includes testing arterial blood gases, Complete Blood Count (CBC), and other blood biomarkers (C-reactive protein (CRP), D-dimer, and ferritin), The therapeutic guidelines include Oxygen therapy, Antibiotics, Cortisone, IL-6 Inhibitors, Venous Thromboembolism Prophylaxis, Mechanical Vitiator (MV), (*BMJ Best Practice*, 2021; CDC, 2020; World Health Organization, 2021)World Health Organization, 2021).

3.1. Conceptual Definition of Variables

Confirmed COVID-19 case: Person with a positive COVID-19 Polymerase Chain Reaction (PCR) test(Killerby et al., 2020). The WHO uses a severity definition for COVID-19. They defined the severity in adults as below:

3.1.1. Critical COVID-19: “Defined by the criteria for acute respiratory distress syndrome (ARDS), sepsis, septic shock, or other conditions that would normally require the provision of life-sustaining therapies such as mechanical ventilation (invasive or non-invasive) or vasopressor therapy.”

3.1.2. Severe COVID-19: “Defined by any of; oxygen saturation < 90% on room air; in adults, signs of severe respiratory distress (accessory muscle use, inability to complete full sentences, respiratory rate > 30 breaths per minute)” .(World Health Organization, 2020)

3.1.3. C-Reactive Protein (CRP): It’s a blood protein that rises in response to inflammation due to infection or trauma. CRP is produced in the liver by factors released from fat cells.(Sino Biological, 2022)

3.1.4. D-Dimer: This is a unique marker of fibrin degradation that is formed by the sequential action of 3 enzymes: thrombin, factor XIIIa, and plasmin (Adam et al., 2009).

3.1.5. Ferritin: This is the main iron-storage protein and is critical to iron homeostasis. Small amounts of ferritin are secreted into the blood circulation. (Para et al., 2022).

3.2. Operational Definition of Variables

3.2.1. **Independent Variables:**

3.2.1.1. C-Reactive Protein (CRP): the CRP level range in blood as follows:

3.2.1.1.1. The level of CRP is Less than 0.3 mg/dL, considered Normal, seen in healthy adults, a range between (0.3 to 1.0) mg/dL.

3.2.1.1.2. Minor elevation: CRP Reading (1.1-9.0) mg/dL.

3.2.1.1.3. Moderate elevation: CRP Reading (9.10-10.0) mg/dL.

3.2.1.1.4. High elevation: CRP Reading (10.1-49.0) mg/dL.

3.2.1.1.5. Sever elevation: CRP Reading (>50) mg/dL. (Nehring et al., 2017)

3.2.1.2. Patients’ Characteristics include Age, gender, length of stay, and other health comorbidities such as (Diabetes, cardiac conditions, immunocompromised, renal disease, chronic liver disease, and pulmonary diseases).

3.2.1.3. Biomarkers:

3.2.1.3.1. D-Dimer: D-dimer is the degradation product of crosslinked (by factor XIII) fibrin. It reflects the ongoing activation of the hemostatic system. The reference concentration of D-dimer is < 250 ng/mL, or < 0.4 μ/mL. (Adam et al., 2009)

3.2.1.3.2. Ferritin: The normal range in the blood is in males: 12-300 ng/mL and females: 10-150 ng/mL, less or more than the range considered an abnormal result. (Para et al., 2022).

3.2.2. **Dependent Variables:**

3.3.2.1.The severity of COVID-19 according to WHO guidelines.

3.3.2.1.1. Severe Illness of COVID-19 in adults; Severe pneumonia confirmed by the presence of one plus one of two.

- The presence of clinical signs of pneumonia (fever, cough, dyspnea).
- Respiratory distress.
- SpO2 < 90% on room air

3.3.2.1.2. Critical COVID-19: acute respiratory distress syndrome (ARDS);

3.3.2.1.2.1.Oxygenation impairment in adults:

- Mild ARDS: 200 mmHg < PaO2/FiO2a ≤ 300 mmHg (with PEEP or CPAP ≥ 5.
- Moderate ARDS: 100 mmHg < PaO2/FiO2 ≤ 200 mmHg (with PEEP ≥ 5 cmH2O).
- Severe ARDS: PaO2/FiO2 ≤ 100 mmHg (with PEEP ≥ 5 cmH2O).

3.3.2.1.2.2.Onset within one week of a known clinical insult (i.e., pneumonia) or new or worsening respiratory symptoms.

3.3.2.1.3. Chest imaging (radiograph, CT scan, or lung ultrasound): bilateral opacities not fully explained by volume overload, lobar or lung collapse, or nodules. The origin of pulmonary infiltrates respiratory failure is not fully explained by cardiac failure or fluid overload.

3.3.2.2.Patients' outcomes: the patient's outcome that patient is either discharged or deceased.

Chapter Four

Methodology

4.0.Introduction

In this section, we have covered the details and analysis of the research methodology, study design, study location, study participants, sample selection criteria, survey instruments, data analysis techniques, and ethical considerations.

4.1.Design of the study:

We utilized a quantitative non-experimental retrospective descriptive and correlation study. This method allowed us to examine the relationship between variables and describe the characteristics of a population or phenomenon. By breaking down the key components of this method, we were able to gather valuable insights and draw accurate conclusions. It was important to understand the different scientific methods available to choose the most appropriate one for our research.

4.1.1. Quantitative: This indicates that the study utilizes numerical data and statistical analysis to draw conclusions. Quantitative research focuses on collecting and analyzing data in a structured and objective manner(Creswell, 2014).

4.1.2. Retrospective: This means that the study analyzes data that has already been collected or recorded in the past. Researchers will examine existing records, databases, or surveys to gather the necessary information for the study(Field, 2013; Portney, 2020). Retrospective studies are useful when it is impractical or unethical to conduct a prospective study.

4.1.3. Descriptive: This aspect of the study involves summarizing and presenting the collected data to describe the characteristics or patterns within the population or phenomenon under investigation. Descriptive statistics, such as mean, median, and standard deviation, are often used to provide a clear picture of the data.(Creswell, 2014; Portney, 2020; Sarstedt, 2019).

4.1.4. Correlation: The study aims to explore the relationship between variables analysis. Incorporating both Analysis of Variance (ANOVA) and the Pearson Chi-Square test into the study can provide a more comprehensive understanding of the relationships between variables. The ANOVA (Analysis of Variance): This statistical method is effective for comparing mean values across different groups. For a continuous dependent variable and one or more categorical independent variables, ANOVA helps determine if there are statistically significant differences in the means across these groups. The Pearson Chi-Square test is used to examine the association between two categorical variables. To explore whether there is a statistically significant relationship between categorical variables, such as patient categorical outcomes (discharge or deceased) or patients' status (severe ill or critical ill). Also adjusted residuals, also known as standardized residuals, are used In the context of a Chi-Square test of independence. They provide a means to identify which specific cells (categories) in a contingency table contribute most to the overall Chi-Square statistic.

4.2. Study Settings:

This study was conducted at Istishari Arab Hospital (IAH) – in Ramallah, Palestine. IAH is one of the largest private hospitals in Palestine. Established in 2016 as part of Arabi Hospitals group to be one of the referral hospitals and operates 240 beds for more than 15

medical and surgical specialties. IAH contains an Intensive Care Unit (ICU) with 26 beds, a Cardiac Care Unit (CCU) with ten beds, PICU with six beds, and the hospital. The hospital opened 12 ICU beds and 30 department beds for COVID-19 patients' treatment. The hospital staff received the three doses of COVID-19 vaccination.

Since 2020, Istishari Arab Hospital in Ramallah has been accredited by the Joint Commission International (JCI), a recognition that reflects its commitment to meeting international healthcare quality and patient safety standards. This accreditation likely has a positive impact on the accuracy of the hospital's data collection and reporting processes. JCI standards are rigorous and focus heavily on improving the quality of patient care, which includes the reliability and precision of clinical data management.

The hospital's adherence to these standards means that there is a systematic approach to collecting, analyzing, and using data to improve patient outcomes and healthcare services. This often involves stringent data validation processes, regular training for staff on data handling, and the implementation of robust information systems. As a result, the data generated and used by Istishari Arab Hospital can be expected to be of high accuracy and reliability, making it a trustworthy source for clinical research, patient care decisions, and policymaking in healthcare. This level of precision in data handling not only enhances patient care but also contributes to the overall improvement of healthcare delivery and administration. (Istishari Arab Hospital, 2023).

4.3. Population:

The population includes the COVID-19 patients treated/referred to or admitted to IAH, including the infected staff from April 10, 2020, until April 30, 2022.

4.4. Sample and Sampling.

This study selected all medical files for all patients who treated at IAH in the period from April 10, 2020, until April 30, 2022, based on the matching to the inclusion criteria this method, referred to as consecutive non-probability sampling, is a practical approach that allows for the inclusion of medical files as they become available or meet the study criteria(Rubin & Babbie, 2016). While it is a convenient method when random sampling is not feasible, it is important to keep in mind that this approach may introduce biases into the sample and limit the generalizability of the findings. (Polit & Beck, 2008).

The study population includes patients who were treated at IAH as in-patients for COVID-19. According to formal statistics from the hospital, 420 inpatients were treated during the mentioned period, and the sample was determined based on the inclusion and exclusion criteria after reviewing the patients' files and the adherence to inclusion and exclusion criteria the total included sample was 142 patients.

4.5. Inclusion criteria:

To be eligible for this study, patients must meet certain criteria. These criteria include:

4.5.1. Being confirmed to have COVID-19 through a nasopharyngeal swab Polymerase chain reaction (PCR) test.

4.5.2. Being an adult who is over 18 years of age.

4.5.3. Being admitted to Istishari Arab Hospital from the emergency department or referred to IAH within 24-48 hours of receiving a positive PCR test result.

4.5.4. Being admitted based on the severity of their illness and their need for non-invasive or invasive mechanical ventilation.

