Clinical outcomes of treatment strategies used in the management of COVID-19 patients in Kenya: Potentially effective therapy options

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STUDENT'S DECLARATION

I certify that this thesis is my original work and has not been presented to an individual or institution either in part or as a whole for the award of a degree. All sources of information cited in this thesis have been acknowledged.

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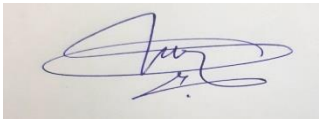
Signature:  **Date: December 8, 2023**

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ABBREVIATIONS AND ACRONYMS

ACE2	:	Angiotensin-Converting Enzyme 2
AKI	:	Acute kidney injury
ALT	:	Alanine aminotransferase
aOR	:	Adjusted odds ratio
AST	:	Aspartate aminotransferase
CCF	:	Congestive cardiac failure
CD	:	Cluster of differentiation
CKD	:	Chronic kidney disease
CP	:	Convalescent Plasma
CQ	:	Chloroquine
CRP	:	C-reactive protein
CT	:	Computed tomography
ESR	:	Erythrocyte sedimentation rate
ESRD	:	End-stage renal disease
HCQ	:	Hydroxychloroquine
HIV	:	Human immunodeficiency virus
HR	:	Hazard ratio
ICU	:	Intensive care unit;
IgG	:	Immunoglobulin
IL	:	Interleukin
KNH	:	Kenyatta National Hospital
LFTs	:	Liver function tests

LMWH	:	Low Molecular Weight Heparin
MERS-CoV	:	Middle East Respiratory Syndrome Coronavirus
MIS	:	Multisystem Inflammatory Syndrome
MRI	:	Magnetic resonance imaging
NK	:	Natural Killer
Nsp	:	nonstructural proteins
OR	:	Odds ratio
ORF	:	Open Reading Frame
PCT	:	Procalcitonin
Pp	:	polyproteins
RBS	:	Random blood sugar
REDCap	:	Research Electronic Data Capture
RNA	:	Ribonucleic Acid
RT-LAMP	:	Reverse Transcriptional Loop-Mediated Isothermal Amplification
SARS-CoV-2	:	Severe Acute Respiratory Syndrome Coronavirus
SC	:	Subcutaneous
SLE	:	Systemic Lupus Erythematosus
SPSS	:	Statistical Package for Social Science
UoN	:	University of Nairobi
VTE	:	Venous thromboembolism
WBC	:	White Blood Cell

OPERATIONAL DEFINITION OF TERMS

Association - is the relation between two variables that may have an impact on how the variables change

Clinical outcomes - is a clinical improvement or worsening of the severity condition in which the patient is found.

Comorbidities - is the existence of prevailing/underlying medical conditions in patients other than the condition/disease of interest

Effectiveness – is the likelihood a treatment shows benefit to a patient when administered

Potentially effective therapy options – refers to treatment regimens that have been shown to improve the severity of the disease

Standard of care - is a specific and appropriate treatment given in the management of COVID-19 according to the national guideline

The management of covid-19 - is the process of treating patients against COVID-19 employing the outlined treatments strategies

Treatments strategies - are the different therapeutic options used in the management of COVID-19 as related to the national guideline or otherwise

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ABSTRACT

Background: The recent outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) identified as coronavirus-19 shown to be of great health concern globally and declared a pandemic by the World Health Organization (WHO). The SARS-CoV infection may be asymptomatic or present clinically with non-specific or specific symptoms ranging from mild to critically ill disease. COVID-19 may be associated with different risk factors in a patient such as diabetes, hypertension, cardiovascular disease, and chronic respiratory disease, which possibly increase complications and mortality. With no available registered drugs or vaccines in the first year of the pandemic, managing the disease was mainly supportive regarding the symptoms observed with an option to repurpose available approved drugs or drugs from in vitro observation used during the SARS-CoV and MERS-CoV pandemics; isolation of infected individuals, and quarantine of whether symptomatic or not, frequent use of disinfectants and hand washing, were used as preventives measures. In sum, the clinical control approaches lie on one hand on drugs which include antiviral, anti-pro-inflammatory cytokine, anti-infectious, and monoclonal antibodies; on the other hand, supportive care including oxygen and mechanical ventilation.

