THE IMPACT OF COMORBIDITIES ON OUTCOME OF PATIENTS ADMITTED WITH CORONAVIRUS DISEASE 2019 INFECTION AT PIETERSBURG HOSPITAL, POLOKWANE, LIMPOPO PROVINCE

by

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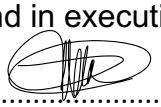
DEDICATION

I dedicate this work to my sons, Mahlogonolo and Tumishang, who brought joy in our lives and afforded us the opportunity to be parents, and to my wife, Lerato, who continues to be my pillar of strength.

DECLARATION

I declare that the mini-dissertation hereby submitted to the University of Limpopo, for the degree of Master of Medicine in Internal Medicine has not previously been submitted by me for a degree at this or any other university; that it is my work in design and in execution, and that all material contained herein has been duly acknowledged.



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Moabelo, KJ (Dr) **Date**

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ABSTRACT

Background: The emergence of the novel Coronavirus disease 2019 (COVID-19), causative agent identified as severe acute respiratory syndrome-coronavirus type 2 (SARS-CoV-2), in late 2019 in Wuhan City, has led to a global outbreak of COVID-19 culminating in the declaration of a pandemic by the World Health Organization (WHO). As of 2nd of October 2022, the cumulative number of cases have reached the 600 million mark, with just over 6.5 million deaths reported to WHO.

Purpose: To determine the relationship between comorbidities and adverse outcome in patients admitted with COVID-19 infection at Pietersburg Hospital from March 2020 to March 2021.

Methods: This was a retrospective study using secondary data extracted from DATCOV portal, a web-based disease surveillance system of patients admitted with laboratory-confirmed SARS-CoV-2 PCR results. Variables extracted from the portal include demographics and clinical data such as comorbidities, management strategies and adverse outcomes (need for oxygenation, organ failure, admission to high care or intensive care unit (ICU) and death). Data was analysed using SSPS 27.0. Variables were presented as numbers, percentages and cross-tabulations.

Results: There were 446 eligible study participants, 225(50.4%) were females and 221(49,6%) were males, and 311(70%) had comorbidities. The median age of patients was 57 (13-96) years. The most prevalent comorbidity was hypertension in 208 patients (46%) followed by diabetes in 153 patients (34%).Both hypertension and diabetes largely contributed to the reported adverse outcome of death. A total of 159 (36%) deaths related to COVID-19 infection were reported during the study period. Using the logistic regression model, the odds of non-survival were significantly associated with two variables, age and ward setting. An increase in patient's age by 1 year, increased the odds of dying by 1.09 as compared to being alive (OR 1.094, 95% CI: 1.038-1.153, p-value<0.001). Being admitted to intensive care unit (ICU) was associated with a higher death rate (OR 0.020, 95% CI: 0.001-0.292, p-value 0.004).

Conclusion: Hypertension and diabetes (p-values of 0.020 and 0.009 respectively) appeared to be significantly related to patient's adverse outcome of non-survival, with hypertension being the common factor in all deaths reported.

Keywords: Covid-19, SARS-CoV-2, Comorbidities, adverse outcome

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ABBREVIATIONS AND ACRONYMS

ACE-2	Angiotensin Converting Enzyme 2 receptor
CDC	Centres for Disease Control and Prevention
COVID-19	Coronavirus disease 2019
HIV	Human Immunodeficiency Virus
ICU	Intensive Care Unit
MERS-CoV	Middle East Respiratory Syndrome coronavirus
NDoH	National Department of Health
NICD	National Institute for Communicable Diseases
PUI	Person Under Investigation
RT-PCR	Reverse Transcriptase Polymerase Chain Reaction
PASC	Post-Acute Sequelae of SARS-CoV-2 infection
SA	South Africa
SARS-CoV2	Severe Acute Respiratory Syndrome-Corona Virus-2
TB	Tuberculosis
WHO	World Health Organization

DEFINITION OF CONCEPTS

Comorbidity	: Co-existing illnesses or diagnoses in relation to the index condition that is the focus of the study (National Centre for Biotechnology Information, 2021a). In this study it refers to pre-existing or newly diagnosed underlying disease other than COVID-19 such as diabetes, hypertension, chronic renal failure, Asthma, Chronic lung disease, malignancy, HIV, Tuberculosis, etc.
Coronavirus disease 2019 (Covid19)	: It is a novel coronavirus due to Severe Acute Respiratory Syndrome-Coronavirus type 2 (SARS-CoV-2) virus responsible for the extremely contagious mild to severe respiratory disease (Merriam-Webster Dictionary, 202). In this study it refers to an infectious respiratory disease caused by a SARS-CoV-2 virus.
Person under investigation (PUI)	: Those who require COVID-19 testing or who have an acute respiratory infection with at least one of the following abrupt onset symptoms: dyspnoea, a cough, a sore throat, or a fever [38°C (measured) or a subjective history of fever], regardless of admissions status (National Institute for Communicable Diseases (NICD), 2020a). In this study it refers to individuals without a laboratory confirmed test but suspected to have a COVID-19 infection based on symptoms and signs observed while awaiting SARS-CoV-2 reverse transcriptase-polymerase chain reaction (RT-PCR) results.

DATCOV	: A COVID-19 admissions sentinel surveillance system that is electronic, hospital-based, and operated by South Africa's National Institute for Communicable Diseases (Jassat, Cohen, Kufa et al., 2020). In this study it refers to the data collection tool used to record the patient with a laboratory confirmed SARS-CoV-2 RT-PCR test.
Adverse outcome or serious illness	: It is characterized as a hospital stay, admission to the intensive care unit (ICU), a high level of care, a diagnosis of acute respiratory distress syndrome (ARDS), intubation, mechanical ventilation, or death.(Centers for Disease Control and Prevention (CDC),2020; NICD, 2021). In this study it means a COVID-19 infected patient who requires Non-invasive ventilation, high flow nasal cannula oxygen, or invasive mechanical ventilation), and/or develops another organ failure and/or requires admission to high care or ICU, and/or dies in a hospital.
Risk factors	: Refers to personal traits and qualities as well as environmental exposure that, according to epidemiological research, raises the risk of contracting a disease. (National Centers for Biotechnology Information,2021b). In this study it refers to behavioural aspect (e.g., smoking), underlying disease(s), and/or therapeutic agents such as immunosuppressive drugs (e.g., chemotherapy, steroids), which

predisposes a person to contract COVID-19 infection.

CHAPTER 1: INTRODUCTION & BACKGROUND

1.1 Introduction and background

In December 2019, the new coronavirus pneumonia outbreak caused by infection with SARS-CoV-2, in Wuhan, Hubei, was classified as a major global public health risk (Ye, Zhang, Zhang et al.,2020). Novel coronavirus causes a severe acute respiratory syndrome that typically manifests with acute respiratory symptoms, including cough, fever, dyspnoea, joint aches, fatigue, and myalgia, as well as a number of flu-like symptoms. But asymptomatic cases have also been documented (Bajgain, Badal, Bajgain et al., 2020; Rothan and Byrareddy, 2020).

With the various waves that have been experienced, COVID-19 cases have been rising globally. The World Health Organization (WHO) Coronavirus dashboard stated that as of September 30, 2022, there have been more than 600 million infections worldwide and almost 6.5 million fatalities (WHO, 2022). As of September 30, 2022, Africa has more over 9.3 million confirmed COVID-19 pandemic cases, similar to other continents. All 55 African nations reported a total of 174 519 deaths, with South Africa(SA) accounting for the majority of cases (WHO, 2022). Additionally, due to its distinct quadruple burden of disease, South Africa's health system was already hampered by the country's population's health demands long before COVID-19 (Lalkhen and Mash,2015).

It has been discovered that age and the presence of underlying comorbidities, which are regarded to be predictors of adverse outcome, affect the likelihood of contracting the SARS-CoV-2 virus (Bajgan et al.,2020). It has been shown that in some patients, COVID-19 infection aggravated co-existing disorders through the host immune response and frequently revealed underlying diseases with rapid progression (Rothan and Byrareddy, 2020). As a result, approximately 20% of those with multiple comorbidities required hospitalization and admission to the intensive care unit (ICU) due to the need for treatment for COVID-19 infection (Bajgan et al., 2020).

Additionally, it has been shown that in this widespread COVID-19 outbreak, having pre-existing comorbidities increases the likelihood that a person will experience

complications like acute respiratory distress syndrome (ARDS), acute renal failure, acute coronary syndrome, one or more organ dysfunction, and death (Bajgan et al., 2020; Callender, Curran, Bates et al., 2020). Therefore, the goal of this study was to investigate how comorbidities affect those with COVID-19 at Pietersburg Hospital, as well as any associated negative consequences.

1.2. Problem statement

According to research, SA has a high prevalence of non-communicable diseases (NCD), with 12 % of the population having type 2 diabetes, obesity and overweight, affecting women (68%) and males (31%) over the age of 15 years, and 35 % having hypertension (Hofman and Madhi, 2020). Chronic comorbid conditions are typically difficult to control for a variety of reasons, including an unorganized healthcare system, disruptions in the supply of medications, and a lack of skills and ability on the side of healthcare professionals (Lalkhen and Mash, 2015). The risk of severe COVID-19 illness and death is higher in those who already have these comorbidities, thus prevention and control in these individuals is crucial (Hofman and Madhi, 2020). Additionally, it has been observed that having numerous comorbidities and being over 65 years old were linked to a worse outcome and a severity of COVID-19 disease progression (Sanyaolu, Okorie, Marinkovic, et al. ,2020).

The majority of COVID-19 infection patients hospitalized require respiratory care due to pneumonia, and those with comorbidities develop severe forms of COVID-19 disease that necessitate high or intensive care with respiratory therapy. The primary cause of COVID-19 admissions to Pietersburg Hospital has also been pneumonia, and many of these patients also had concomitant conditions. However, no prior research has been done on how comorbidities affect patients at the Pietersburg Hospital who have COVID-19 infection or anywhere else in Limpopo Province.

1.3. Significance of the study

In a resource-constrained environment with comorbidities, this study will provide an unbiased examination of COVID-19 epidemiology in a province with a stressed public health system. The study will help with patient care as well as the improvement of management procedures and policies for COVID-19 prevention and response.

Additionally, it will stimulate more investigation and broaden our understanding of COVID-19.

1.4. Research question

- What impact does the presence of comorbidities have on the outcome of patients admitted with COVID-19 infection at Pietersburg Hospital?

1.5. Aim of the study

The aim of the study was to investigate the impact of comorbidities on the outcome of patients with COVID-19 infection at Pietersburg Hospital.

1.6. Objectives

The objectives of this study were as follows:

- To determine comorbidities present in patients with COVID-19 infection at Pietersburg Hospital.
- To evaluate the outcomes of patients admitted with COVID-19 infection at Pietersburg Hospital, particularly survival and deaths.
- To describe the relationship between comorbidities and COVID-19 outcomes (i.e. survival and death) at Pietersburg Hospital.

CHAPTER 2: LITERATURE REVIEW

2.1. Introduction

A literature review was conducted by visiting a variety of sites, including journals, internet search engines, and medical search engines like PubMed and Google Scholar. The terms "COVID-19," "SARS-CoV-2," "comorbidities," "epidemiology," "pathogenesis," "diagnostic," "therapy," and "complications" were used in various combinations to search for papers. After applying filters, only items written in English were chosen.