4.5.5. Patients must have had at least two CRP tests performed within the first week of their admission.

4.6. Exclusion criteria

4.6.1. Patients confirmed by PCR and aged less than 18 years old, pregnant patients.

4.6.2. Patients who present with mild or moderate symptoms.

4.6.3. Pregnant Patient.

4.6.4. A patient who was partially treated before being referred to IAH.

4.7. The Study Instrument and Data Collection

The COVID-19 Mortality Risk (CMR) tool, developed by the Massachusetts Institute of Technology (MIT), uses the XGBoost algorithm to predict mortality in COVID-19 patients. Its performance was evaluated using three validation cohorts, involving a derivation cohort of 3,062 patients, which had an observed mortality rate of 26.84%. This tool components are used for data collection. The data will be divided into four subcategories' patient's characteristics, other biological vs variables, the severity of illness, and the outcome of the disease. The researcher reviews the electronic medical records (EMR) of confirmed COVID-19 patients who were admitted to IAH; the records contain daily progress notes, nursing notes, laboratory findings; D-Dimer, Ferritin, and radiological; CT reports, and the outcome for all patients who meet the inclusion criteria. (Massachusetts Institute of Technology University, 2022)

The data divided into four main categories; First, patients' data will be collected: Sex, Age, social status, Chronic obstructive pulmonary disease (COPD), hypertension, heart failure (HF), Diabetes mellitus (DM), chronic kidney disease (CKD), coronary artery disease length of stay, Hypertension, Immunosuppression, Cancer, smoking, Previous Cerebrovascular Disease,

previous coagulation disease, and the vaccination status. In the second category, the other biomarker CRP was taken upon admission, the second day of admission, two days before and one day before discharge of the deceased. The other biomarkers include platelet, ferritin, D-dimers, and LDH on the day of admission. The third category is the severity of COVID-19 in need of Non-invasive ventilation, Mechanical Ventilation, Vasopressors, Acute Kidney Injury, Renal Replacement Therapy, Remdesivir, and shock (using SOFA scale). As mentioned in the daily progress note and medical reports, the severity will be determined. The fourth category is the outcome of the disease as survivors and non-survivors.

4.8. Statistical and Analysis of Data

The statistical analysis of data using the SPSS software program version 27 for analyzing quantitative descriptive correlation statistics; the data presented as frequencies, percentages, ranges, means, middle and standard deviation as appropriate for a continuous dependent variable and one or more categorical independent variables, ANOVA helps determine if there are statistically significant differences in the means across these groups. The Pearson Chi-Square test is used to examine the association between two categorical variables to explore whether there is a statistically significant relationship between categorical variables, such as patient categorical outcomes (discharge, or deceased) or patients' status (severe ill or critical ill). Also adjusted residuals, also known as standardized residuals, are used in the context of a Chi-Square test of independence. They provide a means to identify which specific cells (categories) in a contingency table contribute most to the overall Chi-Square statistic.

4.9. Ethical considerations

The study was conducted after the approval of the institutional review board IRB of Al-Quds University and the ethical committee of IAH before the start of the study. The patient information is granted as mentioned by keeping confidentiality protected. The research uses encryption, and the data is accessed by the researcher only. The extracted data is used only for research purposes, and the results will be respected as they are. The researcher acknowledges no conflict of interest, and that data will be used for other purposes rather than the aim of the study.

Chapter Five

Findings

5.0. Introduction

This chapter presents the findings of the data analysis. The descriptive analysis illustrated the Patient's characteristics, COVID patients' severity of illness, Patient biomarkers and Patient outcomes with its frequencies and percentages in addition. ANOVA and T-tests examined the differences between means. The T-test examined the variables that had two categories, while for more than two categories, an ANOVA Test was used. Also, a chi-squared test was used to analyze the association between CRP levels and two groups like the outcome (discharged or deceased) and Logistic regression is used because it allows to model the relationship between a predictor variable (CRP levels) and a binary outcome variable example (discharged or dead). Finally using, the Receiver Operating Characteristic (ROC) analysis to predictive model that uses CRP levels and possibly other variables.

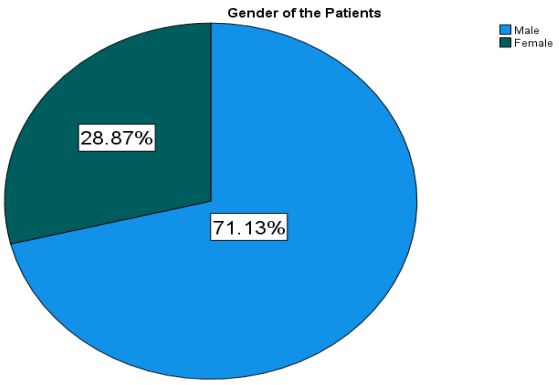
5.1. Descriptive Statistics

The patient's characteristic that was observed was Gender, Age, Place of Residency, marital status, health care worker or Not, Length of stay (LOS), Smoking Status, in addition to if the patient had comorbidities such as Diabetes mellitus, Hypertension, Ischemic heart disease, Heart failure, Previous history of ischemic stroke, Previous history of hemorrhagic stroke, Cardiovascular diseases, History okidney diseasesratory diseases, Immunodeficiency, Chronic obstructive pulmonary disease and Kidney diseases.

5.1.1. Gender

The data showed that the percentage of male patients was 71.1% and the female patients were 28.9% as shown in Figure (5.1).

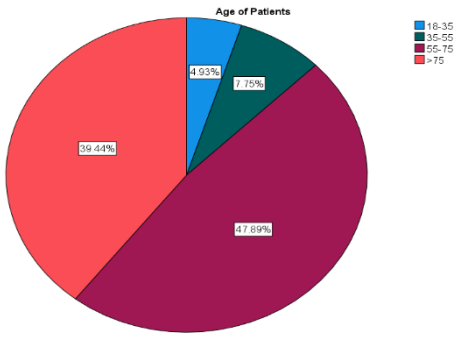
Figure (5. 1) Distribution of patients by gender.



5.1.2. Age

The data showed that the mean age for the patients was 68.04 years (with a standard deviation of 14.497), the median age was 70, the minimum was 23 years, and the maximum was 113 years. Figure 2 shows the distribution of the Ages for the patients 4.9% of the patients included aged (18-35) years, 7.7% (35-55) years, 47.9% (55-75), and 39.4% above 75 years old.

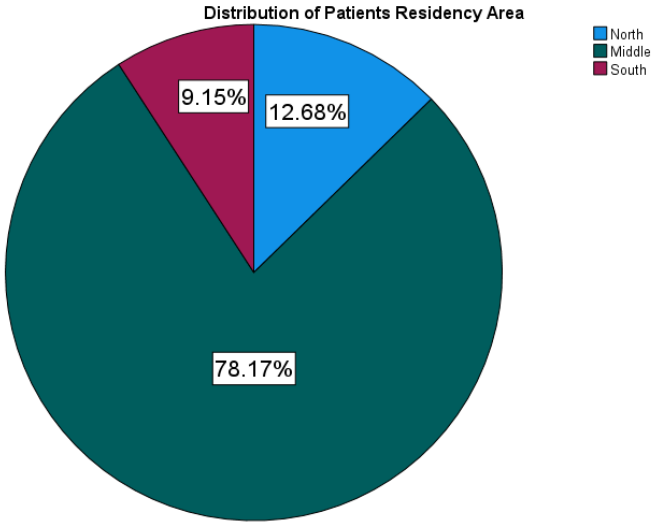
Figure (5. 2) Distribution of Patients by Age.



5.1.3. Distribution of Patient Residency Area

The data showed that the distribution of the sample residency area was divided into three categories. The first category, the North, which represents 12.68%, is represented by Nablus (6.3%), Tulkarem (4.9%), and Jeninn (1.4%). The second category, the Middle, 78.17%, is represented by Ramallah (79.9%), Salfit (2.1%), and Jericho (1.4) %. The third category, the south, is represented by Bethlehem (3.5%), Hebron (4.9%), and Gaza (0.7%).

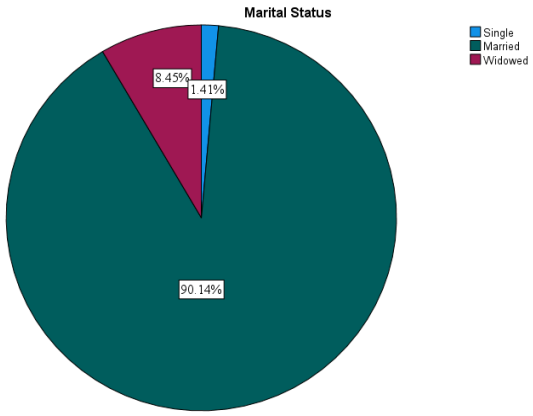
Figure (5. 3)Distribution of Patients Residency Area



5.1.4. Patient Marital Status

The findings of the patients' marital status were single (1.4%), married (90.1%), and widowed (8.5%). As shown in the figure number 4.

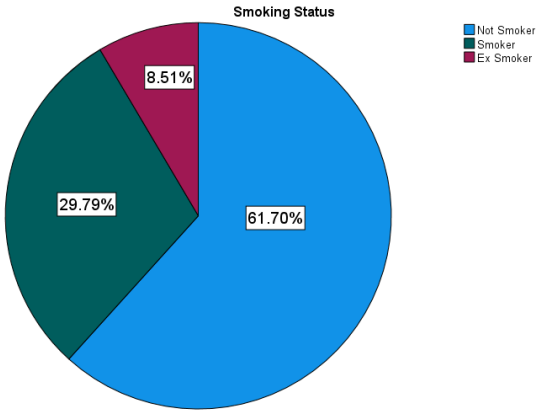
Figure (5. 4) Distribution of patients by Marital Status



5.1.5. Smoking Status

The data shows that smoking status was as Smoker (29.6%), Non-Smoker (61.3%), and Ex-smoker (8.5%). As shown in the figure (5.5).