Objectives: To document the clinical outcomes, adherence to the standard of care, and the influence of co-morbidities on the clinical outcomes of the treatment regimens in the management of COVID-19 in Kenya since the first case was reported

Methods: This was a retrospective cross-sectional study done at Kenyatta National Hospital and Mater Misericordiae hospital in Nairobi County and at Coast General Teaching Hospital in Mombasa County, respectively. The study involved 408 COVID-19 positive patient records files, admitted into the healthcare facilities of interest in Kenya since the first case was reported on 13th March 2020 until 31st December 2021. The collected variables included sociodemographic information, clinical data, pharmacological interventions, and clinical outcomes. Data analysis was done using SPSS version 25. Descriptive statistics such as frequency, mean, and standard deviation, were used to summarize the results. Inferential statistic such as Chi-square, univariable and multivariable logistic regression analysis was used to assess the factors associated with patients discharge. All hypotheses were tested at a 95% confidence interval whereby a p-value of <0.05 was considered statistically significant. Crude odds ratio (cOR) and adjusted odds ratio (aOR) were computed in the logistic regression analyses.

Results: Overall, 76.5% of the patients were discharged, patients in private hospitals had a significantly higher odds (aOR = 10.166, p < 0.001) of being discharged compared to patients in public hospitals, for each unit increase in disease severity, the odds of discharge decrease (aOR = 0.214, p < 0.001). Patients with comorbidities had lower odds of discharge (aOR = 0.281, p < 0.001) compared to those without comorbidities. The use of Tocilizumab (aOR = 0.169, p = 0.04), Baricitinib (aOR = 0.979, p = 0.98), Remdesivir (aOR = 0.518, p = 0.19), supplementary drugs (aOR = 3.979, p = 0.16) were not strongly associated with discharge. The regimen group variable was not a strong predictor of discharge (aOR = 0.297, p = 0.07). Adherence to national guideline was not a significant predictor for discharge (aOR = 1.011, p = 0.98).

Conclusion: Around three-quarters of patients had a favorable treatment outcome. Patients treated in private hospitals were more likely to be discharged compared to patients in public hospitals. Patients treated with mild and moderate disease severity had better treatment compared to those with severe and critical disease. The overall treatment strategies used in Kenya were not strongly associated with a favorable outcome (discharge). The presence of a comorbidity was shown to adversely affect the treatment outcome.

Recommendations: Research is needed to evaluate the efficacy of each drug used in the management of COVID-19 in Kenya. The treatment strategies used so far have not been shown to influence discharge, so there is a need to make improvements by incorporating new molecules into the guidelines, and also make drugs available, accessible, and affordable. Routine training for health care professionals on any updates of the guidelines every time there is new input.

CHAPTER ONE: INTRODUCTION

1.1 Background to the study

In late 2019, an outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was reported and identified to be the causative agent of coronavirus disease 2019 (COVID-19). This came along with health concerns globally. By March 2020, the World Health Organization (WHO) declared COVID-19 a pandemic (Esakandari et al., 2020). Since then, there has been recorded more than 256 million cases with more than 5 million deaths. Africa has recorded more than 6 million cases with more than 150 thousand deaths (World Health Organization, 2022). Since the first case was reported in Kenya on the 13th of March 2020, there was a total of 267,571 cases and a total of 5,354 death as of 22 December 2021 (World Health Organization, 2022).

SARS-CoV-2 infection may clinically present atypically or typically with several symptoms, which vary from asymptomatic to mild or severe illness with possible death (Esakandari et al., 2020). Between 90% to 95% of infected individuals have mild to moderate illness, while 5-10% present with a severe form which may become life-threatening later (Gavriatopoulou et al., 2021). The common symptoms observed include flu-like symptoms such as cough, fever, and shortness of breath. Other reported symptoms are asthenia, malaise, muscle pain, sore throat, and loss of taste and/or smell (Esakandari et al., 2020). In patients of all ages presenting with severe COVID-19, pulmonary findings show severe injury. However, in some individuals with high susceptibility to COVID-19, like the elderly or those having comorbidities, there have been observed severe interstitial pneumonia, acute respiratory distress syndrome (ARDS), and subsequent multiorgan failure, leading to severe respiratory failure and death (Pascarella et al., 2020).

Data have shown that hospitalization and severity of COVID-19 patients were associated with various risk factors in the patients. The case-fatality rate is estimated at 2.3%. However, this increases in those patients depending on the prevailing comorbidities they are associated with. For instance, for those with diabetes the cases fatality rate is 7.3%, for hypertension it is 6.0%, for cardiovascular disease it is 10.5%, and for chronic respiratory disease it is 6.3%. Such underlying conditions are often associated with increased morbidity and mortality (Jakhmola et al., 2020). Different reasons have been advanced to explain the association of comorbidities and COVID-19. In general, having co-morbidities worsens the outcomes of the patients suffering COVID-19. The

SARS-CoV-2 virus damages the vessels endothelium altering circulation. A COVID-19 infection can also lead to the recruitment of the immune cells following an inflammatory response which subsequently leads to impaired organ function (Jakhmola et al., 2020).