2.2. Epidemiology of Covid-19 infection

Wuhan City, Hubei Province of China, was the site of the first Covid-19 infections, which appeared after a cluster of pneumonia cases with no known cause was identified there in late December 2019 (NICD, 2020b). On February 11th, 2020, a novel coronavirus (2019-nCoV), also known as COVID-19, or SARS-CoV-2 was identified as the causal culprit (WHO, 2020a). Since then, cases have been found in more than 100 countries, including South Africa, leading the WHO declaring COVID-19 outbreak a pandemic on March 11th, 2020 (WHO, 2020a).

2.3. Basic pathogenesis and clinical manifestation

Although the initial cases were postulated to have resulted from contact with an animal host, it is now believed that the virus spreads to humans through bronchial secretions released when a sick person sneezes or coughs (SA Corona Virus Online Portal, 2020). The virus can also spread via contact with infected hands or surfaces and subsequent contact of the exposed hands with the eyes, nose, or mouth (Attaway, Scheraga, Bhimraj et al., 2021).

The betacoronavirus SARS-CoV-2 is a member of the subgenus Sarbecovirus of the family Coronaviridae, which causes unusual respiratory illness in people. The severe acute respiratory syndrome (SARS), the common cold, and the Middle East respiratory syndrome coronavirus (MERS-CoV) are just a few of the disorders that have been linked with a broad group of RNA-viruses which are single-stranded and enveloped,

known as coronaviruses (Mitchell, Chiwele and Costello, 2021). The spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins are its four primary structural proteins, and they play a significant role during entry into the host cell (Attaway et al., 2021).

The virus's main target in respiratory diseases is the lung epithelial cells. The S-protein on SARS-CoV-2 attaches to the ACE-2 receptor, which is how the virus spreads to a host. The upper respiratory tracts of humans have a high expression of ACE-2 receptors. In addition to the lungs, human mucosal surfaces and epithelial cells that surround organs like the conjunctiva, liver, kidney, and heart as well as gut cells all have ACE-2 receptors (Mustafa, Giles and Pepper, 2020; Rothan and Byrareddy, 2020).

The respiratory tract's epithelial cell undergoes proteolytic cleavage when the SARS-CoV-2 S-spike protein attaches to the ACE-2 receptor. The host cell is then infected because of viral endocytosis, maturation, replication, and shedding inside the cytoplasm. As a response, the infected cells release pro-inflammatory cytokines (cytokine storm), which may cause microangiopathic vasculopathy and B-cell secretion of SARS-CoV-2 antibodies (Attaway et al., 2021).

After an average of 5.2 days of incubation, COVID-19 infection starts to show clinical symptoms (Rothan and Byrareddy, 2020). From the start of COVID-19 symptoms through death, it takes roughly 6 to 41 days, with a median of 14 days. Depending on the patient's age and immune state, the incubation period varies. Compared to the younger patients, the incubation period is shorter in the elderly over 70 (Rothan and Byrareddy, 2020).

The most frequent presenting symptoms, according to a comprehensive review and meta-analysis, were fever, cough, exhaustion, and dyspnoea (Yang, Zheng, Gou et.al, 2020). In a study of 41 hospitalized patients in Wuhan, China, it was discovered that fever (98%) cough (76%) and myalgia or weariness (44%) are the most prevalent symptoms during the beginning of an illness. Less common symptoms include sputum production (28%) headache (8%) haemoptysis (5%) and diarrhoea (3%) (Huang, Wang, Li et al., 2020). Out of 40 patients, 22 experienced the start of dyspnoea, with a median time from the disease onset of about 8 days.

COVID-19 and earlier coronaviruses display similar clinical symptoms such as fever, dry cough, dyspnoea, and bilateral ground-glass opacities on imaging. However, COVID-19 displayed certain distinct clinical characteristics, such as targeting of the upper airway. This was demonstrated by symptoms of the upper respiratory tract, such as rhinorrhoea, sneezing, and sore throat. Similar to MERS-CoV or SARS-CoV, COVID-19 also causes gastrointestinal symptoms (Rothan and Byrareddy, 2020).

2.4. Diagnosis of Covid 19

An in-lab molecular test is used to identify COVID-19. Sputum, tracheal aspirates, and broncho-alveolar lavage fluid are examples of lower respiratory tract samples that are sent for testing. Upper respiratory tract samples include nasopharyngeal and oropharyngeal swabs (NICD, 2020c).

Nucleic acid amplification tests, such as the Real Time Polymerase Chain Reaction (RT-PCR) molecular test, which detects SARS-CoV-2 genetic material and has high sensitivity and high specificity for diagnosing SARS-CoV-2 infection, are among the diagnostic procedures used to detect infection with the SARS-CoV-2 virus. The Point of Care Antigen Test, an immunoassay that detects the presence of a particular viral antigen and has subpar sensitivity and specificity, is another test that is employed (CDC, 2021).

It is not advised to utilize serology or antibody tests during an acute illness because they are not sensitive enough to identify the current infection. These tests are used to identify previous exposure to the SARS-CoV-2 virus. Currently, serology testing is only used for public health surveillance (CDC, 2021; WHO, 2020b). RT-PCR is therefore regarded as the gold standard test for detecting COVID-19 infection (Goudouris, 2020).

Any person in South Africa who exhibits acute respiratory symptoms (those lasting less than 14 days), such as coughing, sore throat, shortness of breath, anosmia, or any other clinical illness that favours with COVID-19, or who is asymptomatic but is a close contact of a confirmed case, should be tested (NICD, 2020c).

2.5. Treatment and outcome

According to their clinical presentation, COVID-19 patients are divided into three categories (mild, moderate, and severe), and these have a significant impact on the available therapy options (Attaway et al., 2021).

Controlling COVID-19 infection is based on the following principles: isolation of suspected and confirmed patients at a suitable location; infection prevention and control measures; symptom management (such as fever treatment); optimized supportive care (such as giving oxygen to patients who are hypoxemic and short of breath); and organ support in severe or critical illness (Mitchell et al., 2021).

Globally, it is predicted that 91.5 million patients have recovered from COVID-19 infection, and more will. Survivors of SARS-CoV-2 infection may have to battle with long term sequelae of severe inflammation from the disease with the following reported as common complications that arise from individuals infected with COVID-19 pneumonia, namely; post intensive care syndrome, venous thromboembolism, cardiovascular impairment, pulmonary impairment, acute kidney injury, neurological manifestations and post-acute sequelae of SARS-CoV-2 infection (PASC) (Africa Centres for Disease Control and Prevention, 2021; Attaway et al., 2021).

In a largest, geographically inclusive retrospective study done in the US, the in-hospital mortality rate stood at 10.6% in March 2020 with an increased trend towards 19.7 % witnessed in April 2020. A drop to 9.3 % became evident in November and this was largely due to better understanding of the disease, improved clinical care and ventilation strategies (Finelli, Gupta, Petigara et al., 2021). South Africa experienced more in-patient mortality during the second wave (Jassat, Mudara, Ozougwu et al., 2021a). The Limpopo province was also hard-hit, with 90% deaths reported during the second wave. The case fatality rate was 27.5% (Tshitangano, Setati, Mphekgwana et al., 2022). During the surge of the epidemic in the first wave, the Mthatha Regional Hospital, serving majority of rural areas similar to Pietersburg Hospital, experienced the highest recorded in-hospital mortality rate of 46%, a figure way above the Eastern Cape provincial rate (27.5%) and national rate of 18.3% between March and July (Kaswa, Yogeswaran and Cawe, 2021). High volume of patients experienced together with inadequate staff personnel, more pressure on bed and oxygen availability and

limited access to ICU, late presentation to hospital, contributed largely to reported in-hospital mortality (Kaswa et al.,2021).

2.6. Comorbidities in patients with COVID-19 infection

The effects of comorbidities on a variety of diseases have been extensively studied globally (Callender et al.,2020; Gasmi, Peana, Pivina et al.,2021). People with underlying health difficulties have been demonstrated to have severe, life-threatening sickness and a significant mortality rate, according to a systematic review and meta-analysis on the frequency of comorbidities in the Middle East Respiratory Syndrome coronavirus (MERS-CoV) (Badawi and Ryoo, 2016).

The non-communicable diseases (NCDs) such as hypertension, type 2 diabetes, obesity and overweight, are prevalent and contribute to the burden of disease in SA (Hofman and Madhi, 2020). With a prevalence of 19 percent and 0.7 percent, respectively, among persons aged 15 to 49 in 2020, HIV and TB are epidemics that coexist with the high rate of NCDs (Jassat, Cohen, Tempia et al., 2021b). According to the most recent data from 2019, over 7.5 million persons in SA are thought to be HIV positive. About 2.3 million of the 7.5 million people with HIV did not obtain treatment despite being eligible (Jassat et al., 2021b), and this typically occurs in conjunction with a high incidence of TB (Mash, Presence-Vollenhoven, Adeniji et al., 2021).

At the beginning of the epidemic, it was thought that HIV-positive individuals would largely experience extremely high case fatality rates due to their compromised immunity (Blumberg, Jassat, Mendelson et al., 2020). However, there was paucity of data at the time due to few research carried out in underdeveloped nations with high rates of chronic communicable diseases like HIV and TB. Therefore, there was insufficient data to support the idea that HIV or TB infection alone increases the chance of contracting SARS-CoV-2 or has negative COVID-19 consequences (Blumberg et al., 2020; Rossouw, Boswell, Nienaber et al., 2020). However, Blumberg et al. (2020) found that those with additional comorbid conditions (such as diabetes mellitus and hypertension) had an increased risk of developing severe disease.

Only four studies emanating from Africa reported a link between comorbidities and COVID-19, with many studies coming out of Europe, America, and Asia (Ratshikhopha, Muvhali, Naicker et al.,2022). The African Covid-19 Critical Care

Outcomes Study (ACCCOS), a significant multicentre, prospective, observational cohort study, involved 64 institutions from ten different African nations, with South Africa as one of them. Their main concern was the in-hospital mortality of critically ill Covid-19 patients admitted to high-care settings like the intensive care unit. Their research revealed a link between higher mortality and comorbidities such HIV/AIDS, diabetes, chronic liver disease, renal disease, and the severity of organ malfunction at the time of admission as well as a lack of critical care amenities (Biccard, Gopalan, Miller et al.,2021).

Studies "were not clear on whether HIV or TB are risk factors for disease severity and death in COVID patients" since they were conducted in high-income nations with lower rates of HIV and TB (Jassat et al, 2021b). These studies were conducted in communities that were distinct from those in South Africa, where there was a lower prevalence of TB and HIV..

Jassat et al. (2021b) discovered that HIV and TB were synergistically connected with a moderate risk of in-hospital COVID-19 mortality in a national cohort research they did in South Africa. They also found that age, sex, and other comorbidities were also associated with this risk. People with HIV who were antiretroviral therapy naive were at increased risk.

The most prevalent comorbidities, according to research done in the United States (US), were diabetes, obesity, and hypertension. Of the 5700 patients who were admitted with COVID-19, 14.2% of those who were discharged or died received intensive care unit (ICU) treatment, 12.2% underwent invasive mechanical ventilation, 3.2% underwent kidney replacement therapy, and 21% passed away (Richardson, Hirsch, Narasimhan et al., 2020). Being a large study, having enrolled 5700 patients with COVID-19, the study was done in a single geographical area.