Figure (5. 5) Distribution of Patients by Smoking Status



5.1.6. Present of Comorbidities

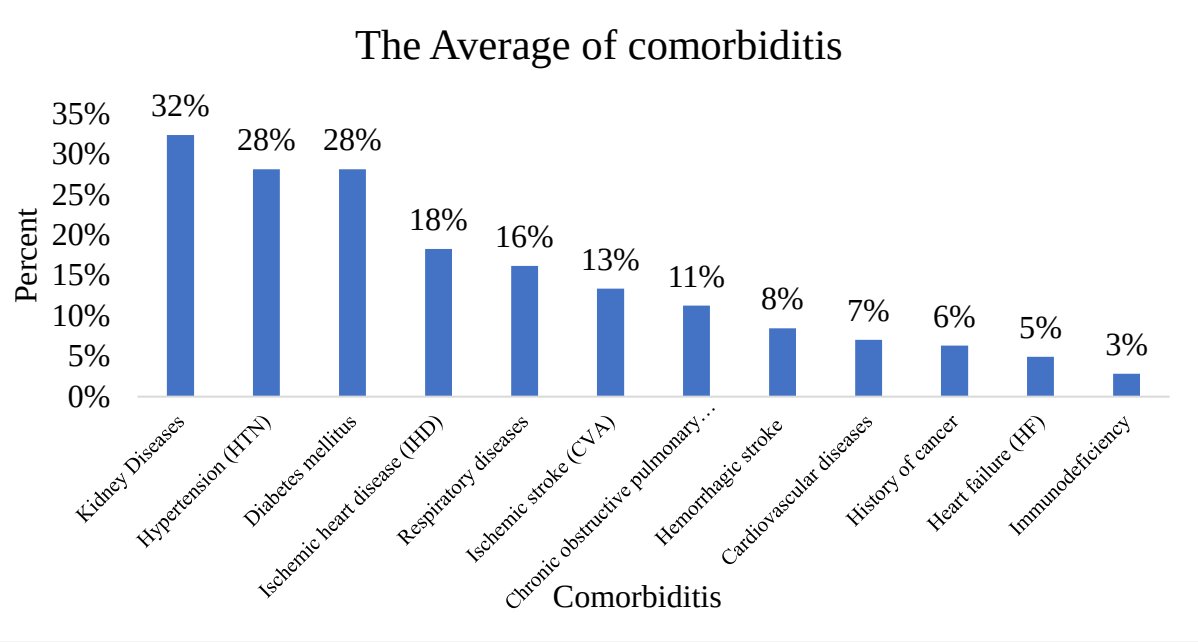
The average comorbidity score was 1.77, with a standard deviation of 1.74. with a maximum of 9 and a minimum of zero comorbidities. Most patients had kidney disease, with a

mean of 32%, followed by diabetes mellitus (DM) and hypertension (HTN), with means of 28% each. Immunodeficiency had the lowest comorbidity rate, with an average of 3%. Table 1 and figure shows the distribution of comorbidities.

Table (5. 1) Distribution of patients by comorbidities

Comorbidities	Mean	Yes
Hypertension (HTN)	28%	40.00
Heart failure (HF)	5%	7.00
Ischemic heart disease (IHD)	18%	26.00
Ischemic stroke (CVA)	13%	19.00
Hemorrhagic stroke	8%	12.00
Cardiovascular diseases	7%	10.00
Diabetes mellitus	28%	40.00
Respiratory diseases	16%	23.00
History of cancer	6%	9.00
Chronic obstructive pulmonary disease (COPD)	11%	16.00
Immunodeficiency	3%	4.00
Kidney Diseases	32%	46.00

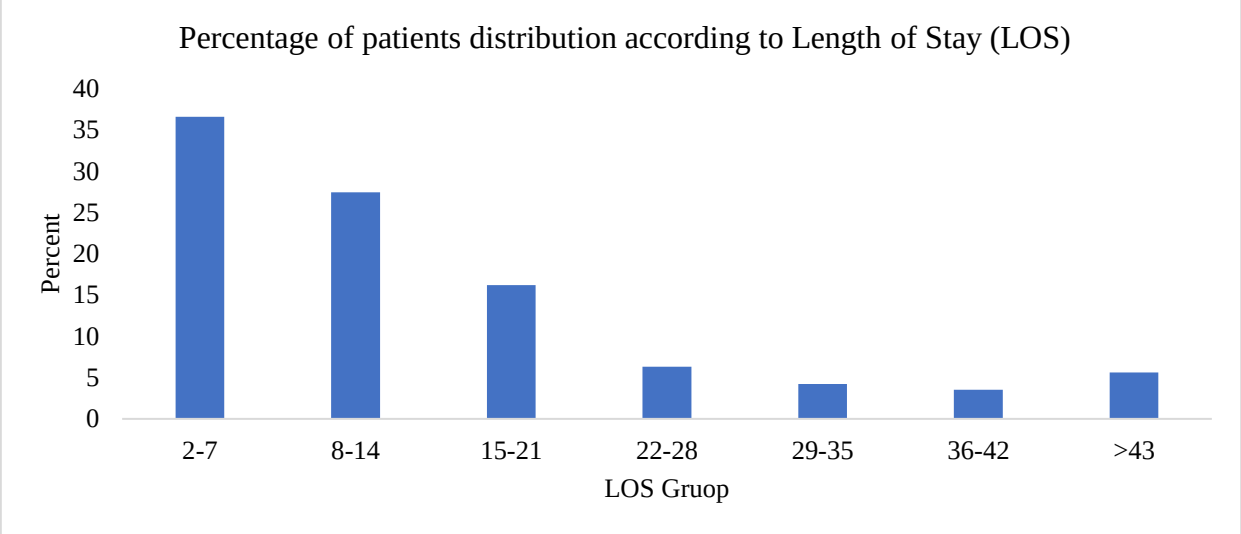
Figure (5. 6) The Average of Comorbidities



5.1.7. Length of stay (LOS

The average LOS was 20.82 days (with a standard deviation of 42.87) the minimum l2 days and maximum 312 days, and the percentiles 75,50,25 was 18,11,6. Figure 7 illustrates that LOS groups (2-7) days 36.6%, (8-14) days 27.5%, (15-21) days 16.2%, (22-28) days 6.3%, (29-35) days 4.2%, (36-42) days 3.5%, (>43) days 5.6%).

Figure (5. 7) Distribution of patients According to Length of Stay (LOS)



5.1.8. COVID–19 Patients' Severity of Illness. And patient status (outcome).

The patients were divided into severely ill (n=54, 38%) and critically ill (n=88, 62%). The study included patients who were discharged (n=60, 42.3%) and those who died (n=82, 57.7%). As presented in Figure (5.8).

Figure (5. 8) Distribution of Patients according to Outcome (Deceased or Discharged) and according to Severity of illness (Severe or Critical).

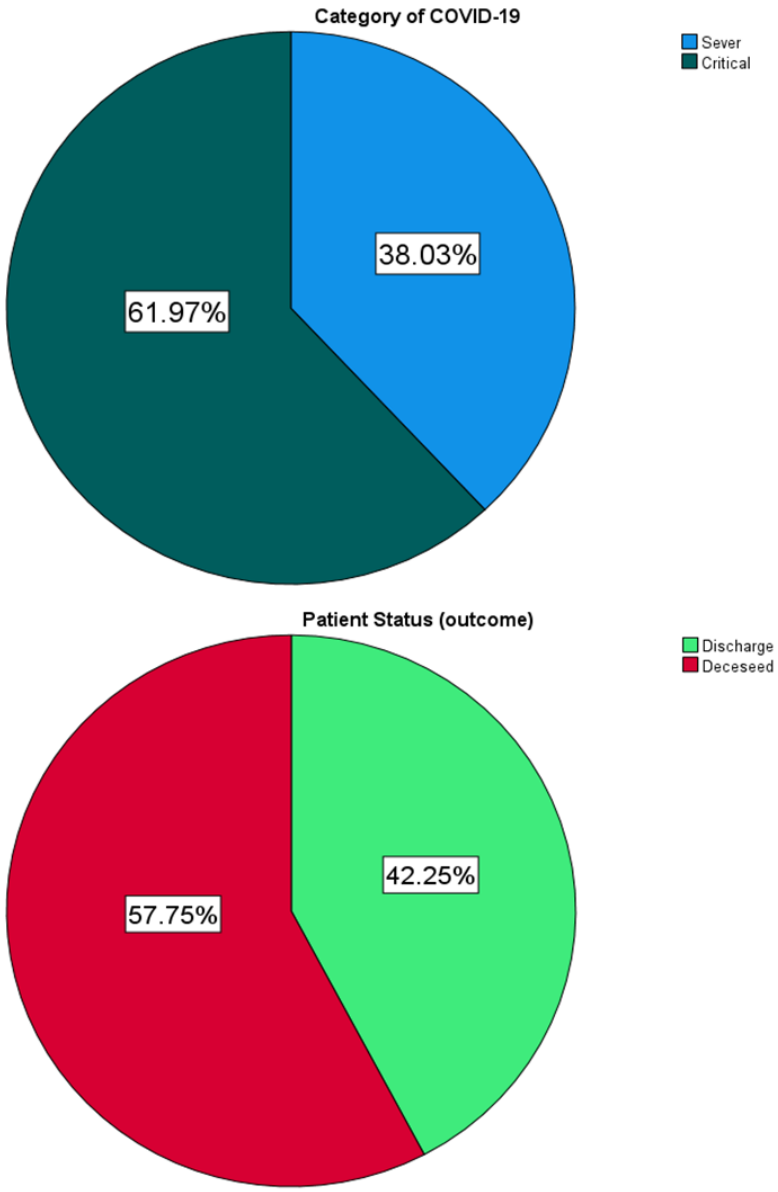


Table (5.2) shows the frequency of patients with severe illness and critically ill frequency in the severe category by gender, with male N=41 (76%) and females=13 (24%). And in critical category N=60 (68%) and female N= 28(32%). Patients who complain of severe illness are distributed by the residency area: North N=3 (6%), Middle N=48(88%), and South N=3(6%). Also, patients who complained from critical illness were distributed by the residency area North N=15 (17%), Middle N=63(71%), and South N=10(12%).

Table (5. 2) Frequency of severity of illness between Gender and Residency

Category of COVID-19	Gender				Residency					
	Male		Female		North		Middle		South	
	N	%	N	%	N	%	N	%	N	%
Severe (54)	41.0	76%	13.0	24%	3.0	6%	48.0	88%	3.0	6%
Critical (88)	60.0	68%	28.0	32%	15.0	17%	63.0	71%	10.0	12%

N=number of patients.

% = The percentage of patients.