When COVID-19 broke out, there were no available registered drugs or vaccines at the moment. For this reason, managing the disease was mainly supportive in regard to the symptoms observed with more emphasis on preventive measures. Isolation of infected individuals and quarantine of whether symptomatic or not, frequent use of disinfectants, and hand washing were some of the recommended approaches to curbing COVID-19 (Esakandari et al., 2020; Pascarella et al., 2020; Uzunova et al., 2020). COVID-19 management has proven to be challenging for health workers due to the fact that the disease usually starts out with non-specific flu-like symptoms which later develop into further complications and other non-pulmonary manifestations (Mendelson et al., 2020). Given the emergency of the infection, there was a need to repurpose available approved drugs such as Remdesivir, lopinavir-ritonavir, and hydroxychloroquine, for the clinical management of COVID-19 (Maciorowski et al., 2020; Tiwari et al., 2021). Many of the pharmacological treatments used in the management of SARS-CoV-2 came from medications previously used during the SARS-CoV or MERS-CoV pandemics or from in vitro observations (Pascarella et al., 2020).

The pathogenesis of COVID-19 involves lung inflammation and immune deficiency as a result of an immune response and overproduction of cytokines. Therefore, the clinical control approaches lie, on one hand, on drugs which include antiviral, anti-pro-inflammatory cytokine, anti-infectious agents, and monoclonal antibodies. On the other hand, supportive care including oxygen and mechanical ventilation are also applied (Esakandari et al., 2020; Gavriatopoulou et al., 2021). Additionally, some other treatment methods were tried out, like herbal medicine and convalescent plasma. In some countries in Asia and Africa which have a history of traditional medicine, this treatment option was proposed in their guidelines. The WHO supported the idea claiming that alternative traditional medicines may have some benefits (Esakandari et al., 2020; Iwuoha et al., 2020).

Due to the lack of an effective therapeutic options, which is yet to be established, research is being conducted on the control and prevention of the disease (Uzunova et al., 2020). However, in regard to the pathogenesis of the disease, there are some well-defined objectives to consider in its

management which include, identifying the patients who need treatment, correcting hypoxia, reducing the viral load, managing the hyper-inflammation phase, and managing the hypercoagulability phase (Stratton et al., 2021).

1.2 Problem Statement

After the COVID-19 became a worldwide pandemic, various treatment protocols have been proposed but with no conclusive cure so far. Patient management at the moment relies on providing supportive care on one hand and a combination of various repurposed drugs on the other hand. There are several research studies being conducted worldwide currently to understand the pathophysiology, epidemiological characteristics, clinical features of COVID-19 patients, and their impact on the outcomes of treatment regimens. A study in China that assessed the clinical outcomes of COVID-19 treatment regimens with various drugs, reported that the early administration of interferon-beta-1b alone or in combination with oral ribavirin for COVID-19 patients was associated with an improved clinical outcome and earlier discharge as opposed to Lopinavir-ritonavir, intravenous ribavirin, umifenovir, corticosteroids, interferon-alpha-2b, antibiotics or Chinese medicines, which failed to show consistent clinical benefits (Wong et al., 2021). However, to the best knowledge of the principal investigator, no such study covering this pivotal aspect has been conducted in Kenya so far. This required a study that could portray the current situation on COVID-19 treatments with a focus on the clinical outcomes.

1.3 Justification of the study

At the time of conducting this study, only a few studies in Africa in general and Kenya in particular on COVID-19 clinical outcomes of treatment had been published. However, such studies were focusing mostly on the clinical and epidemiological features, clinical management, interaction of COVID-19 with HIV, tuberculosis, diabetes, and their impact on the disease outcomes but with no keen reference to adherence to treatment guidelines and clinical outcomes. A study in Kenya (Ombajo et al., 2020) and in DR Congo (Nachega et al., 2020), reported the epidemiological and clinical characteristics and prevalence of COVID-19 patients, while other studies from South Africa (Mendelson et al., 2020) and Burkina-Faso (Skrip et al., 2020) reported on the clinical management and mortality of COVID-19 patients. Data on the treatment outcomes was lacking, hence the need for an extensive study to address the issue. The aim of this study is to assess the

different strategies used to tackle this novel infection. This was to provide precise data on the clinical outcomes of the treatment regimens and inform evidence-based guidelines for COVID-19 management. This will support healthcare workers in their present and coming efforts in the management of this infection and also inform policy. The findings of this study will be shared with other institutions to help in building suitable management guidelines for COVID-19.