In a similar vein, 41 hospitalized patients in China as of January 2, 2020, had been identified as having COVID-19 infection. Less than half of infected people (32%) had concomitant conditions, which included diabetes (20%), hypertension (15%), and cardiovascular disease (15%). The majority of infected people (73%) were men (Huang et al., 2020). Even early on during the emergence of the pandemic, it became evident that there was a high baseline prevalence of clinically significant comorbidities in most of the hospitalized patients.

According to a study article, the most frequent comorbidities seen in patients with COVID-19 infection were hypertension, diabetes, and cardiovascular illnesses. Having several comorbidities was linked to a higher chance of illness severity, however, there was no correlation between these risk factors and a higher risk of death (Bajgain et al., 2020).

Smoking, pregnancy, immunosuppressive treatment, and long-term steroid usage are other possible risk factors linked to SARS-CoV-2 virus infection and subsequent unfavourable outcome. In a significant meta-analysis, individuals with COVID-19 were found to have a higher risk of illness severity and in-hospital mortality if they currently smoke or have smoked in the past. It has been demonstrated that smoking increases the expression of the ACE-2 receptor, a host receptor exploited by the SARS-CoV-2 virus to enter the mucosa (Reddy, Charles, Sklavounos et al.,2020).

Data available indicates that patients with malignancy, particularly those with lung and haematological malignancies, are more likely to develop severe COVID-19 infection and die from it (Uzzo, Kutikov and Geynisman, 2021). Depending on the type of chemotherapy used, the current body of literature presents contradictory findings regarding the relationship between active oncologic therapy and poor outcomes. For instance, a higher risk for aggressive chemotherapy with myelosuppressive drugs was seen in a large British population-based cohort research (Clift, Coupland, Keogh et al.,2020).

Anti-inflammatory and immunosuppressive medications called corticosteroids are frequently used in COVID-19 (Wang, Yang, Chen et al.,2021). They have acquired popularity because of the pandemic. It is important to remember that although beneficial in certain COVID-19 cases, persons using oral corticosteroids for other ailments may be more susceptible to getting COVID-19 and having a more severe case of it (Richards and Feldman, 2020).When used during severe COVID-19 infection, corticosteroids should be used with caution because they appear to be linked to a delayed viral clearance, especially in patients with the infection (Wang et al.,2021).

Due to the physiological and immunological changes brought on by pregnancy, pregnant women may be more susceptible to contracting the SARS-CoV-2 virus and developing complications later in life (Wang, Iiu, Wu et al,2021).

The majority of the reviewed literature discusses NCDs that are widespread in our environment, but it says little about communicable diseases like HIV and TB, which are also widespread there. There is an anticipation of a varied disease burden and outcome due to Pietersburg Hospital's rural location, resource limitations, and different disease profile. Therefore, it is crucial to determine how comorbid illnesses like HIV and TB, which are both common, affect the prognosis of people with COVID-19 disease.

CHAPTER 3: RESEARCH METHODOLOGY

3.1. Introduction

The sample strategies of study, data extraction techniques, and methods and materials used for data collecting are all covered in this chapter. Additionally, it goes into great detail to outline the steps taken to obtain the study's data as well as significant ethical issues. It provides a broader definition of the population and details the measures used to guarantee the study's validity and reliability.

3.2. Study design

This study examined adult patients who were hospitalized to Pietersburg Hospital between March 2020 and March 2021 with COVID-19 infection. It was a retrospective, descriptive analysis.

3.3. Study setting

The study was carried out at Pietersburg Hospital, a public tertiary referral facility offering specialist care located in the City of Polokwane within the Capricorn district, in the province of Limpopo. It receives referral from all health care facilities in the province. The hospital includes 20 wards with 504 useable beds out of 701 permitted beds, including adult and paediatric intensive care units and cardiology and cardiothoracic intensive care units. Out of the above-mentioned total bed number, 90-beds in three wards- namely COVID-19 ICU, isolation ward, and PUI ward were established to accommodate COVID-19 patients and PUIs. Medical professionals, nurses, pharmacists, allied health professionals including physiotherapists, occupational therapists, speech therapists, and audiologists, as well as dieticians, dentists, and clinical technicians, make up the staff composition.

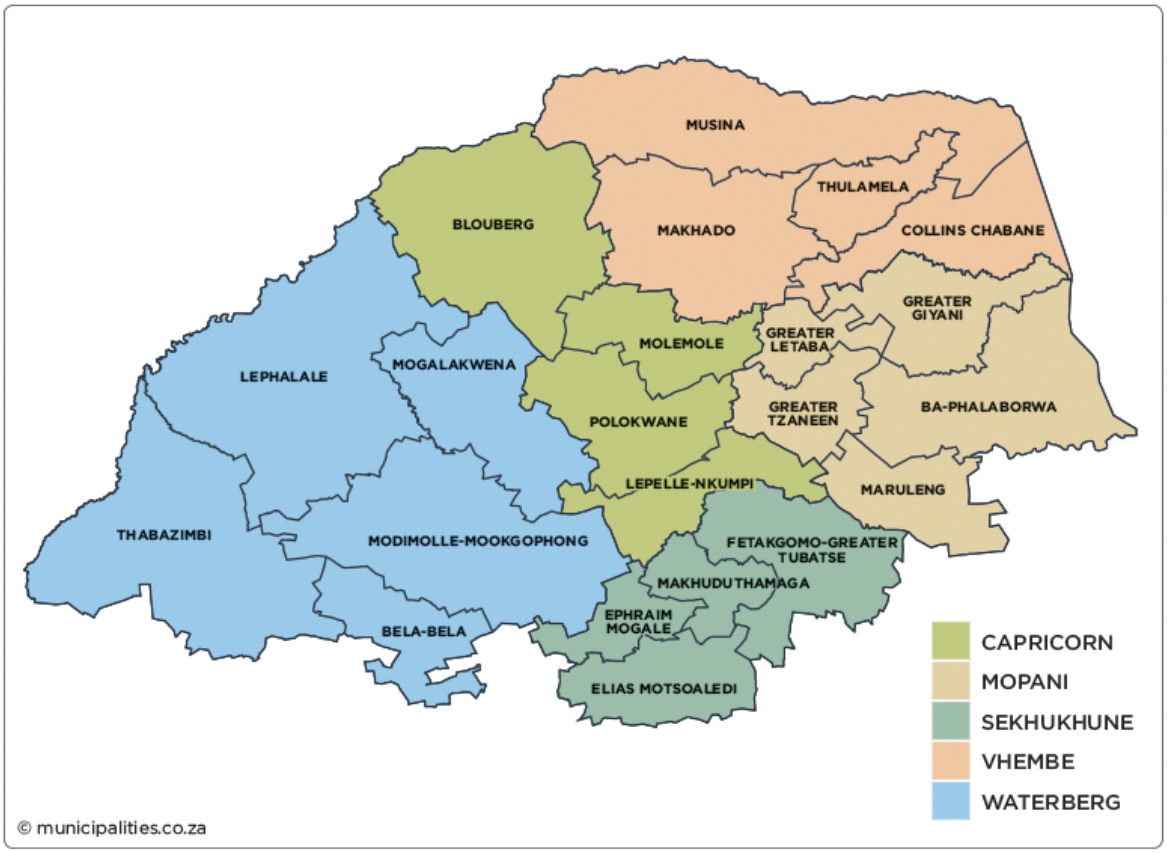

Figure 3.3.1: The population map of Limpopo Province and its districts and municipalities.

https://municipalities.co.za/provinces/view/5/limpopo [Accessed 13 October 2022]

3.4. Study Population

Population group enrolled in this study included all adults and adolescents outside paediatric age group (i.e., ≤12 years old) with a confirmed SARS-CoV-2 PCR test admitted to our isolation wards including ICU at Pietersburg Hospital between March 2020 to March 2021.

Inclusion criteria

- All adults (> 12 years) patients
- Confirmed cases of SARS-CoV-2 infection by positive results on polymerase chain reaction (PCR) testing of a nasopharyngeal or oropharyngeal swab in patients admitted for pneumonia in Pietersburg Hospital.

Exclusion criteria

- Paediatric patients because my specialty is in adult medicine. According to the hospital policy, any patient above the age of 12 years belong to Internal Medicine and that is where my interest lies.
- Persons under investigation (PUI), as they do not have a laboratory, confirmed the test, but suspected to have COVID-19 infection based on symptoms and signs observed while awaiting SARS-CoV-2 reverse transcriptase-polymerase chain reaction results.

3.5. Sampling Technique and Sampling Size

Sampling is the method of choosing a group of people from a population in order to estimate the characteristics of the full population (Singh and Masuku, 2014). Based on eligibility requirements, participants were chosen using a census sample technique. In a census study, every member of a population or group is counted in relation to a specific attribute at one moment in time (House, 2001). The researcher used participants based on accessibility and shared characteristics in this census survey. Any person who was admitted to the isolation unit and met the qualifying requirements was therefore enrolled in the trial. To obtain a 95-percent confidence level with a 5-percent margin of error, the sample size of 385 patients or so was required.

3.6. Data Collection

In this study, the researcher made use of secondary data collected by the National Institute for Communicable Diseases (NICD) DATCOV portal, which is a web-based disease surveillance system (version v2.4.35) from March 2020 to March 2021. An application to make use of this data was sought from the NICD and permission was granted prior to collection of the data.

The data collection tool was adapted from DATCOV portal and modified for the purpose of the study and was presented to the Department of Internal Medicine at Pietersburg Hospital for further inputs. The tool included four sections, namely, demographics, comorbidities (self-reported, based on clinical diagnosis, and/or on treatment), onset and admission and patient outcomes (Annexure A).

3.7. Data Analysis

SPSS 27.0(IBM Corporation, Armonk, New York, USA), a statistical analysis programme, was used to analyse the data. In order to determine which comorbidities were present in COVID-19 infection patients at Pietersburg Hospital, descriptive statistics were used. The means and medians were used to present continuous variables. Cross-tabulations, percentages, and numbers were used to present categorical variables. The Chi-square test was employed to ascertain whether categorical variables were associated. Using a multivariate logistic regression model, the link between comorbidities and survival as a result was examined. For the examination of several outcomes in connection with numerous independent factors, a multivariate model was utilized. In this study, COVID-19 survival was the endpoint, while age, gender, race, and comorbidities were the independent variables. The odds ratio and 95% confidence interval of the chosen predictor variables were used to express the results. The Chi-square test was used to determine the significance of the data. A P-value of less than 0.05 was used as a criteria for the undesirable adverse occurrence of non-survival.

3.8. Internal and External Validity of the Study

If a research tool regularly yields the same results when used in similar situations, it is said to be reliable (Heale and Twycross, 2015). On April 1, 2020, Tygerberg Hospital in the Western Cape province piloted the data collection tool. It was extended to specified public health sector institutions in each province that reported admissions of Covid-19 patients following a successful pilot (Jassat et al.,2020).

The degree to which an idea is accurately measured is what is meant by "validity" (Heale and Twycross, 2015). Numerous reports based on DATCOV data were generated and used at different levels for public health initiatives. The information from DATCOV was used by the Ministerial Advisory Committee and the Incident Management Team, two organizations established to oversee the outbreak response (Jassat et al., 2020).

3.9. Ethical Consideration

Participants' rights and all ethical guidelines for conducting research involving human beings were upheld. Prior to data collection, study protocol was authorized by the Turfloop Research Ethics Committee (TREC) of the University of Limpopo, project number TREC/99/2022:PG (Annexure B).