Table 5.3 shows the frequency of patients based on smoking status and severity of illness. Patients in severe illness smoke N=26 (48%), non-smokers N= 24(45%), and ex-smokers N=4 (7%). In critically ill patients, smoke N=16 (18%), Nonsmokers N=63 (63%), and EX-smoker N=8 (10%).

Table (5. 3) Frequency of severity of illness and smoking status.

Category of COVID-19	**Smoking status**					
	Non-Smoker		Smoker		Ex-Smoker	
	N	%	N	%	N	%
Sever (54)	24.0	45%	26.0	48%	4.0	7%
Critical (88)	63.0	72%	16.0	18%	9.0	10%

N=number of patients.

% = the percentage of patients.

Table (5.4) shows the patients discharged and deceased frequency by gender and area of residency, first discharged male N=42 (70%) and female N=18 (30%) patients, second diseased male N=59(72%) and female N= 23(23%) patients. Patient discharged distributed by the residency area North N=5 (8.3%) Middle N= 52(86.6%) and South N=3(5%). Deceased patients distributed by the residency area North N=13 (16%) Middle N=59(72%) and South N=10(12%).

Table (5. 4) Frequency of Patient status, Gender, and Residency area.

	Gender				Residency					
	Male		Female		North		Middle		South	
Patient Status (outcome)	N	%	N	%	N	%	N	%	N	%
Discharged (60)	42.0	70%	18.0	30%	5.0	8.3%	52.0	86.6%	3	5%
Deceased (82)	59.0	72%	23.0	28%	13.0	16%	59.0	72%	10.0	12%

5.1.9. Patient Vital Signs

The data indicates that the average readings for vital signs during the first measurement were as follows: BP (systolic) 127 mmHg and (diastolic) 73.3 mmHg, with an average heart rate of 84.3 beats per minute, respiratory rate of 36.2 breaths per minute, the temperature of 37.5°C, and saturation of 85.06%.

5.1.10. Ventilation Assistance

Figure (5.9) and Table (5.5) showing the distribution of patients across different Ventilation Assistance; Nasal Cannula (92.9%) (7.1%), Face Mask (90.9%) (9.1%), High Flow (28.6%) (71.4%), Non-Invasive (11.4) (88.6), Invasive (4.7) (59.3) and their outcomes (Discharged or Deceased) respectively.

Figure (5.9.) Ventilation Assistance according to patient Outcomes (disgorged discharged or deceased).

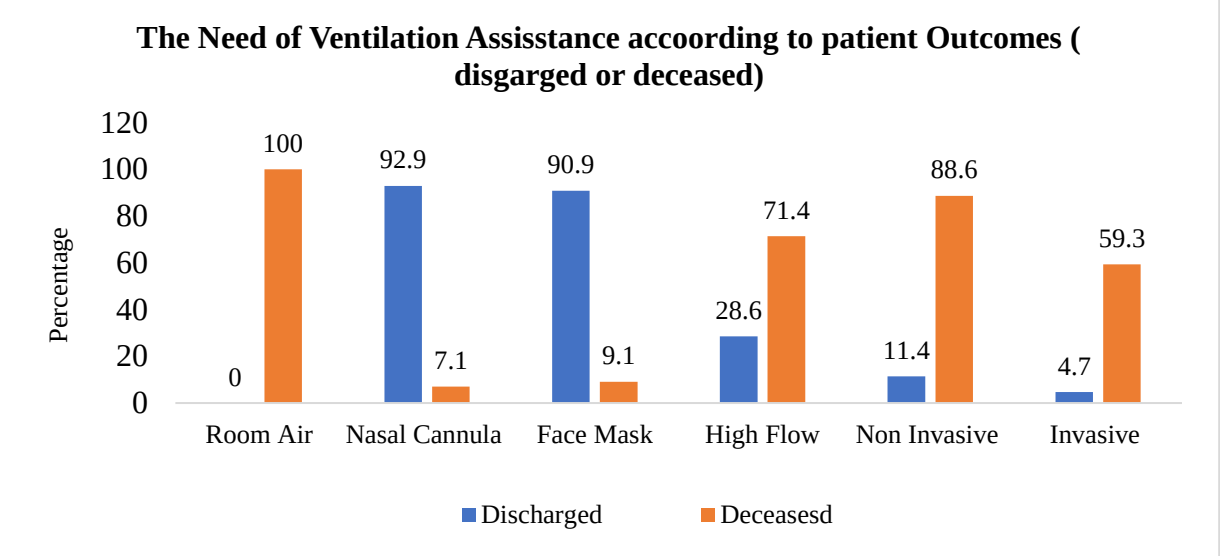
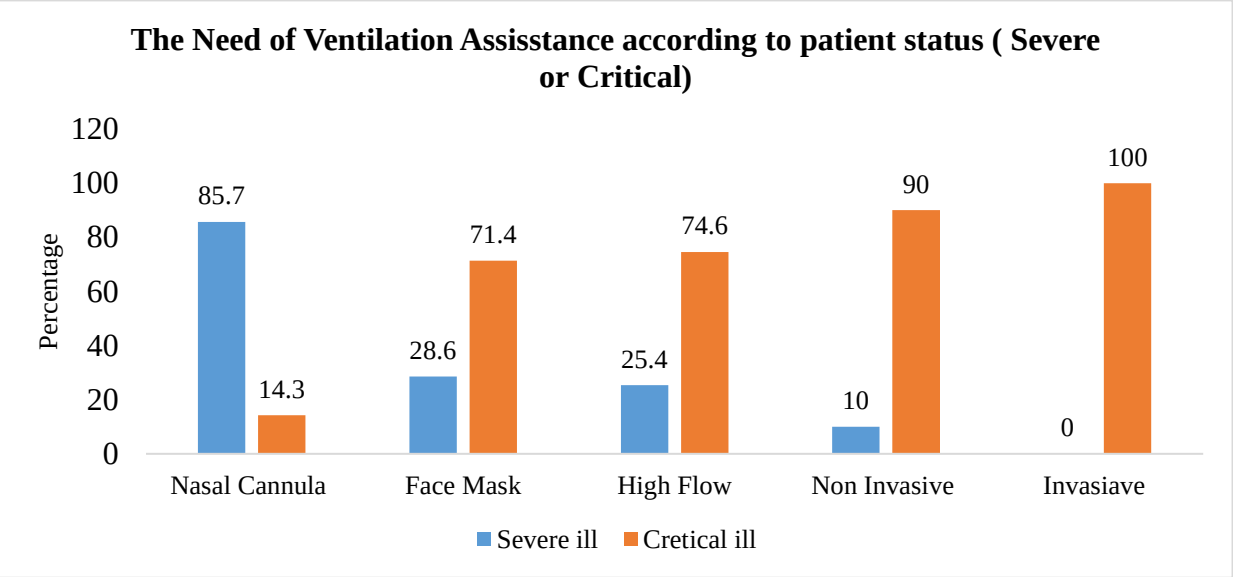


Table (5.5) Ventilation Assistance according to patient Outcomes (discharged or deceased)

Ventilation procedure	Discharged		Deceased	
	N	percentage	N	percentage
Nasal Cannula	13	92.9	1	7.1
Face Mask	10	90.9	1	9.1
High Flow	18	28.6	45	71.4
Non-Invasive	8	11.4	62	88.6
Invasive	2	4.7	41	59.3

Figure (5.10) and Table 5 show the distribution of patients across different oxygen delivery methods (Room Air (0%) (100%), Nasal Cannula (85.7%) (14.3%), Face Mask (28.6%) (71.4%), High Flow (25.4%) (74.6%), Non-Invasive (10%) (90%), Invasive (0%) (100%) and patients' status (severe ill or critical ill) respectively.

Figure 5.10. The Need for Ventilation Assistance according to patient status (Severe or Critical).



5.1.11. Patients Biomarkers

Table (5.6) shows the distribution of biomarker levels during the patient's admission, healthcare providers conducted routine sampling to measure biological biomarkers. The CRP1 levels on the day of admission had an average of 162.58 mg/dl (with a standard deviation of 90.86), the CRP 2 the second day of admission had an average of 172.6 mg/dl (with a standard deviation of 86.4), and the CRP 3 the two days before discharge or deceased had an average of 157.7 mg/dl (with a standard deviation of 105.7), an whereas the CRP4 levels before the discharge or deceased day had an average of 169.27 mg/dl (with a standard deviation of 132.56).

The frequency distribution for D-Dimer (average 2.38 FEU), Ferritin (average 2875.49 ng/ml), Platelet count (average 321.7 mcL), and the average LDH test (416 U/L).

Table (5. 6) Frequency of biomarkers.

Frequency Statistics of Biomarkers	CRP1 (mg/dl)	CRP2 (mg/dl)	CRP4 (mg/dl)	CRP4 (mg/dl)	Platelets count (mcL)	Ferritin (ng/ml)	D-dimer (FEU)	LDH (U/L)
N=	142	142	142	142	142	142	142	142
Mean	162.58	172.6	157.7	169.27	321	2875.49	2.38	416.0
Median	150.72	189.6	16	170.50	332	539.20	1.30	407.5
Std. Deviation	90.86	86.4	105.7	132.56	123	20944.17	3.83	196.9
Minimum	3.03	12.9	3.2	0.67	84	12.00	0.10	22.0
Maximum	411.48	420.4	489	587.76	555	248300.00	30.3	764.0

Table (5.7) shows the distribution of average readings for each CRP categories. For On-admission group, the CRP1 results were distributed as follows: Normal N=0 (0%), Minor elevation N=10 (0.7%), Moderate elevation N=0 (0%), CRP2 results were distributed as follows: Normal N= 0 (0%), Minor elevation N=0 (0%), Moderate elevation N=0 (0%), High elevation N=13 (9.2%), Severe elevation N=129 (90.8%). CRP3 results were distributed as follows: Normal N=0 (0%), Minor elevation N=2 (1.4%), Moderate elevation N=1 (0.7%), High elevation N=28 (19.7%), Severe elevation N=111 (78.2%). And CRP4 results were distributed

as follows: Normal N=1 (0.7%), Minor elevation N=13 (9.2%), Moderate elevation N=2 (1.4%), High elevation N=27 (19%), Severe elevation N=99 (69.7%).

Table (5. 7) Distributions of CRP Categories.