The Provincial Research Committee of the Limpopo Department of Health gave approval for the study, with approval code LP 2022-05-029 (Annexure C). Additionally, the management of Pietersburg Hospital, reference number 4/2/2, and the Pietersburg-Mankweng Research Ethics Committee (PMREC), project number PMREC 31 August UL 2022/B (Annexure D), both gave authorization (Annexure E). Additionally, NICD gave permission for the usage of the DATCOV Portal's data.

The names of patients were not disclosed in the study. Instead, study participants were allocated unique numbers only known to the researcher. The data collected was completely anonymized. An application for waiver of informed consent was made (Annexure G)

3.10. Conclusion

This chapter provided a brief overview of the research methodology, research design, sampling technique, and data collection procedures used in the study. It continued by outlining ethical concerns around data collecting, data analysis and presentation, and the length at which validity of the study was ensured.

CHAPTER 4: PRESENTATION/ INTERPRETATION OF FINDINGS

4.1. Introduction

The study design, the study environment, the study population, the inclusion, and exclusion criteria, data collection, and analysis, validity, reliability, and bias, and finally the ethical consideration were covered in the preceding chapter. This section provides a summary of the researcher's results and conclusions based on data that was gathered and examined with the assistance of a statistician. Regarding their applicability to the study's goal, the discussion and interpretation of the results will give some light. As a result, the following will be covered in this chapter:

a. Demographics and clinical characteristics of patients with COVID-19 infection.
b. Comorbidities present in patients with COVID-19 infection.
c. Outcomes of patients admitted with COVID-19 infection.
d. Relationship between comorbidities and COVID-19 outcomes.

4.2. Demographics and clinical characteristics of participants

During the period of the study, a total of 463 patients with confirmed COVID-19 infection were admitted at Pietersburg hospital. Of 463 patients, 446 patients were included in the study and only 17 were excluded as they did not meet the inclusion criteria (Figure 4.2.1).

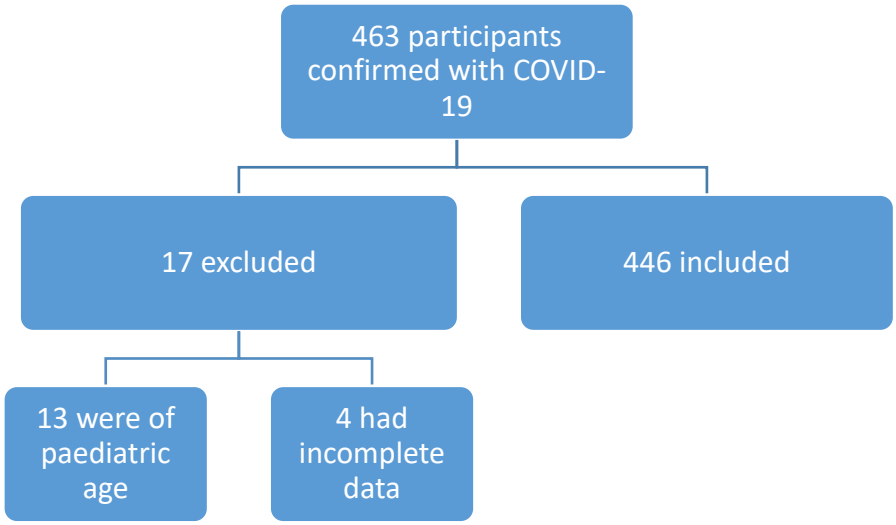

Figure 4.2.1: Study participants who met inclusion criteria

They comprised of 225 (50.4 %) females and 221(49.6%) males, with a median age of 57 (13-96) years (figure 4.2.2).

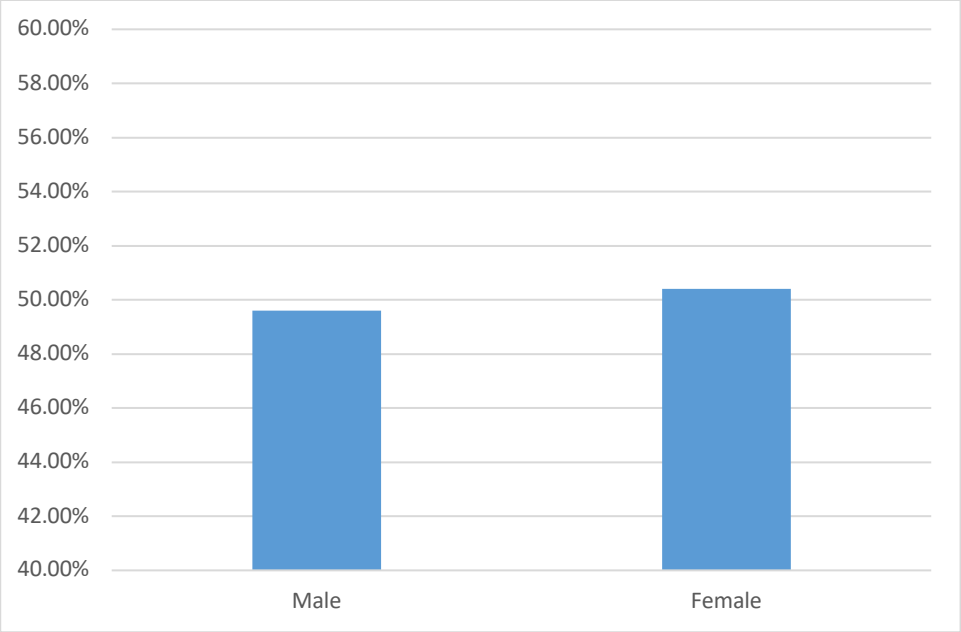

Figure 4.2.2: Distribution of patients by gender (n=446)

The ethnic groups of the study participant is shown in Figure 4.2.3. The majority of the patients were of Black African race, with 414(93%) participants .

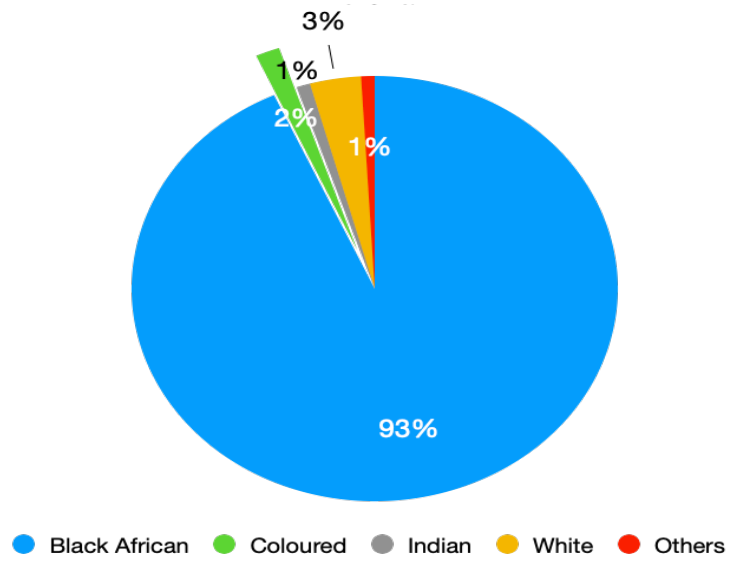

Figure 4.2.3: Ethnic group distribution of study participants

The majority of patients admitted were in the age category between 50 to 69 years of age. The younger patients were not severely affected by the pandemic during the period of study. The statistics indicate that the teenage group falling within the age category of 10-19 years only contributed 1.8 % of the disease burden (Figure 4.2.4).

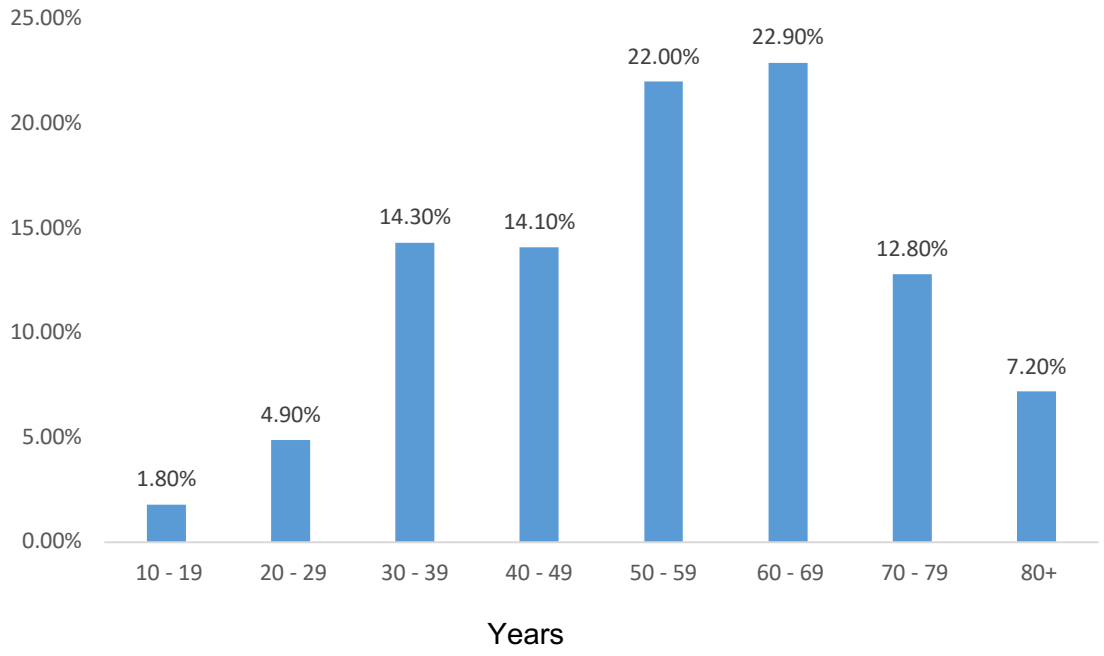

Figure 4.2.4: Age groups of patient with COVID-19 infection seen in the study

4.3. Comorbidities present in patients with COVID-19 infection

Of 446, 311(70%) had comorbidities, namely, hypertension (208 [46%]), diabetes (153 [34%]), HIV (54 [12%]), chronic renal failure (32[7%]), cardiac disease (27[6%]), asthma (20[4%]), chronic pulmonary disease (14[3%]), malignancy (13[3%]) and active tuberculosis (5[1%]) (Table 4.3.1). Out of 153 patients with diabetes, 24 (16%) patients were reported to be newly-diagnosed with diabetes.

Table 4.3.1:Comorbidities present in patients with COVID-19

Comorbidities		Female	Male
Hypertension	No	97 (47.1%)	102 (50.7%)
	Yes	109 (52.9%)	99 (49.3%)
Diabetes	No	128(64.0%)	120(59.7%)
	Yes	72(36.0%)	81(40.3%)
Diabetes status	Newly-diagnosed	13(5.8%)	11(5.0%)
	Pre-existing	55(24.4%)	57(25.8%)
Cardiac disease	No	175(93.1%)	174(92.6%)
	Yes	13(5.8%)	14(6.3%)
Chronic Pulmonary Disease	No	185(98.9%)	174(93.5%)
	Yes	2(1.1%)	12(6.5%)
Asthma	No	176(93.1%)	183(96.3%)
	Yes	13(6.9%)	7(3.7%)
Chronic Renal Failure	No	171(90.5%)	174(92.6%)
	Yes	18(9.5%)	14(7.4%)
Malignancy	No	176(95.7%)	180(97.3%)
	Yes	8(4.3%)	5(2.7%)
Tuberculosis Active	No	173(99.4%)	167(97.7%)
	Yes	1(0.6%)	4(2.3%)
Tuberculosis Past	No	97(96.0%)	100(91.7%)
	Yes	4(4.0%)	9(8.3%)
HIV Positive	No	97(78.9%)	73(72.3%)
	Yes	26(21.1%)	28(27.7%)

4.4. Outcomes of patients admitted with COVID-19 infection

Throughout the period of study, a total of 159 (36%) deaths related to COVID-19 infection were reported whilst 287 persons survived. In contrast, 82 (37.1%) male patients died compared to just 77 (34.2%) female patients; nevertheless, there was no statistically significant difference between the two groups (p-value = 0.525 Table 4.5.1). A total of 394 patients with COVID-19 were admitted in the general ward whilst

a combined number of 52 persons required admission to an advanced level of care (i.e. high care and ICU respectively). The majority of patients who were hospitalized and admitted to the general ward, required supplemental oxygenation (83%) whereas 72 did not require supplemental oxygen probably due to their non-severity of the disease. However, only 31(7%) patients needed to be mechanically ventilated and were admitted in ICU. Given the high number of patients who were admitted (446), more than 31 patients surely needed escalation to ICU (Table 4.4.1). However, due to resource constraints, with few number of ICU beds available at Pietersburg hospital to cater to the majority of patients, most could not access it.

Table 4.4.1. Outcomes of patients admitted with COVID-19 infection

Clinical characteristics		Frequency	Percentage
Supplemental Oxygen	No	72	16.1%
	Yes	374	83.9%
Mechanical Ventilation	No	415	93.0%
	Yes	31	7.0%
Ward setting	General Ward	394	88.3%
	High Care	3	0.7%
	Intensive Care Unit	49	11.0%

4.5. Relationship between comorbidities and COVID-19 outcomes

In terms of comorbidities present, only hypertension and diabetes (p-values of 0.020 and 0.009 respectively) appeared to be significantly related to patient's adverse outcome of non-survival, with hypertension being the common factor in all deaths reported. In patients who had comorbidities other than hypertension and diabetes, no significant difference was observed in patients who reached the adverse event of death (p-value > 0.05), (Table 4.5.1). Communicable diseases, such as active TB and HIV, with the only 5 and 54 cases reported respectively, did not show any significant impact with regard to non-survival outcome, p-values 0.286 and 0.193, with the majority of them surviving. Regarding patients with respiratory illnesses , chronic pulmonary disease and asthma collectively, fared better as they had more survival than deaths. (Table 4.5.1) Smoking as a risk factor, did not seem to contribute much negatively to the adverse outcome as expected, probably due to lesser individuals self-reporting to be current or previous smokers.

Table 4.5.1. Relationship between comorbidities and COVID-19 outcomes

Variables		Output		
		Alive	Died	P-value
Gender	Female	148 (65.8%)	77 (34.2%)	0.525
	Male	139 (62.9%)	82 (37.1%)	
Hypertension	No	137 (68.8%)	62 (31.2%)	0.020
	Yes	120 (57.7%)	88 (42.3%)	
Diabetes	No	170(68.5%)	78(31.5%)	0.009
	Yes	85(55.6%)	68(44.4%)	
Diabetes status	Newly-diagnosed	14(58.3%)	10(41.7%)	0.004
	Pre-existing	58(51.8%)	54(48.2%)	
Cardiac Disease	No	221(63.3%)	128(36.7%)	0.674
	Yes	16(59.3%)	11(40.7%)	
Chronic Pulmonary Disease	No	222(61.8%)	137(38.2%)	0.853
	Yes	9(64.3%)	5(35.7%)	
Asthma	No	223(62.1%)	136(37.9%)	0.107
	Yes	16(80.0%)	4(20.0%)	
Chronic Renal Failure	No	218(63.2%)	127(36.8%)	0.670
	Yes	19(59.4%)	13(40.6%)	
Malignancy	No	222(62.4%)	134(37.6%)	0.238
	Yes	6(46.2%)	7(53.8%)	
Tuberculosis Active	No	215(63.2%)	125(36.8%)	0.286
	Yes	2(40.0%)	3(60.0%)	
Tuberculosis Past	No	136(69.0%)	61(31.0%)	0.088
	Yes	6(46.2%)	7(53.8%)	
HIV Positive	No	120(70.6%)	50(29.4%)	0.193
	Yes	33(61.1%)	21(38.9%)	
Smoking	Never smoked	99(59.6%)	67(40.4%)	0.955
	Current smoker	6(46.2%)	7(53.8%)	
	Previous smoker	14(63.6%)	8(36.4%)	
Obesity	No	75(57.3%)	56(42.7%)	0.535
	Yes	32((52.5%)	29(47.5%)	

Using the logistic regression model, the two predictor variables, age and the ward setting were significantly associated with the odds of non-survival. Older age is a significant risk for COVID-19 related death. The odds of dying increase by 1.09 times for every additional year of age (OR 1.094, 95 percent CI: 1.038-1.153, p-value 0.001).Being admitted to the general ward reduced the odds of dying by 2 % compared to being in ICU (OR 0.020, 95% CI: 0.001-0.292, p-value = 0.004), (Figure 4.5.1).

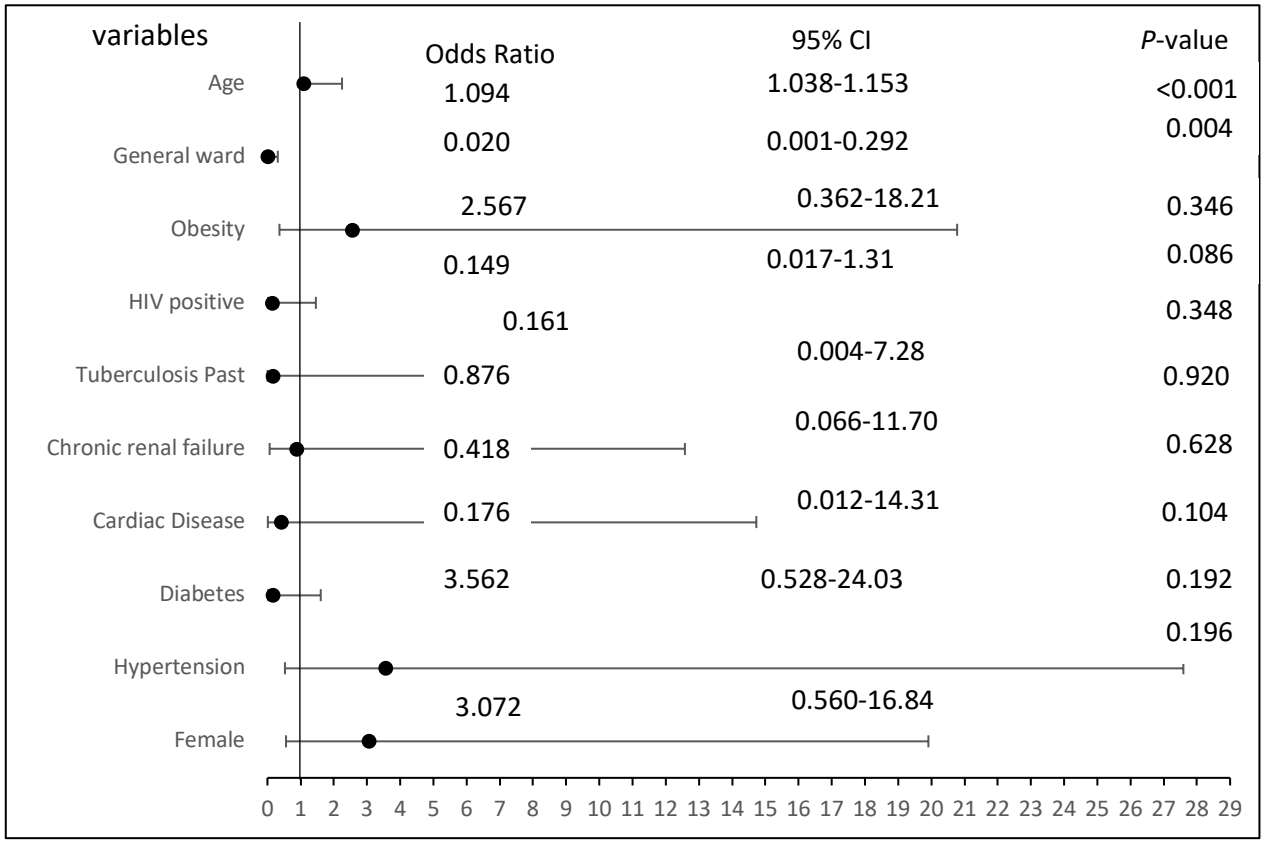

FIGURE 4.5.1 Variables and Odd ratios in a logistic regression model.

4.6. Conclusion

Hypertension and diabetes were the commonest comorbidities present in most patients in our study and had a significant influence on the outcomes of the study. The most prevalent communicable diseases (HIV and TB) in our setting seemingly did not contribute significantly to the outcomes. It can be as a result of under-investigation of the conditions. It also became evident that older age was associated with a significant risk of COVID-19 related death. Admission to the ICU was associated with poorer outcomes as compared to the general ward.

CHAPTER 5 : DISCUSSION, RECOMMENDATIONS, CONCLUSION

5.1. Introduction

In this chapter, we provide a general summary of the findings, talk about the impact the study will have on society as a whole, provide recommendations based on the findings, and then examine the difficulties and study limits.

5.2. Discussion

Hypertension and diabetes were the common comorbidities present in most patients in our study and had a significant influence on the outcomes of the study. The most prevalent communicable diseases (HIV and TB) in our setting seemingly did not contribute significantly to the outcomes. The non-communicable diseases (NCDs) such as hypertension, type 2 diabetes, obesity and overweight, are prevalent and contribute to the burden of disease in SA (Hofman and Madhi, 2020). With a prevalence of 19 percent and 0.7 percent, respectively, among persons aged 15 to 49 in 2020, HIV and TB are epidemics that coexist with the high rate of NCDs (Jassat, Cohen, Tempia et al., 2021b). According to the most recent data from 2019, over 7.5 million persons in SA are thought to be HIV positive. About 2.3 million of the 7.5 million people with HIV did not obtain treatment despite being eligible (Jassat et al., 2021b), and this typically occurs in conjunction with a high incidence of TB (Mash, Presence-Vollenhoven, Adeniji et al., 2021).

A research done in the US has shown that the most prevalent comorbidities were diabetes, obesity and hypertension (Richardson, Hirsch, Narasimhan et al.,2020), a data which is comparable to ours, although in our case obesity was not significant as a result of not being objectively measured. In China during the early period of COVID-19 pandemic, they have noted a prevalence of diabetes (20%), hypertension (15%) and cardiovascular disease (15%) in 41 hospitalized patients (Huang et al., 2020).

In our study, about 49 (11%) patients required admission to the ICU, with only 31(7%) of them requiring to be mechanically ventilated. As compared to the data emanating from the US, one study reported 809 (14.2%) patients received ICU care, with 695 (12.2%) of them receiving mechanical ventilation (Richardson, Hirsch, Narasimhan et

al.,2020). The disparity in terms of available access to advance care cannot be ignored. Our study was done in a setting with limited resources as compared to the one done in the US.

Identification of vulnerable populations is crucial to lowering the risk of contracting severe COVID-19 due to the high prevalence of non-communicable diseases, obesity, HIV, and TB in South Africa (Ratshikhopa et.al, 2022).