Distributions of CRP Categories								
Category	CRP1		CRP2		CRP3		CRP4	
	N	%	N	%	N	%	N	%
Normal	0	0	0	0%	0	0%	1	0.70%
Minor elevation	1	0.70%	0	0%	2	1.4%	13	9.20%
Moderate elevation	0	0	0	0%	1	0.7%	2	1.40%
High elevation	11	7.70%	13	9.2%	28	19.7%	27	19.00%
Severe elevation	130	91.50%	129	90.8%	111	78.2%	99	69.70%

Table (5.8) shows the distribution of CRP1 results to the COVID-19 category, with severe elevation in critically ill patients N= 86 (66.1%) and severely ill N= 44 (33.8%). In the high elevation CRP levels, critical ill patients N= 1 (9.1%) while in severe ill N= 10 (90.9%). In the Minor elevation CRP levels, Critical ill patients N= 1 (100%) while in severe ill N= 10 (90.9%).

Table (5. 8) Distribution of CRP1 admission Grouping and COVID-19 Category.

		Category of COVID-19				Total	
		Sever		Critical			
		N	%	N	%	N	%
CRP1	Minor elevation	0	0.0%	1	100%	1	0.7%
	High elevation	10	90.9 %	1	9.1%	11	7.7%
	Sever elevation	44	33.8%	86	66.1%	130	91.5%

Table (5.9) shows the distribution of CRP2 results to the COVID-19 category, with severe elevation in critically ill patients N= 86 (66.1%) and severely ill N= 44 (33.9%). In the high elevation CRP levels, critically ill patients N= 2 (16.6%) while in severely ill N= 10 (83.3%).

Table (5. 9) Distribution of CRP2 and COVID-19 Category.

		Category of COVID-19				Total	
		Sever		Critical			
		N	%	N	%	N	%
CRP 2	High elevation	10	83.3%	2	16.6%	12	7.7%
	Sever elevation	44	33.9	86	66.1	130	91.5%

Table (5.10) shows the distribution of CRP3 results to the COVID-19 category, with severe elevation in critically ill patients N= 81 (81.8%) and severely ill N= 18 (18.2%). In the high elevation CRP levels, critical ill patients N=7 (26%) while in severe ill N= 20 (74%). In the Moderate elevation CRP levels, critical ill patients N= 0 (0) % while in severe ill N= 2 (100%). In the Minor elevation CRP level in critical ill patients N=0 (0%), sever ill N=13 (100%). And In the Normal CRP level in critically ill patients N=0 (0%), sever ill N=1 (100%).

Table (5. 10) Distribution of CRP3 and COVID-19 Category

		Category of COVID-19				Total	
		Sever		Critical			
		N	%	N	%	N	%
	Normal	1	100%	0	0.00%	1	0.7%

CRP3	Minor elevation	13	100%	0	0.00%	13	9.2%
	Moderate elevation	2	100%	0	0.00%	2	1.4%
	High elevation	20	74.%	7	26%	27	19.0%
	Sever elevation	18	18.2%	81	81.8%	99	69.7%
Total		54	38.03%	88	61.97%	142	100.0%

Table (5.11) shows the distribution of CRP4 results to the COVID-19 category, with severe elevation in critically ill patients N= 81 (81.82%) and severely ill N= 18 (18.18%). In the high elevation CRP levels, critical ill patients N=7 (25.93%) while in severe ill N= 20 (74.07%). In the Moderate elevation CRP levels, critical ill patients N= 0 (0) % while in severe ill N= 2 (100%). In the Minor elevation CRP level in critical ill patients N=0 (0%), sever ill N=13 (100%). And in In the Normal CRP level in critical ill patients N=0 (0%), sever ill N=1 (100%).

Table (5. 11) Distribution of CRP4and COVID-19 Category.

		Category of COVID-19				Total	
		Sever		Critical			
		N	%	N	%	N	%
CRP4	Normal	1	100.00%	0	0.00%	1	0.7%
	Minor elevation	13	100.00%	0	0.00%	13	9.2%
	Moderate elevation	2	100.00%	0	0.00%	2	1.4%
	High elevation	20	74.07%	7	25.93%	27	19.0%
	Sever elevation	18	18.18%	81	81.82%	99	69.7%
Total		54	38.03%	88	61.97%	142	100.0%

Table (5. 12) shows the distribution of CRP1 results to patient's outcome discharge or deceased. In the severe elevation in deceased patients N= 81 (62%) and discharged patients N= 49 (38%). In the high elevation CRP levels, deceased patients N= 1 (9%) while in discharged N= 10 (91%). In the Minor elevation CRP levels, deceased patients N= 0 (0%) while in discharged N= 1 (100%).

Table (5. 12) Distribution of CRP1 and patient outcomes.

		Patient Status (outcome)				Total	
		Discharge		Deceased			
		N	%	N	%	N	%
CRP 1	Minor elevation	1	100%	0	0%	1	0.70%
	High elevation	10	91%	1	9%	11	7.70%
	Sever elevation	49	38%	81	62%	130	91.50%
Total		60	42%	82	58%	142	100.00%

Table (5. 13) shows the distribution of CRP2 results to patient's outcome discharge or deceased. In the Severe elevation in deceased patients N= 81 (63%) and discharged patients N= 48 (37%). In the high elevation CRP levels, discharged patients N= 12 (92%) while in deceased N= 1 (8s%).

Table (5. 13) Distribution of CRP2 and patients outcome.

		Patient Status (outcome)			
		Discharge		Deceased	
		N	%	N	%
CRP 2	High elevation	12	92%	1	8%
	Sever elevation	48	37%	81	63%
Total		60	42%	82	58%

Table (5. 14) shows the distribution of CRP3 results to patient's outcome discharge or deceased. In the severe elevation in deceased patients N= 81 (98.8%) and discharged patients N= 30 (50%). In the high elevation CRP levels, deceased patients N= 1 (1.2%) while in discharged N= 27 (45%). In the Moderate elevation CRP levels, deceased patients N= 0 (0%) while in discharged N= 2 (3.3%).

Table (5. 14) Distribution of CRP3 and patient outcomes.

		Patient Status (outcome)			
		Discharge		Deceased	
		N	%	N	%
CRP 3	Minor elevation	2	3.3%	0	0.0%
	Moderate elevation	1	1.7%	0	0.0%
	High elevation	27	45.0%	1	1.2%
	Severe elevation	30	50.0%	81	98.8%
Total		60	100.0%	82	100.0%

Table (5.15) shows the distribution of CRP4 results to the patient's outcome discharge or deceased. In the severe elevation in deceased patients N= 77 (93.7%) and discharged N= 22 (36.7%). In the high elevation CRP levels, deceased patients N=5 (8%) while in discharged N= 22 (36.7%). In the Moderate elevation CRP levels, deceased patients N= 0 (0) % while in discharged ill N= 2 (3.3%). In the Minor elevation CRP level in deceased patients N=0 (0%), discharged N=13 (21.7%).

Table (5. 15) Distribution of CRP4 before discharge grouping and patient outcomes.

		Patient Status (outcome)				Total	
		Discharge		Deceased			
		N	%	N	%	N	%
CRP 4	Normal	1	100.00%	0	0.00%	1	0.70%
	Minor elevation	13	100.00%	0	0.00%	13	9.20%
	Moderate elevation	2	100.00%	0	0.00%	2	1.40%
	High elevation	22	81.48%	5	18.52%	27	19.00%
	Severe elevation	22	22.22%	77	77.78%	99	69.70%
Total		60	42.25%	82	57.75%	142	100.00%

5.2. Research questions statistics

What is the relationship between the CRP test and the severity prognosis (severely ill and critically ill) in COVID-19 patients?

5.2.1. CRP and Severity Prognosis either severe illness or critically ill (Chi-Square Test).

Table (5.16) shows the results of the chi-square test for CRP on admission day CRP1 group and patient status (severe illness or critical illness); there is a statistically significant association between these two categorical variables. The (p-value is less than 0.001), including Phi and Cramer's V, with p-values also less than 0.001.

Table (5. 16) Chi-Square test CRP1 and Prognosis Severe.

Chi-Square Tests for CRP on admission and Severity prognosis			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	14.631	2	.001

Likelihood Ratio	15.529	2	.000
Linear-by-Linear Association	4.948	1	.026
N of Valid Cases	142	-	-
Symmetric Measures	Value	Approximate Significance	
Phi	.321	.001	
Cramer's V	.321	.001	
N of Valid Cases	142	.001	

Table (5.17) An adjusted residual of (3.8) in the highly elevated CRP1 for patient status (severe illness) indicates that there are significantly more patients with severe illness in the highly elevated CRP1 group than would be expected by chance. An adjusted residual of (3.4) in the "severe elevated CRP1" group for patient status (critical) suggests that there are significantly more patients with critical illness in the "severe elevated CRP1" group than would be expected by chance.

Table (5. 17) Adjusted Residual; CRP1 and Severity Prognosis.

		Category of COVID-19			
		Severe		Critical	
		N	Adjusted Residual	N	Adjusted Residual
CRP1	Minor elevation	0	-.8	1	.8
	High elevation	10	3.8	1	-3.8
	Severe elevation	44	-3.4	86	3.4
Total		54		88	

Table (5.18) shows the results of the chi-square test for CRP second day of admission CRP2 group and patient status (severe illness or critical illness); there is a statistically significant association between these two categorical variables. The (p-value is less than 0.001), including Phi and Cramer's V, with p-values also less than 0.001.

Table (5. 18) Chi-Square test CRP2 and Prognosis Severe.

Chi-Square Tests for CRP2 and Severity Prognosis			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	13.179	1	0.000
Likelihood Ratio	13.250	1	0.000
Linear-by-Linear Association	13.086	1	0.000
N of Valid Cases	142	-	-
Symmetric Measures	Value	Approximate Significance	
Phi	0.305	.001	
Cramer's V	0.305	.001	
N of Valid Cases	142	.	

Table (5.19) shows an adjusted residual of (3.6) in the highly elevated CRP2 for patient status (severe illness), indicates that there are significantly more patients with severe illness in the high elevated CRP2 group than would be expected by chance. An adjusted residual of (3.6) in the severe elevated CRP2 for patient status (critical illness) suggests that there are

significantly more patients with critical illness in the severe elevated CRP2 than would be expected by chance.