The prevalence of comorbidities in patients with COVID-19 infection predisposes them to worse clinical outcomes compared to those without, according to a number of local and international literature. Naturally, not every pre-existing comorbidity has the same dangers. For instance, in this global outbreak, the three most significant pre-existing conditions hypertension (16%), cardiovascular disease (12.11%), and diabetes (7.87%) were primarily linked to illness severity and unfavourable outcomes (Callender et.al., 2020). A higher risk of serious adverse outcomes was also linked to having several comorbidities. In certain studies, aging was linked to an increased risk of disease severity, with older patients (60 years and older) suffering more COVID-19 complications than younger individuals (Ye et al.,2020; Guan et al., 2020, and Ratshikhopa et al., 2022).

According to this study, COVID-19 negative outcomes were linked to co-existing diabetes and hypertension. Furthermore, as people aged, the risk of not surviving increased by 1.09 times. The odds ratio below one was considered a protective factor. The majority of patients treated throughout the study period were elderly (between 50 and 69 years old) with coexisting disorders, increasing their risk of developing severe disease.

In this study, the in-hospital mortality was 159 (36%) at Pietersburg hospital. In a largest, geographically inclusive retrospective study done in the US, the in-hospital mortality rate stood at 10.6% in March 2020 with an increased trend towards 19.7 % witnessed in April 2020. A drop to 9.3 % became evident in November and this was largely due to better understanding of the disease, improved clinical care and ventilation strategies (Finelli, Gupta, Petigara et al., 2021). South Africa experienced more in-patient mortality during the second wave (Jassat, Mudara, Ozougwu et al., 2021a). The Limpopo province was also hard-hit, with 90% deaths reported during the second wave. The case fatality rate was 27.5% (Tshitangano, Setati, Mphekgwana et

al., 2022). During the surge of the epidemic in the first wave, the Mthatha Regional Hospital, serving majority of rural areas similar to Pietersburg Hospital, experienced the highest recorded in-hospital mortality rate of 46%, a figure way above the Eastern Cape provincial rate (27.5%) and national rate of 18.3% between March and July (Kaswa, Yogeswaran and Cawe, 2021). High volume of patients experienced together with inadequate staff personnel, more pressure on bed and oxygen availability and limited access to ICU, late presentation to hospital, contributed largely to reported in-hospital mortality (Kaswa et al.,2021).

There was no significant association between non-survival as an outcome and communicable diseases such as active TB and HIV, respiratory illnesses like asthma and chronic obstructive pulmonary disease. This correlates with the findings by ACCCOS multicentre cohort study with the exception that in their case, HIV was associated with increased mortality in adults admitted with COVID-19 (Biccard et al.,2021). In our case, there were less patients reported to have had HIV or active TB. This could be attributed to the under-investigation of patients who were admitted.

Obesity has been strongly connected with the probability of a catastrophic COVID-19 result in the literature. Even though it has been associated with comorbidities including hypertension, diabetes, and cardiovascular illnesses, this was frequently linked to the physiological effect it has on the lungs. Obesity reduces lung capacity which ultimately leads to invasive ventilation, made worse by the pneumonia caused by the Covid-19 virus (Gasmi et al.,2021). In our investigation, obesity was determined based on the clinician's clinical judgment as the standard method of calculating body mass index (BMI) was not used. This might have been because the COVID-19 was so severe that the majority of patients became oxygen dependent, making it challenging to measure. Another explanation could be that even individuals with mild COVID-19 infections were not properly identified because calculating BMI is not a typical practice in our setting. Therefore, in our study, the effect of obesity was not statistically significant and we acknowledge the limitation that obesity was not objectively measured hence the result should be taken with caution.

5.3. Summary and Interpretation of Research Findings

The study found that pre-existing comorbidities were linked with adverse outcomes. The presence of comorbidities did not confer similar risks to the outcomes of COVID-19. Hypertension(42.3%) and diabetes(44.4%) were associated with poor adverse events, with hypertension being a common factor in all deaths reported. Several studies support this outcome and further on, add that the increasing age worsens the poor outcome (Callender et al., 2020; Gasmi et al., 2021). In this study, the age of a patient also contributed significantly to the outcome, as an increase in age by 1 fold led to more adverse outcome (P value <0.001). For the duration of the study, 159 people (or 36% of the entire population) have passed away as a result of COVID-19 which was higher than the national and other global studies.

5.4. Limitations of the study

This is a retrospective study, therefore limitations are unavoidable. The collection of data relied mostly on Healthcare personnel to enter data onto the portal, therefore some pertinent information might have not been captured. Data is from a convenience sample of hospitalized adult patients from a single centre, not a representation of a whole population. Patients were not followed up post discharge in this study, hence the study outcome might have been underreported as some patients who were discharged or transferred to other facilities could have suffered the adverse events thereafter. Obesity was not objectively measured and together with underestimation of TB and HIV, could have influenced the association with outcomes. However, the strength of study is drawn from a large sample size.

5.5. Contributions of the study

This study offers an objective analysis of COVID-19 epidemiology in a resource limited setting plagued by co-morbidities and located in a province with an overwhelmed public health system. The study assists in patient management and should aid in the improvement of management protocols and policies for COVID-19 prevention and response. If there is a causal relationship between chronic diseases and severe COVID-19 patients, it will be easier for the health sector to identify at-risk groups and evaluate their risks in order to reduce COVID-19 consequences. This will guide proper planning of healthcare.

5.6. Conclusion

According to the study, individuals who have COVID-19 on a background of hypertension and diabetes, were more likely to die from the infection when multi-morbidity, advanced age, and a failing medical facility with few resources are present.

In brief, the study brought to light the importance of reinforcing primary health care to improve on its plight to reduce morbidity related to non-communicable diseases such as hypertension, diabetes, which were commonly associated with worse adverse outcomes. This global pandemic also revealed some health system failures/challenges related to the ailing infrastructure and resource limitations including personnel to manage a pandemic of such magnitude.

To research how this epidemic affects individuals with comorbid conditions and to follow up on the patients who survived, a larger, countrywide investigation is required. This will help with the analysis of COVID-19's long-term effects.

5.7. Recommendations

- Future studies should look at multiple sites within the province to assess the impact on a larger scale.
- Primary Health Care should be strengthened to curb the high number of non-communicable diseases and to achieve disease control if already afflicted.

REFERENCES

Africa Centres for Disease Control & Prevention. 2021. Guidance on Diagnosis and Management of People with Post-Acute COVID-19 Syndrome. Available at: https://africacdc.org/download/guidance-on-diagnosis-and-management-of-people-with-post-acute-covid-19-syndrome/ [Accessed 19 Jun. 2021].

Attaway, A.H., Scheraga, R.G., Bhimraj, A., Biehl, M. & Hatipoğlu, U. 2021. Severe covid-19 pneumonia: pathogenesis and clinical management. *BMJ*, [online] p.n436. Available at: https://www.bmj.com/content/372/bmj.n436 [Accessed 13 Jun. 2021].

Badawi, A. & Ryoo, S.G. 2016. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. *International Journal of Infectious Diseases*, [online] 49, pp.129–133. Available at: https://www.sciencedirect.com/science/article/pii/S1201971216311006 [Accessed 8 Nov. 2020].

Bajgain, K.T., Badal, S., Bajgain, B.B. & Santana, M.J. 2020. Prevalence of comorbidities among individuals with COVID-19: A rapid review of current literature. *American Journal of Infection Control*, [online] 49(2021). Available at: https://www.ajicjournal.org/action/showPdf?pii=S0196-6553%2820%2930637-4 [Accessed 17 Mar. 2021].

Biccard, B.M., Gopalan, P.D., Miller, M., Michell, W.L., Thomson, D., Ademuyiwa, A., Aniteye, E., Calligaro, G., Chaibou, M.S., Dhufera, H.T., Elfagieh, M., Elfiky, M., Elhadi, M., Fawzy, M., Fredericks, D., Gebre, M., Bayih, A.G., Hardy, A., Joubert, I. and Kifle, F. (2021). Patient care and clinical outcomes for patients with COVID-19 infection admitted to African high-care or intensive care units (ACCCOS): a multicentre, prospective, observational cohort study. *The Lancet*, [online] 397(10288), pp.1885–1894. doi:10.1016/S0140-6736(21)00441-4. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8137309/ [Accessed 16 July 2022].

Blumberg, L., Jassat, W., Mendelson, M. & Cohen, C. 2020. The COVID-19 crisis in South Africa: Protecting the vulnerable . *S Afr Med J*, 110(9), pp.823–824.

Mitchell, A., Chiwele, I. and Costello, J. (2021). *Coronavirus disease 2019 (COVID-19) - Symptoms, diagnosis and treatment | BMJ Best Practice*. [online]. bestpractice.bmj.com. Available at: https://bestpractice.bmj.com/topics/en-gb/3000201 [Accessed 19 Jun. 2021].

Callender, L.A., Curran, M., Bates, S.M., Mairesse, M., Weigandt, J. & Betts, C.J. 2020. The Impact of Pre-existing Comorbidities and Therapeutic Interventions on COVID-19. *Frontiers in Immunology*, [online] 11(1991). Available at: https://pubmed.ncbi.nlm.nih.gov/32903476/ [Accessed 14 Aug. 2021].

Centers for Disease Control & Prevention. 2020. *Coronavirus Disease 2019 (COVID-19)*. [online] Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/evidence-table.html [Accessed 27 Mar. 2021].

Clift, A.K., Coupland, C.A.C., Keogh, R.H., Diaz-Ordaz, K., Williamson, E., Harrison, E.M., Hayward, A., Hemingway, H., Horby, P., Mehta, N., Benger, J., Khunti, K., Spiegelhalter, D., Sheikh, A., Valabhji, J., Lyons, R.A., Robson, J., Semple, M.G., Kee, F. and Johnson, P. 2020. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. *BMJ*, [online] 371, p.m3731. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7574532/ [Accessed 4 Oct. 2021].

Finelli, L., Gupta, V., Petigara, T., Yu, K., Bauer, K.A. and Puzniak, L.A. 2021. Mortality Among US Patients Hospitalized With SARS-CoV-2 Infection in 2020. *JAMA Network Open*, 4(4), p.e216556. doi:https://doi.org/10.1001/jamanetworkopen.2021.6556 [Accessed 07 Jun. 2023]

Gasmi, A., Peana, M., Pivina, L., Srinath, S., Benahmed, A.G., Semenova, Y., Menzel, A. and Dadar, M. (2021). Interrelations between COVID-19 and other disorders. *Clinical Immunology*, [online] 224(108651), pp.1–12. doi:10.1016/j.clim.2020.108651. Available at: https://www.sciencedirect.com/science/article/pii/S1521661620308111?via%3Dihub#s0040 [Accessed 21 September 2022] .

Goudouris, E.S. 2020. Laboratory diagnosis of COVID-19. *Jornal de Pediatria*, [online] 97(1). Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456621/ [Accessed 29 Jun. 2021].

Heale, R. & Twycross, A. 2015. Validity and reliability in quantitative studies. *Evidence Based Nursing*, [online] 18(3), pp.66–67. Available at: https://ebn.bmj.com/content/18/3/66 [Accessed 29 Mar. 2021].

Hofman, K. & Madhi, S. 2020. The Unanticipated costs of COVID-19 to South Africa's quadruple disease burden. *S Afr Med J*, 110(8), pp.698–699.

House, C. 2001. *Statistical Aspects of a Census*. [online] *Google Scholar*. Available at:https://ageconsearch.umn.edu/record/235076/files/Statistical_Aspects_of_a_Census.pdf. [Accessed 30 Aug. 2021].

Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X., Cheng, Z., Yu, T., Xia, J., Wei, Y., Wu, W., Xie, X., Yin, W., Li, H., Liu, M. & Xiao, Y. 2020. Clinical Features of Patients Infected with 2019 Novel Coronavirus in Wuhan, China. *The Lancet*, [online] 395(10223). Available at: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30183-5/fulltext [Accessed 8 Nov. 2020].

Jassat, W., Cohen, C., Kufa, T., Goldstein, S., Masha, M., Cowper, B., Slade, D., Greyling, C., Soorju, S., Kai, R., Walaza, S. & Blumberg, L. 2020. *DATCOV: A Sentinel Surveillance Programme for Hospitalized Individuals with COVID-19 in South Africa, 2020*. [online] www.nicd.ac.za. Available at: https://www.nicd.ac.za/wp-content/uploads/2020/06/COVID-19-Special-Public-Health-Surveillance-Bulletin-10-June-2020-005.pdf [Accessed 29 Jun. 2021].

Jassat, W., Cohen, C., Tempia, S., Masha, M., Goldstein, S., Kufa, T., Murangandi, P., Savulescu, D., Walaza, S., Bam, J.-L., Davies, M.-A., Prozesky, H.W., Naude, J., Mnguni, A.T., Lawrence, C.A., Mathema, H.T., Zamparini, J., Black, J., Mehta, R. and Parker, A. 2021a. Risk factors for COVID-19-related in-hospital mortality in a high HIV and tuberculosis prevalence setting in South Africa: a cohort study. *The Lancet HIV*, 8(9). doi:https://doi.org/10.1016/s2352-3018(21)00151-x [Accessed 07 Jun. 2023].

Jassat, W., Mudara, C., Ozougwu, L., Tempia, S., Blumberg, L., Davies, M.-A., Pillay, Y., Carter, T., Morewane, R., Wolmarans, M., Von Gottberg, A., Bhiman, J.N., Walaza, S., Cohen, C. and DATCOV author group. 2021b. Difference in mortality among individuals admitted to hospital with COVID-19 during the first and second waves in South Africa: a cohort study. *The Lancet Global Health*, [online] 9(9), pp.e1216–e1225. doi:https://doi.org/10.1016/S2214-109X(21)00289-8 [Accessed 07 Jun. 2023].

Kaswa, R., Yogeswaran, P. and Cawe, B. 2021. Clinical outcomes of hospitalised COVID-19 patients at Mthatha Regional Hospital, Eastern Cape, South Africa: A retrospective study. *South African Family Practice*, 63(1). doi: https://doi.org/10.4102/safp.v63i1.5253. [Accessed 7 Jun. 2023].

Lalkhen, H. & Mash, R. 2015. Multimorbidity in non-communicable diseases in South African primary healthcare. *South African Medical Journal*, [online] 105(2), p.134. Available at: http://www.scielo.org.za/scielo.php?script=sci_arttext&pid=S0256-95742015000200024 [Accessed 24 Aug. 2021]

Mash, R.J., Presence-Vollenhoven, M., Adeniji, A., Christoffels, R., Doubell, K., Eksteen, L., Hendrikse, A., Hutton, L., Jenkins, L., Kapp, P., Lombard, A., Marais, H., Rossouw, L., Stuve, K., Ugoagwu, A. and Williams, B. 2021. Evaluation of patient characteristics, management and outcomes for COVID-19 at district hospitals in the Western Cape, South Africa: descriptive observational study. *BMJ Open*, [online] 11(1), p.e047016. doi:10.1136/bmjopen-2020-047016. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7839306/ [accessed 16 July 2022]

Meriam-Webster Dictionary. 2021. *Definition of COVID-19*. [online] Available at: https://www.merriam-webster.com/dictionary/COVID-19 [Accessed 28 Mar. 2021].

Mustafa, F., Giles, R. & Pepper, M.S. 2020. Rapid evolution of our understanding of the pathogenesis of COVID-19 - implications for therapy. *S Afr Med J*, [online] 110(12), pp1180-1185. Available at: http://www.samj.org.za/index.php/samj/article/view/13118/9612 [Accessed 27 Mar. 2021].

National Center for Biotechnology Information. 2021a. *Comorbidity - MeSH - NCBI*. [online] www.ncbi.nlm.nih.gov. Available at: https://www.ncbi.nlm.nih.gov/mesh/?term=comorbidities [Accessed 13 Jun. 2021].

National Center for Biotechnology Information. 2021b. *Risk Factors - MeSH - NCBI*. [online] www.ncbi.nlm.nih.gov. Available at: https://www.ncbi.nlm.nih.gov/mesh/68012307 [Accessed 3 Oct. 2021].

National Institute for Communicable Diseases. 2020a. *Coronavirus disease 2019 (COVID-19) Quick Reference for Health Workers*. [online] Available at: https://www.nicd.ac.za/wp-content/uploads/2020/04/COVID-19-Quick-reference-NDoH-Criteria-2-April-update.pdf [Accessed 27 Mar. 2021].

National Institute for Communicable Diseases.2020b. *Novel coronavirus outbreak in Wuhan City, China*. [online] Available at: https://www.nicd.ac.za/novel-coronavirus-outbreak-in-wuhan-city-hubei-province-of-china/ [Accessed 3 Sep. 2020].

National Institute for Communicable Diseases. 2020c. *Clinical management of suspected or confirmed Covid-19 disease*. [online]. Available at: https://www.nicd.ac.za/wp-content/uploads/2020/08/Clinical-management-of-suspected-or-confirmed-COVID-19-V5-24-August-2020.pdf [Accessed 29 Jun. 2021].

National Institute for Communicable Diseases. 2021. COVID-19 HOSPITAL SURVEILLANCE UPDATE. [online]. Available at: https://www.nicd.ac.za/wp-content/uploads/2021/03/NICD-COVID-19-Weekly-Sentinel-Hospital-Surveillnace-update-Week-10-2021.pdf [Accessed 27 Mar. 2021].

Ratshikhopha, E., Muvhali, M., Naicker, N., Tlotleng, N., Jassat, W. and Singh, T. (2022). Disease Severity and Comorbidities among Healthcare Worker COVID-19 Admissions in South Africa: A Retrospective Analysis. *International Journal of Environmental Research and Public Health*, 19(9), p.5519. doi:10.3390/ijerph19095519. [online] Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9104097/ [Accessed 16 July 2022]

Reddy, R.K., Charles, W.N., Sklavounos, A., Dutt, A., Seed, P.T. & Khajuria, A. 2020. The effect of smoking on COVID-19 severity: A systematic review and meta-analysis. *Journal of Medical Virology*, [online] (93), pp.1045–1056. Available at: https://onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.26389 [Accessed 30 Sep. 2021].

Richards, G.A. & Feldman, C. 2020. The use of corticosteroids for COVID-19 infection. *African Journal of Thoracic and Critical Care Medicine*, [online] 26(3), p.87. Available at: https://journals.co.za/doi/pdf/10.7196/AJTCCM.2020.v26i3.106 [Accessed 3 Oct. 2021].

Richardson, S., Hirsch, J.S., Narasimhan, M., Crawford, J.M., McGinn, T., Davidson, K.W., Barnaby, D.P., Becker, L.B., Chelico, J.D., Cohen, S.L., Cookingham, J., Coppa, K., Diefenbach, M.A., Dominello, A.J., Duer-Hefele, J., Falzon, L., Gitlin, J., Hajizadeh, N., Harvin, T.G. & Hirschwerk, D.A. 2020. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized with COVID-19 in the New York City Area. *JAMA*, [online] 323(20), pp.2052–2059. Available at: https://jamanetwork.com/journals/jama/fullarticle/2765184 [Accessed 26 Mar. 2021].

Rossouw, T., Boswell, M., Nienaber, A. & Moodley, K. 2020. Comorbidity in context: Part 1. Medical considerations around HIV and tuberculosis during the COVID-19 pandemic in South Africa. *S Afr Med J*, 110(7), pp.621–624.

Rothan, H.A. & Byrareddy, S.N. 2020. The Epidemiology and Pathogenesis of Coronavirus Disease (COVID-19) Outbreak. *Journal of Autoimmunity*, [online] 109(102433), p.102433. Available at: https://pubmed.ncbi.nlm.nih.gov/32113704/ [Accessed 8 Nov. 2020].

SA Corona Virus Online Portal. 2020. *About - SA Corona Virus Online Portal*. [online] Available at: https://sacoronavirus.co.za/information-about-the-virus-2/ [Accessed 3 Sep. 2020].

Sanyaolu, A., Okorie, C., Marinkovic, A., Patidar, R., Younis, K., Desai, P., Hosein, Z., Padda, I., Mangat, J. & Altaf, M. 2020. Comorbidity and its Impact on Patients with COVID-19. *Sn Comprehensive Clinical Medicine*, [online] pp.1–8. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7314621/ [Accessed 24 Oct. 2020].

Singh, A.S. & Masuku, M.B. 2014. SAMPLING TECHNIQUES & DETERMINATION OF SAMPLE SIZE IN APPLIED STATISTICS RESEARCH: AN OVERVIEW. *International Journal of Economics, Commerce and Management.,* [online] 2(11), p.3. Available at: https://www.ijecm.co.uk/wp-content/uploads/2014/11/21131.pdf [Accessed 1 Oct. 2021].

Tshitangano, T.G., Setati, M.E., Mphekgwana, P.M., Ramalivhana, N.J. and Matlala, S.F. (2022). Epidemiological Characteristics of COVID-19 Inpatient Deaths during the First and Second Waves in Limpopo Province, South Africa. *Journal of Respiration*, 2(2), pp.111–122. doi:https://doi.org/10.3390/jor2020009 [Accessed 07 Jun. 2023]

Uzzo, R.G., Kutikov, A. & Geynisman, D.M. 2021. *UpToDate*. [online] www.uptodate.com. Available at: https://www.uptodate.com/contents/covid-19-risks-for-infection-clinical-presentation-testing-and-approach-to-infected-patients-with-cancer#H1048496786 [Accessed 3 Oct. 2021].

Wang, C.-L., liu, Y.-Y., Wu, C.-H., Wang, C.-Y., Wang, C.-H. & Long, C.-Y. 2021. Impact of COVID-19 on Pregnancy. *International Journal of Medical Sciences*, [online] 18(3), pp.763–767. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7797535/ [Accessed 4 Oct. 2021].

Wang, J., Yang, W., Chen, P., Guo, J., Liu, R., Wen, P., Li, K., Lu, Y., Ma, T., Li, X., Qin, S., Zhang, Y. & Wang, Y. 2021. The proportion and effect of corticosteroid therapy in patients with COVID-19 infection: A systematic review and meta-analysis. *PLOS ONE*, [online] 16(4), p.e0249481. Available at: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0249481 [Accessed 3 Oct. 2021].

World Health Organization. 2020a. Pneumonia of unknown cause – China. *World Health Organization*. [online] Available at: https://www.who.int/csr/don/05-january-2020-pneumonia-of-unkown-cause-china/en/ [Accessed 3 Sep. 2020].

World Health Organization. 2020b. *Episode #14 - COVID-19 - Tests*. [online] www.who.int. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/media-resources/science-in-5/episode-14---covid-19---tests?gclid=EAIaIQobChMI_Kea77K98QIVUuztCh2CPQoREAAYASAAEgJ82fD_BwE [Accessed 29 Jun. 2021].