Table (5. 19) Adjusted Residual; CRP2 and Severity Prognosis.

		Category of COVID-19						Total	
		Severe			Critical				
		N	%	Adjusted Residual	N	%	Adjusted Residual	N	%
CRP2	High elevation	11	20.4%	3.6	2	2.3%	-3.6	13	9.2%
	Severe elevation	43	79.6%	-3.6	86	97.7%	3.6	129	90.8%
Total		54	100.0 %		88	100.0 %		142	100.0 %

Table (15.20) shows the association between CRP3, and patient status (severe illness or critical illness) has been found to be statistically significant according to the results of the chi-square test. The p-value is less than 0.001, which also includes Phi and Cramer's V, with p-values less than 0.001 as well.

Table (5. 20) Chi-Square test CRP3 and Prognosis Severe

Chi-Square Tests for CRP3 and Severity Prognosis			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	46.151[a]	3	0.000
Likelihood Ratio	48.721	3	0.000
Linear-by-Linear Association	38.437	1	0.000

N of Valid Cases	142	
Symmetric Measures	Value	Approximate Significance
Phi	0.570	0.000
Cramer's V	0.570	0.000
N of Valid Cases	142	.

Table (5.21) shows that in Severe Illness, Patients with minor elevated CRP3 have a significantly higher likelihood (adjusted residual of 1.8) of severe illness. Patients with moderate elevated CRP also have a significantly higher likelihood (adjusted residual of 1.3) of severe illness. Patients with high elevated CRP3 have a slightly higher likelihood (adjusted residuals of 6.3). Patients with severe elevated CRP3 have a significantly lower likelihood (adjusted residual of -6.8) of severe illness. On the other hand, Critical Illness Patients with severe elevated CRP3 have a significantly higher likelihood (adjusted residual of 6.8) of critical illness. Patients with moderate CRP3, minor elevated CRP3, and high elevated CRP3 all have a significantly lower likelihood (adjusted residuals of -1.8, -1.3, and -6.2, respectively) of critical illness.

Table (5. 21) Adjusted Residual; CRP3 and Severity Prognosis.

Category of COVID-19					
		Severe		Critical	
		N	Adjusted Residual	N	Adjusted Residual
CRP3	Minor elevation	2	1.8	0	-1.8
	Moderate elevation	1	1.3	0	-1.3
	High elevation	25	6.2	3	-6.2
	Severe elevation	26	-6.8	85	6.8

Total	54		88	

Table (5.22) shows the association between CRP on the day before discharge CRP4 and patient status (severe illness or critical illness) has been found to be statistically significant according to the results of chi-square test. The p-value is less than 0.001, which also includes Phi and Cramer's V, with p-values less than 0.001 as well.

Table (5. 22) Chi-Square test CRP4 and Severity Prognosis

Chi-Square Tests for CRP4 on the day before discharge and severity prognosis			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	57.506	4	.001
Likelihood Ratio	63.851	4	.000
Linear-by-Linear Association	49.154	1	.026
N of Valid Cases	142	-	-
Symmetric Measures	Value	Approximate Significance	
Phi	.636	.001	
Cramer's V	.636	.001	
N of Valid Cases	142	.001	

Table (5.23) shows that in Severe Illness, Patients with minor elevated CRP4 have a significantly higher likelihood (adjusted residual of 4.8) of severe illness. Patients with high elevated CRP 4 also have a significantly higher likelihood (adjusted residual of 4.8) of severe illness. Patients with normal elevated CRP4 and moderate CRP4 have a slightly higher

likelihood (adjusted residuals of 1.3 and 1.8, respectively) of severe illness. Patients with severe elevated CRP4 have a significantly lower likelihood (adjusted residual of -7.4) of severe illness. On the other hand, Critical Illness Patients with severe elevated CRP4 have a significantly higher likelihood (adjusted residual of 7.4) of critical illness. Patients with normal elevated CRP4, moderate CRP4, minor elevated CRP4, and high elevated CRP4 all have a significantly lower likelihood (adjusted residuals of -1.3, -1.8, -4.8, and -4.8, respectively) of critical illness.

Table (5. 23) Adjusted Residual; CRP4 and Severity Prognosis

		Category of COVID-19			
		Severe		Critical	
		N	Adjusted Residual	N	Adjusted Residual
CRP2	Normal	1	1.3	0	-1.3
	Minor elevation	13	4.8	0	-4.8
	Moderate elevation	2	1.8	0	-1.8
	High elevation	20	4.3	7	-4.3
	Severe elevation	18	-7.4	81	7.4
Total		54		88	

5.2.2. CRP and Patient Outcomes; Discharge or Deceased (Chi-Square Test).

Table (5.24) shows the results of chi-square test for CRP1 on admission day CRP1 group and patient outcomes (discharge or deceased); there is a statistically significant

association between these two categorical variables. The (p-value is less than 0.001), including Phi and Cramer's V, with p-values also less than 0.001.

Table (5. 24) Chi-Square test CRP1 and Patient outcomes (Discharge or Deceased)

Chi-Square Tests for CRP1 on day admission and Patient Outcomes (discharge or deceased)			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	13.148	2	.001
Likelihood Ratio	14.47	2	.000
Linear-by-Linear Association	10.97	1	.026
N of Valid Cases	142	-	-
Symmetric Measures	Value	Approximate Significance	
Phi	0.304	.001	
Cramer's V	0.304	.001	
N of Valid Cases	142	-	

Table (5.25) An adjusted residual of (3.4) in the high elevated CRP1 group for patient status (Discharge) indicates that there are significantly more patients with severe illness in the high elevated CRP1 group than would be expected by chance. An adjusted residual of (3.6) in the "severe elevated CRP1" group for (Deceased) suggests that there are significantly more patients with Discharge in the severe elevated CRP 1 group than would be expected by chance.

Table (5. 25) Adjusted Residual; CRP1 and Patient outcomes (Discharge or Deceased).

Adjusted Residual; CR1 and Patient outcomes (Discharge or Deceased)					
		Patient Status (outcome)			
		Discharge		Deceased	
		N	Adjusted Residual	N	Adjusted Residual
P1	Minor elevation	1	1.2	0	-1.2
	High elevation	10	3.4	1	-3.4
	Severe elevation	49[a]	-3.6	81	3.6
Total		60		82	

Table (5.26) shows the association between CRP2 and patient outcome (discharge or deceased has been found to be statistically significant according to the chi-square test results). The p-value is less than (0.001), including Phi and Cramer's V, with p-values less than (0.001) as well.

Table (5. 26) Chi-Square test CRP2 and Patient outcomes (Discharge or Deceased).

Chi-Square Tests for CRP2 and Patient Outcomes (discharge or deceased)			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	14.694	1	0.000
Likelihood Ratio	12.522	1	0.000
Linear-by-Linear Association	16.085	1	0.000
N of Valid Cases	14.590	1	0.000

Symmetric Measures	Value	Approximate Significance
Phi	0.322	0.000
Cramer's V	0.322	0.000
N of Valid Cases	142	-

Table (5.27) An adjusted residual of (3.8) in the high elevated CRP2 group for patient status (Discharge) indicates that there are significantly more patients with severe illness in the high elevated CRP2 group than would be expected by chance. An adjusted residual of (3.8) in the severe elevated CRP2 for (Deceased) suggests that there are significantly more patients with critical illness in the severe elevated CRP2 group than would be expected by chance.

Table (5. 27) Adjusted Residual; CRP2 and Patients outcome (Discharge or Deceased)

		Patient Status (outcome)			
		Discharge		Deceased	
		N	Adjusted Residual	N	Adjusted Residual
CRP 2	High elevation	12	3.8	1	-3.8
	Severe elevation	48	-3.8	81	3.8
Total		60		82	

Table (5.28) Shows the association between CRP3, and patient outcomes (discharge or deceased) has been found to be statistically significant according to the results of chi-square test. The p-value is less than 0.001, which also includes Phi and Cramer's V, with p-values less than 0.001 as well.

Table (5. 28) Chi-Square test CRP3 and Patient outcomes (Discharge or Deceased).

Chi-Square Tests for CRP3 and Patient Outcomes (discharge or deceased)			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	48.327	3	0.000
Likelihood Ratio	55.260	3	0.000
Linear-by-Linear Association	38.989	1	0.000
N of Valid Cases	48.327	3	0.000
Symmetric Measures	Value	Approximate Significance	
Phi	0.583	0.000	
Cramer's V	0.583	0.000	
N of Valid Cases	142	-	

Table (5. 29) Adjusted Residual; CRP3 and Patient outcomes (Discharge or Deceased)

		Patient Status (outcomes)			
		Discharge		Deceased	
		N	Adjusted Residual	N	Adjusted Residual
CRP 3	Minor elevation	2	1.7	0	-1.7
	Moderate elevation	1	1.2	0	-1.2
	High elevation	27	6.5	1	-6.5
	Severe elevation	30	-7.0	81	7.0
Total		60		82	

Table 5.30 shows the association between CRP4 patient outcomes (discharge or deceased) has been found to be statistically significant according to the results of chi-square test. The p-value is less than 0.001, which also includes Phi and Cramer's V, with p-values less than 0.001 as well.

Table (5. 30) Chi-Square test CRP4 and Patient outcomes (Discharge or Deceased).

Chi-Square Tests for CRP4 on the day before discharge and Patient Outcomes (discharge or deceased)			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	55.175	4	<.001
Likelihood Ratio	62.675	4	<.001
Linear-by-Linear Association	44.762	1	<.001
N of Valid Cases	142	-	-
Symmetric Measures	Value	Approximate Significance	
Phi	0.623	<.001	
Cramer's V	0.623	<.001	
N of Valid Cases	142	-	

Table (5.31) shows that in discharged Patients with minor elevated CRP4 have a significantly higher likelihood (adjusted residual of 4.4) of discharged patients. Patients with high elevated CRP4 also have a significantly higher likelihood (adjusted residual of 4.4).