World Health Organization. 2022. *WHO COVID-19 dashboard*. [online] covid19.who.int. Available at: https://covid19.who.int/ [Accessed 2 Oct. 2022].

Yang, J., Zheng, Y., Gou, X., Pu, K., Chen, Z., Guo, Q., Ji, R., Wang, H., Wang, Y. & Zhou, Y. 2020. Prevalence of Comorbidities in the Novel Wuhan Coronavirus (COVID-19) infection: A Systematic Review and meta-analysis. *International Journal of Infectious Diseases*, [online] 94(2020). Available at: https://www.sciencedirect.com/science/article/pii/S1201971220301363 [Accessed 24 Oct. 2020].

Ye, C., Zhang, S., Zhang, X., Cai, H., Gu, J., Lian, J., Lu, Y., Jia, H., Hu, J., Jin, C., Yu, G., Zhang, Y., Sheng, J. & Yang, Y. 2020. Impact of comorbidities on patients with COVID-19: A large retrospective study in Zhejiang, China. *Journal of Medical Virology*, [online] 92(11), pp.2821–2829. Available at: https://onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.26183 [Accessed 24 Oct. 2020].

ANNEXURE A: Data collection tool

Section A: Demographics													
Date of birth (yyyy/mm/dd)								Gender (Please mark with an X)		Race (Please mark with an X)			
								Male	Female	African	whit e	Coloured	Indian/Asia

Pregnant or post-partum (6 weeks after delivery)? (Please mark with an X if applicable)	☐
Is the patient a health care worker?	☐

If yes, please select	Doctor	Nurse	Allied Health	Laborat ory	Param edic	Admin/Porter

Section B: Comorbidities (Mark with an X, multiple if applicable) *Y=yes N= No HIV=Human Immunodeficiency Virus ART Antiretroviral therapy											
Hypertension			Diabetes			Cardiac disease			Chronic pulmonary disease		
Y	N	Unkn own	Y	N	Unkno wn	Y	N	Unknown	Y	N	Unknown

Chronic renal failure			Malignancy			If Malignancy, Type of malignancy
Y	N	Unknown	Y	N	Unknown	

Tuberculosis, Active disease on treatment			Tuberculosis, Past disease, completed treatment		
Y	N	Unknown	N	Y	Unknown

HIV Positive	Y	N	Unknown	If positive complete below

HIV on ART			HIV Viral suppression			HIV Latest VL	HIV Latest CD4
Y	N	Unknown	Y	N	Unknown		

Smoker (current or former)			Obesity			Other(s)
Y	N	Unknown	Y	N	Unknown	

Current Medication

☐ Immunosuppressive drugs ☐ Chemotherapy ☐ Steroids

☐ ARV, if yes, Specify regimen ☐ ACE-inhibitor ☐ NSAIDs

Section C: Onset and Admission

Admission reason ☐ Covid symptoms ☐ Isolation ☐ Other

Onset date of first/earliest symptom

Date of positive COVID-19 Diagnosis

Admission date

Setting of care (Please mark with an X)

General ward	High care	Intensive Care Unit

☐ Is the patient on oxygen?

☐ Is the patient ventilated?

Section D: Patient Outcomes

Discharge alive	Transfer to other facility	Died	Died (Non-COVID)

Outcome Date

ANNEXURE B: ETHICAL CLEARANCE LETTER (TREC)

University of Limpopo
Department of Research Administration and Development
Private Bag X1106, Sovenga, 0727, South Africa
Tel: (015) 268 3935, Fax: (015) 268 2306, Email: anastasia.ngobe@ul.ac.za

TURFLOOP RESEARCH ETHICS COMMITTEE

ETHICS CLEARANCE CERTIFICATE

MEETING: **23 May 2022**

PROJECT NUMBER: **TREC/99/2022: PG**

PROJECT:

Title:	The Impact of Comorbidities on Outcome of Patients Admitted with Coronavirus Disease 2019 Infection at Pietersburg Hospital, Polokwane, Limpopo Province.
Researcher:	K Moabelo
Supervisor:	Dr PM Mangena
Co-Supervisor/s:	Dr ME Setati Dr MJ Nchabeleng
School:	Medicine
Degree:	Master of Medicine in Internal Medicine

PROF D MAPOSA
CHAIRPERSON: TURFLOOP RESEARCH ETHICS COMMITTEE

The Turfloop Research Ethics Committee (TREC) is registered with the National Health Research Ethics Council, Registration Number: **REC-0310111-031**

Note:

i) **This Ethics Clearance Certificate will be valid for one (1) year, as from the abovementioned date. Application for annual renewal (or annual review) need to be received by TREC one month before lapse of this period.**

ii) **Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee, together with the Application for Amendment form.**

iii) **PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.**

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ANNEXURE C: Approval letter (Provincial research committee, Limpopo Province)

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF
HEALTH

Ref : LP_2022-05-029
Enquires : Ms PF Mahlokwane
Tel : 015-293 6028
Email : Phoebe.Mahlokwane@dhsd.limpopo.gov.za

KOENA MOABELO

PERMISSION TO CONDUCT RESEARCH IN DEPARTMENTAL FACILITIES

Your Study Topic as indicated below**;**

THE IMPACT OF COMORBIDITIES ON OUTCOME OF PATIENTS ADMITTED WITH CORONAVIRUS DISEASE 2019 INFECTION AT PIETERSBURG HOSPITAL, POLOKWANE, LIMPOPO PROVINCE

1. Permission to conduct research study as per your research proposal is hereby Granted
2. Kindly note the following:
    a. Present this letter of permission to the office of Clinical Executive Director a week before the study is conducted.
    b. This permission is for **Pietersburg and Mankweng Hospitals ONLY**
    c. In the course of your study, there should be no action that disrupts the routine services, or incur any cost on the Department.
    d. After completion of study, it is mandatory that the findings should be submitted to the Department to serve as a resource.
    e. The researcher should be prepared to assist in the interpretation and implementation of the study recommendation where possible.
    f. The approval is only valid for a 1-year period.
    g. If the proposal has been amended, a new approval should be sought from the Department of Health
    h. Kindly note that, the Department can withdraw the approval at any time.

Your cooperation will be highly appreciated

_____ 06/06/2022

Head of Department **Date**

pp

Private Bag X9302, Polokwane
Fidel Castro Ruz House, 18 College Street, Polokwane 0700. Tel: 015-293 6000/12. Fax: 015 293 6211.
Website: http/www.limpopo.gov.za

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ANNEXURE D: Ethical clearance (Polokwane-Mankweng Research Ethics Committee (PMREC)

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF HEALTH
Tel: (015) 287 5400, Fax: (015) 268 2306, Email: ananiaspoopedi@gmail.com

POLOKWANE MANKWENG RESEARCH ETHICS COMMITTEE (PMREC)

ETHICS CLEARANCE CERTIFICATE

MEETING: 31 August 2022

PROJECT NUMBER: PMREC 31 August UL 2022/B

PROJECT: Post-graduate Research

Title: The impact of comorbidities on outcome of patients admitted with coronavirus disease 2019 infection at Pietersburg hospital, Polokwane, Limpopo province.

Researcher: Dr K Moabelo

Supervisor: Dr. PM Mangena

Co-Supervisor/s: Dr MJ Nchabeleng and Dr ME Setati

Department: Internal Medicine

Degree: Master of Medicine in Internal Medicine

Approval date: 20 September 2022

Expiry date: 20 September 2023

PMREC Decision: Approved

SIGNED:

Chairperson: Pietersburg/Mankweng Complex Research Ethics Committee

School of Medicine

University of Limpopo

REC 300408-006

Note:
i) Conduct the project strictly in accordance with the proposal submitted and granted ethics approval, including any amendments made to the proposal required by the HREC
ii) Application for annual renewal (or annual review) needs to be received by PMREC one month before lapse of this period.
iii) Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee, together with the Application for Amendment form.
iv) Provide a progress report' for every year of approval and provide a final report' when the project is complete. Advise in writing if the project has been discontinued.
v) PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.

NB: Please note that failure to comply with the conditions of approval may result in withdrawal of approval for the project.

ANNEXURE E: Hospital research approval

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF

HEALTH

PIETERSBURG HOSPITAL

REF : **4/2/2**

ENQ : **MOLOKOMME N**

TO : **Dr K MOABELO**

(PRINCIPAL INVESTIGATOR)

FROM : **Dr MC MASIPA**

ACT CEO: PIETERSBURG HOSPITAL

DATE : **12 SEPTEMBER 2022**

RE : **REQUEST FOR RESEARCH**

1. The above matter refers.
2. Your request to conduct research is hereby granted.
3. You will be expected to avail the report to the institution upon completion.

Thanking you in advance.

Dr MC MASIPA

ACTING CHIEF EXECUTIVE OFFICER

PIETERSBURG HOSPITAL

13/09/2022.

DATE

ANNEXURE F: Request for sharing of data

Dr KJ Moabelo

Pietersburg Hospital

Cnr Dorp and Hospital street

Polokwane

0699

To: DATCOV team

RE: PERMISSION TO USE DATA FOR RESEARCH PURPOSE

Kindly receive my formal request to use data on DATCOV App for research purpose.

I am currently a Medical Registrar in Internal medicine under the supervision of Dr Mangena, HOD of Internal Medicine. As part of my training, I must do research towards an MMed degree. My research topic is on "**The impact of comorbidities on outcome of patients admitted with Coronavirus disease 2019 infection at Pietersburg hospital**" over a period of 12 months (from March 2020 to March 2021).

Ethical clearance to conduct research will still be sought from both the University of Limpopo and the Limpopo Department of Health.

I request permission/authorization to extract DATCOV data limited to Pietersburg Hospital patients only.

Your assistance in that regard is highly valued.

Regards

Dr Moabelo KJ

MBBCh

Internal Medicine Registrar

Student number: 202176657

ANNEXURE G: WAIVER FOR INFORMED CONSENT

PMREC WAIVERS TO INFORMED CONSENT

Section 1. PROTOCOL/PROPOSAL INFORMATION

Protocol/proposal number (for official use ONLY):	
Protocol/proposal title:	The impact of comorbidities on outcome of patients admitted with Coronavirus disease 2019 at Pietersburg hospital, Polokwane, Limpopo province.
Principal investigator:	DR K MOABELO

Indicate applicable with an "X"

Independent research	Contract research	Post-graduate research X	Undergraduate research

Section 2. REQUEST FOR ALTERATION OR WAIVER OF INFORMED CONSENT

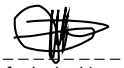
Indicate applicable with an "X"

X	2A A waiver of informed consent
	2B An alteration of inform consent
	2C A waiver of parent/guardian permission
	2D A waiver of assent because minors are nor capable of assent
	2E A waiver of assent because the research holds out a prospect of direct and indirect benefit

Section 3. DECLARATION

I, the principal investigator, declare that:

STATEMENT	DETAIL and/or EXPLANATION
3A The research involves no more than minimal risk to the research participants,	The research is a retrospective study with less likelihood to cause any harm to the participants.
3B The waiver or alteration will not adversely affect the rights and welfare of the research participants,	Participants' right were respected by ensuring their identity is protected in the form of unique identifiers.
3C The research could not practicably be carried out without the waiver or alteration, and	
3D Whenever appropriate, the research subjects will be provided with additional pertinent information after participation.	



Signature of principal investigator

07/09/2022

Date

REMARKS (for official use ONLY):