Patients with normal elevated CRP4 and moderate CRP4 have a slightly higher likelihood (adjusted residuals of 1.2 and 1.7, respectively). Patients with severe elevated CRP4 have a significantly lower likelihood (adjusted residual of -7.3) of discharged patients. On the other hand, Critical Illness Patients with severe elevated CRP4 have a significantly higher likelihood (adjusted residual of 7.3) of deceased patients. Patients with normal elevated CRP4, moderate CRP4, minor elevated CRP4, and high elevated CRP4 all have a significantly lower likelihood (adjusted residuals of -1.2, -1.7, -4.4, and -4.6, respectively) of critical illness.

Table (5. 30) Adjusted Residual; CRP4 and Patient outcomes (Discharge or Deceased).

		Patient Status (outcomes)			
		Discharge		Deceased	
		N	Adjusted Residual	N	Adjusted Residual
CRP2	Normal	1	1.2	0	-1.2
	Minor elevation	13	4.4	0	-4.4
	Moderate elevation	2	1.7	0	-1.7
	High elevation	22	4.6	5	-4.6
	Severe elevation	22	-7.3	77	7.3
Total		60		82	

5.2.3. The CRP and Length of Stay LOS (ANOVA 0.05.)

Table (5.32) shows the ANOVA test for CRP1; the p-value is 0.714, which is greater than the typical significance level of 0.05. This suggests no statistically significant difference in

CRP1 levels across the LOS groups. In CRP4, the p-value is 0.561, which is also greater than 0.05. Similar to CRP1, this indicates no statistically significant difference in CRP4 levels across the LOS groups.

Table (5. 31) The CRP and Length of Stay LOS (ANOVA).

ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
CRP1	Between Groups	35808.596	6	5968.099	.714	.639
	Within Groups	1128126.141	135	8356.490		
	Total	1163934.737	141			
CRP2	Between Groups	86546.038	6	14424.340	.814	.561
	Within Groups	2391239.717	135	17712.887		
	Total	2477785.756	141			

5.2.4. The CRP and Gender (independent T-Test 0.05.)

Table (5.33) indicates that the p-value for the independent t-test comparing CRP1 levels and CRP4 between two gender groups is (0.388) and (0.410), which is greater than the typical significance level of 0.05. This means that the difference in CRP levels between the two gender groups is not statistically significant.

Table (5. 32) The CRP and Gender (independent T-Test).

		t-test for Equality of Means					
		df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
CRP1	Equal variances assumed	140	.388	-14.57656	16.83964	-47.86943	18.71631
	Equal variances not assumed	67.786	.410	-14.57656	17.59847	-49.69577	20.54265
CRP2	Equal variances assumed	140	.794	-6.44025	24.62937	-55.13384	42.25335
	Equal variances not assumed	78.292	.789	-6.44025	24.02723	-54.27198	41.39148

5.2.5. The CRP and Age of Patients (ANOVA 0.05.)

Table (5.34) indicates that the p-value for ANOVA comparing CRP1 levels and CRP4 between groups of ages is (0.409) and (0.003) respectively, which in CRP1 is greater than the typical significance level of 0.05. This means that the difference in CRP1 levels between the two gender groups is not statistically significant. And in CRP4, it is less than the typical significance level of 0.05. This means that the difference in CRP4 levels between the two gender groups is statistically significant. When comparing age groups (40-60) in the CRP4 using the

Post Hok test, the p-value (0.048) was less than the standard significance level of 0.05. This indicates a statistically significant difference between this age group (46-60) and the others. There was also a statistically significant difference found in the age group o (>75) with a P-value of 0.016. The difference in the age group of (>75) had a P-value of .016.

Table (5. 33) The CRP and Age (ANOVA).

		Sum of Squares	df	Mean Square	F	Sig.
CRP1	Between Groups	33047.489	4	8261.872	1.001	.409
	Within Groups	1130887.248	137	8254.651		
	Total	1163934.737	141			
CRP4	Between Groups	266670.332	4	66667.583	4.131	.003*
	Within Groups	2211115.424	137	16139.529		
	Total	2477785.756	141			

Multiple Comparisons

Tukey HSD

Dependent Variable	(I) Age Groups	(J) Age Groups	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
CRP4	18-30	31-45	54.69571	70.67933	.938	-140.6935	250.0849
		46-60	24.54381	58.80876	.994	-138.0298	187.1174
		61-75	-65.11644	54.43779	.754	-215.6068	85.3739
		>75	-80.34082	54.94815	.589	-232.2420	71.5604
	31-45	18-30	-54.69571	70.67933	.938	-250.0849	140.6935
		46-60	-30.15190	55.44543	.983	-183.4278	123.1240
		61-75	-119.81215	50.78581	.133	-260.2068	20.5825
		>75	-135.03653	51.33250	.070	-276.9424	6.8694
	46-60	18-30	-24.54381	58.80876	.994	-187.1174	138.0298
		31-45	30.15190	55.44543	.983	-123.1240	183.4278
		61-75	-89.66025*	32.28158	.048	-178.9009	-.4196
		>75	-104.8846*	33.13498	.016	-196.4845	-13.2848
	61-75	18-30	65.11644	54.43779	.754	-85.3739	215.6068
		31-45	119.81215	50.78581	.133	-20.5825	260.2068
		46-60	89.66025*	32.28158	.048	.4196	178.9009
		>75	-15.22438	24.55462	.972	-83.1043	52.6555
	>75	18-30	80.34082	54.94815	.589	-71.5604	232.2420
		31-45	135.03653	51.33250	.070	-6.8694	276.9424
		46-60	104.88463*	33.13498	.016	13.2848	196.4845
		61-75	15.22438	24.55462	.972	-52.6555	83.1043

*. The mean difference is significant at the 0.05 level.

5.2.6. The CRP and Complications (independent T-Test 0.05.).

Table (5. 35) shows that the independent t- test of CRP1 and complications Cardiogenic shock Sepsis / Septic shock, Hepatic disfunction, Hyper Coagulopathy, Heart Failure, Myocardial Infarction, Acute Respiratory distress syndrome (ARDS) that, the p-value independent t-test between CRP1 and complication is greater than the typical significance level of 0.05 there is no statistically significant relationship. On the other hand, the p-value for the independent test between CRP4 and ARDS and Acute Kidney (AKI) is less than 0.001, which indicates a highly significant result.

Table (5. 34) The CRP and Complications (independent T-Test 0.05.).

Biomarkers	Complication	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval	
						Lower	Upper
CRP1	Cardiogenic shock	140	0.105	-34.173	20.949	-75.590	7.243
	Sepsis / Septic shock	140	0.102	-25.894	15.731	-56.996	5.206
	Hepatic disfunction	140	0.639	15.575	33.159	-49.981	81.133
	Hyper Coagulopathy	140	0.788	-10.266	38.026	-85.447	64.913
	Heart Failure	140	0.849	-7.907	41.509	-89.973	74.158
	Myocardial Infarction	140	0.519	16.568	25.629	-34.102	67.237
	Acute Respiratory distress syndrome	140	0.038	-32.544	15.520	-63.228	-1.860
	Acute Kidney injury	140	0.537	-10.963	17.731	-46.018	24.091
CRP4	Cardiogenic shock	140	0.005	-86.457	29.976	-145.721	-27.192
	Sepsis / Septic shock	140	0.995	0.157	23.173	-45.657	45.972
	Hepatic disfunction	140	0.010	-142.047	47.286	-216.654	-29.677

	Hyper Coagulopathy	140	0.010	-142.047	54.182	-249.169	-34.925
	Heart Failure	140	0.038	-124.791	59.646	-242.714	-6.868
	Myocardial Infarction	140	0.023	-84.327	36.765	-157.013	-11.641
	Acute Respiratory distress syndrome	140	<0.001	-181.142	17.161	-215.070	-147.214
	Acute Kidney injury	140	<0.001	-123.051	23.726	-169.958	-76.143

Chapter Six

Discussion

6.0.Introduction

In this chapter, we delve into the critical analysis and interpretation of the findings obtained from the extensive examination of COVID-19 patients, their biomarkers, and clinical outcomes, with a particular focus on the C-Reactive Protein (CRP) test. The preceding chapters have provided an in-depth exploration of the findings.

Our primary objective in this discussion is to elucidate the significance of CRP as a prognostic marker for COVID-19 patients' severity (severe ill or critical ill) clinical outcomes (discharged or deceased)by addressing two fundamental research questions: firstly, the relationship between the CRP test and the severity prognosis of COVID-19 patients categorized as severely ill or critically ill, and secondly, the ability of the CRP test to predict the prognosis of COVID-19 patients, specifically, their likelihood of recovery or unfortunate demise.

These statistical tools enable us to explore potential associations and predictive capabilities of CRP levels in the context of COVID-19 patient characteristics, severity of illness, and ultimate outcomes. This discussion chapter serves as the culmination of our research journey, where aim to synthesize the findings, provide nuanced interpretations, and draw meaningful conclusions. Moreover, it offers valuable insights into the clinical relevance of CRP as a potential tool for predicting the course and outcome of COVID-19, contributing to the growing body of knowledge in the battle against this global pandemic.

6.1.The patients' characteristics

The study included 142 patients selected through convenience sampling. Of these, 71.1% were male and 28.9% were female.

Based on the findings, the sample residency area can be divided into three categories. The North category accounts for 12.68% and includes Nablus (6.3%), Tulkarem (4.9%), and Jenin (1.4%). The Middle category comprises 78.17% and includes Ramallah (79.9%), Salfit (2.1%), and Jericho (1.4%). The South category is represented by Bethlehem (3.5%), Hebron (4.9%), and Gaza (0.7%).

The average length of stay (LOS) for the patients was 20.82 days, with a standard deviation of 42.87. The minimum LOS was 2 days, and the maximum was 312 days. The 25^{th}, 50^{th}, and 75^{th} percentiles were 6, 11, and 18, respectively. Most patients (36.6%) had a LOS of 2-7 days, while 27.5% had a LOS of 8-14 days. 16.2% had a LOS of 15-21 days, 6.3% had a LOS of 22-28 days, 4.2% had a LOS of 29-35 days, 3.5% had a LOS of 36-42 days, and 5.6% had a LOS of over 43 days.

COVID-19 patients were classified as severely ill (N=54, 42.3%) or critically ill (N=88, 62%). The study included discharged patients (N=60, 42.3%) and those who died (N=82, 57.7%).

6.2. The CRP and Patient Status (severe ill or critical ill)

The chi-square test findings indicate a statistically significant association between CRP levels one day of addition (CRP 1 and 2) and patient status (severe illness or critical illness). The p-value, which is less than (0.001), signifies a strong statistical significance. Additionally, the analysis includes Phi and Cramer's V statistics, both of which also yield p-values less than (0.001).

The chi-square test findings indicate a statistically significant association between CRP levels one day before discharge or deceased (CRP 3 and 4) and patient status (severe illness or critical illness). The p-value, which is less than (0.001), signifies a strong statistical significance. Additionally, the analysis includes Phi and Cramer's V statistics, both of which also yield p-values less than (0.001).

Furthermore, the relationship between CRP 4 levels and the severity of illness among patients. In cases of Severe Illness, patients with minor elevations in CRP1 exhibit a significantly higher likelihood, as evidenced by an adjusted residual of (4.8). Similarly, patients with high elevated (CRP4) also display a substantially increased likelihood, supported by an adjusted residual of (4.8). Patients with normal elevated (CRP4) and moderate (CRP4) levels have a slightly higher likelihood, with adjusted residuals of (1.3) and (1.8), respectively, for severe illness. On the contrary, patients with severe elevations in (CRP4) exhibit a significantly lower likelihood of severe illness, indicated by an adjusted residual of (-7.4).

Conversely, (Critical Illness) Patients with severe elevations in CRP4 demonstrate a significantly higher likelihood, as reflected by an adjusted residual of (7.4). Patients with normal elevated CRP4, moderate CRP4, minor elevated CRP4, and high elevated CRP4 all exhibit significantly lower likelihoods of critical illness, as denoted by adjusted residuals of -1.3, -1.8, -4.8, and -4.8, respectively. These findings shed light on the intricate relationship between CRP levels and the severity of illness among COVID-19 patients, emphasizing the importance of CRP as a potential prognostic indicator; this result is supported by the articles of study by Sadeghi-Haddad-Zavareh et al., 2021 on CRP levels in COVID-19 patients also emphasizes the significance of CRP as a predictor of disease severity and progression. They found that patients with a CRP level >64.75 mg/L were more likely to develop severe forms of the disease. Their results align with our findings, which indicate a significant association between CRP levels and

patient severity of illness status. Both studies underscore the importance of CRP as a biomarker for predicting clinical outcomes in patients, particularly in the context of COVID-19.

6.3. The CRP and Patient outcomes (Discharge or Deceased).

Based on findings of the chi-square tests, which reveal a significant association between CRP levels on admission (CRP1) and patient outcomes, either discharged or deceased. The findings are statistically robust with a p-value less than 0.001, further substantiated by Phi and Cramer's V values, also indicating significance at p-values less than 0.001.

Notably, the adjusted residuals provide deeper insights. A residual of 3.4 in the high elevated CRP group for discharged patients suggests a higher-than-expected frequency of severely ill patients in this category. Conversely, a residual of 3.6 in the severe elevated CRP group for deceased patients indicates an unexpectedly high number of critically ill patients.

Furthermore, examining CRP levels on the day before discharge (CRP2) also shows a significant association with patient outcomes. Discharged patients with minor to high elevated CRP levels exhibit higher-than-expected frequencies (adjusted residuals of 4.4), whereas those with normal or moderate levels show slightly elevated likelihoods (residuals of 1.2 and 1.7). In stark contrast, patients with severe elevated CRP levels have a much lower likelihood of being discharged (residual of -7.3) but a significantly higher probability of being in the deceased category (residual of 7.3).

These findings indicate a clear gradient in patient outcomes based on CRP levels, with elevated levels correlating with more severe clinical outcomes. This relationship underscores the importance of CRP as a predictive biomarker in patient management and prognosis while mentioned by study involving COVID-19 patients admitted to a New York healthcare system found that higher CRP concentrations were strongly associated with adverse outcomes like

venous thrombo-embolism, acute kidney injury, critical illness, and mortality. It concluded that systemic inflammation, as measured by CRP, has a significant association with critical illness and mortality in COVID-19 patients, emphasizing the potential of CRP-based approaches for risk stratification and treatment. This aligns with our findings of a clear gradient in patient outcomes based on CRP levels, further substantiating the importance of CRP as a predictive biomarker in patient management and prognosis.(Smilowitz et al., 2021).

Chapter Seven

Conclusion

7.0. Introduction

During the COVID-19 pandemic, understanding factors predicting patient outcomes has been paramount. This study highlights C-Reactive Protein (CRP) as an indicator of disease severity. It examines the relationship between CRP levels and patient outcomes (discharge or deceased) and the severity of illness (severe illness or critical illness) in COVID-19 patients. Utilizing chi-square tests and adjusted residuals, we seek to establish a definitive correlation between CRP levels and patient outcomes. The findings provide significant insights into CRP's prognostic value in clinical settings, enhancing knowledge about COVID-19 and aiding healthcare professionals in patient management. The study concludes with actionable recommendations, acknowledges its limitations, and suggests avenues for future research.

7.1.Recommendation

The pandemic has presented numerous challenges to the global healthcare community. One of the most pressing issues is identifying reliable biomarkers that can predict patient outcomes. This study has shed light on the correlation between CRP with patients' status and patient outcomes. These findings provide valuable insights into the clinical trajectory of COVID-19 and offer actionable data that can influence both clinical practice and public health strategies.

Given the significance of CRP as a prognostic tool, it is crucial to translate these insights into practical applications. To this end, we recommend implementing the following

suggestions across various healthcare domains, from individual patient management to broader public health policies. By doing so, healthcare providers and policymakers can improve patient care, optimize resource allocation, and enhance overall health outcomes during the pandemic and future healthcare crises.

By adopting these following recommendations, healthcare providers and policymakers can respond to the pandemic more efficiently and effectively. This will ultimately lead to better patient prognosis and resource management.

1. Customizing Treatment Plans: Treatment plans can be tailored to individual patients by using CRP levels to manage potential complications more aggressively.
2. Raising Awareness: Healthcare professionals can be educated on the importance of CRP in assessing COVID-19 severity, enabling them to interpret results more effectively.
3. Holistic Patient Assessment: CRP monitoring can be integrated into a wider range of clinical parameters for a more comprehensive patient assessment.
4. Patient Education: Patients and their families can be informed about the significance of CRP levels, improving their understanding of the disease process and treatment methods.
5. Resource Prioritization: CRP level data can be used to prioritize resource allocation for high-risk patients, such as ICU beds and ventilators.
6. Pandemic Preparedness: Pandemic response plans can include CRP level monitoring for quicker identification of high-risk cases and more effective containment strategies.
7. Development of a CRP-Based Artificial Intelligence model for enhancing and improving patient outcomes.

7.2.Limitations

1. Generalizability: The study's findings may not be universally applicable across different populations or non-COVID-19 patients.
2. Data Constraints: The reliance on a single biomarker like CRP may overlook the multifactorial nature of diseases like COVID-19.

7.3.Future Studies

1. The study conducted at one of the referring center's hospitals pivots to conduct broader population studies. The research should be extended to diverse populations to validate and refine the findings.
2. This is the first study to try to find the power of CRP as a prediction tool for COVID-19 severity and mortality in Palestine. It's crucial for comparative Biomarker Analysis studies. Future research should compare CRP with other biomarkers to develop a more comprehensive prognostic model.

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Appendix

(Appendix 1): Data Collection Tool.

Demographic data	
Items	Answer
Case serial number	
Gender	
Age	
Occupation	
Marital status	
Pregnancy	
City	
Weight (Kg)	
Height (cm)	
Smoking Status	
PCR test	
Date of admission	
Date of death	
Date of positive test	
Date of having at least one symptom	
Signs and symptoms	
Fever	
Fatigue	
Myalgia	
Loss of taste	
Loss of smell	
Cough	
Dry cough	
Productive cough	
Shortness of breath	
Chest discomfort	
Sore throat	
Runny nose	
Congested nose	
Sneezing	
Rash	
Headache	
Seizure	
Abdominal pain	
Diarrhea	
Constipation	
Nausea	
Vomiting	

Sweating	
Hoarseness of voice	
Neurological abnormalities	
Joint pain	
Chills	
Vital sings	
Blood pressure	
Heart rate	
Temperature	
Oxygen saturation	
Respiratory rate	
Comorbidities	
Diabetes mellitus	
Hypertension	
Ischemic heart disease	
Heart failure	
Previous history of ischemic stroke	
Previous history of hemorrhagic stroke	
Cardiovascular diseases	
History of cancer	
Respiratory diseases	
Obesity; BMI >40	
Immunodeficiency	
chronic obstructive pulmonary disease	
kidney diseases	
Oxygen requirements	
Room Air	
Nasal Cannula	
Face mask	
High flow	
Noninvasive ventilation	
Invasive ventilation	
Complications	
Cardiogenic shock	
Septic shock	
Hepatic dysfunction	
Hyper Coagulopathy status	
Thrombocytopenia	
Anemia	
Hypoproteinemia	
Heart failure	
Arrhythmia	
Myocardial infarction	
Sepsis	

Lung injury	
Acute kidney injury	
Kidney failure	
Laboratory results	
CRP on admission CRP1	
CRP second day of admission CRP2	
CRP two days before disagreeing or deceased CRP3	
CRP one day before discharge or deceased CRP4	
Ferritin level	
d-dimer level	
LDH level	
Platelet level	

(Appendix 2): Al-Quds University IRB approval.

Al-Quds University
Jerusalem
School of Public Health

جامعة القدس
القدس
كلية الصحة العامة

التاريخ : 17/6/2022

عزيزتي الطالب محمد عواد المحترم
برنامج ماجستير: السياسات والادارة الصحية

الموضوع: موافقة لجنة اخلاقيات البحث العلمي

قامت اللجنة الفرعية لأخلاقيات البحث التابعة لكلية الصحة العامة بمراجعة مشروع الرسالة

بعنوان:
" The Power of C-Reactive Protein biomarker in Detecting the Severity Progress of COVID-19 Patients Illness"

المقدم من (مشرف الرسالة/ د.عاطف الريماوي).

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