1.4 Research questions

1. What are the clinical outcomes of the treatment strategies used in the management of COVID-19 patients in Kenya?
2. Do health care professionals adhere to guidelines with reference to treatment among COVID-19 patients in Kenya?
3. What is the influence of underlying co-morbidities on the clinical outcomes of the various treatment strategies used in the management of COVID-19 in Kenya?

1.5 Study Objectives

1.5.1 Broad Objective

To document the clinical outcomes, adherence to the standard of care, and the influence of co-morbidities on the clinical outcomes of the treatment strategies used in the management of COVID -19 in Kenya since the first case was reported.

1.5.2 Specific Objectives

1. To document the clinical outcomes of the treatment strategies used in the management of COVID-19 patients in Kenya.
2. To investigate adherence to treatment guidelines with reference to drug contraindications among COVID-19 patients in Kenya.
3. To assess the influence of underlying co-morbidities on the clinical outcomes of the various treatment strategies used in the management of COVID-19 in Kenya.

1.6 Hypotheses

1.6.1 Null hypotheses

H_0: There is no significant difference in the clinical outcomes of the various therapeutic options for the management of COVID-19.

H_0: Underlying co-morbidities do not significantly influence the clinical outcomes of the various therapeutic options for the management of COVID-19

1.6.2 Alternative hypotheses

H_1: There is a statistically significant difference in the clinical outcomes of the various therapeutic options for the management of COVID-19.

H_1: Underlying co-morbidities significantly influence the clinical outcomes of the various therapeutic options for the management of COVID-19

CHAPTER TWO: LITERATURE REVIEW

2.1. Virology and Etiology

Known and isolated from human nasal secretions longtime ago in 1965, this virus was named coronavirus due to its resemblance with the solar corona under an electron microscope. It was reported to affect humans causing respiratory infection; hence it was designated as Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) (Dhama et al., 2020; Esakandari et al., 2020; Tiwari et al., 2021). This novel infection, responsible for COVID-19, shares some similarities in its genome sequence like the SARS-CoV in their subgenera suggesting it is a betacoronavirus, which was then named by the International Committee on Taxonomy of Viruses as SARS-CoV-2 (Dhama et al., 2020; Esakandari et al., 2020; Mcintosh, 2021). The coronaviruses are from the order Nidovirales, family Coronaviridae, subfamily Orthocoronavirinae which have four genera including alpha, beta having an origin from mammals(bat) and gamma, delta with an avian and mammal (pigs) origin. (Dhama et al., 2020; Esakandari et al., 2020)

The coronavirus (SARS-CoV-2) is an RNA virus enveloped which contains a helical viral nucleocapsid, non-segmented positive single-stranded, with a genome of about 30 bp in length containing 14 Open Reading Frame (ORF) (Dhama et al., 2020; Ezzikouri et al., 2020; Park, 2020). The ORF is found on the 5’ end encoding two polyproteins (pp1a, pp1ab) and 15 nonstructural proteins (NSPs) while the 3’ end contains four structural proteins including spike, envelope, membrane, nucleocapsid, and eight accessory proteins (Dhama et al., 2020; Ezzikouri et al., 2020).

Fixed on the viral envelope, the spike (S) protein which is an antigen mediates entry into the cell. It possesses two subunit S1 and S2, the S1 bind to the cell surface receptor the angiotensin-converting enzyme 2 (ACE2) while the S2 serve in membrane fusion (Dhama et al., 2020; Esakandari et al., 2020; Ezzikouri et al., 2020). Additionally, the spike protein is among the main protein to elicit the host immune response (Dhama et al., 2020). The membrane (M) protein embedded in the envelope plays an important role in viral assembly and is responsible for the viral envelope shape (Dhama et al., 2020; Esakandari et al., 2020). The envelope (E) protein encircles the nucleocapsid and is involved in many functions including the pathogenesis, assembly, and release of the newly formed virion (Dhama et al., 2020; Park, 2020). The viral RNA genome is found in the nucleocapsid protein (N), which has a part in the genome formation, assists the

membrane protein during the assembly of the virion, and boosts the virus transcription (Dhama et al., 2020; Park, 2020).

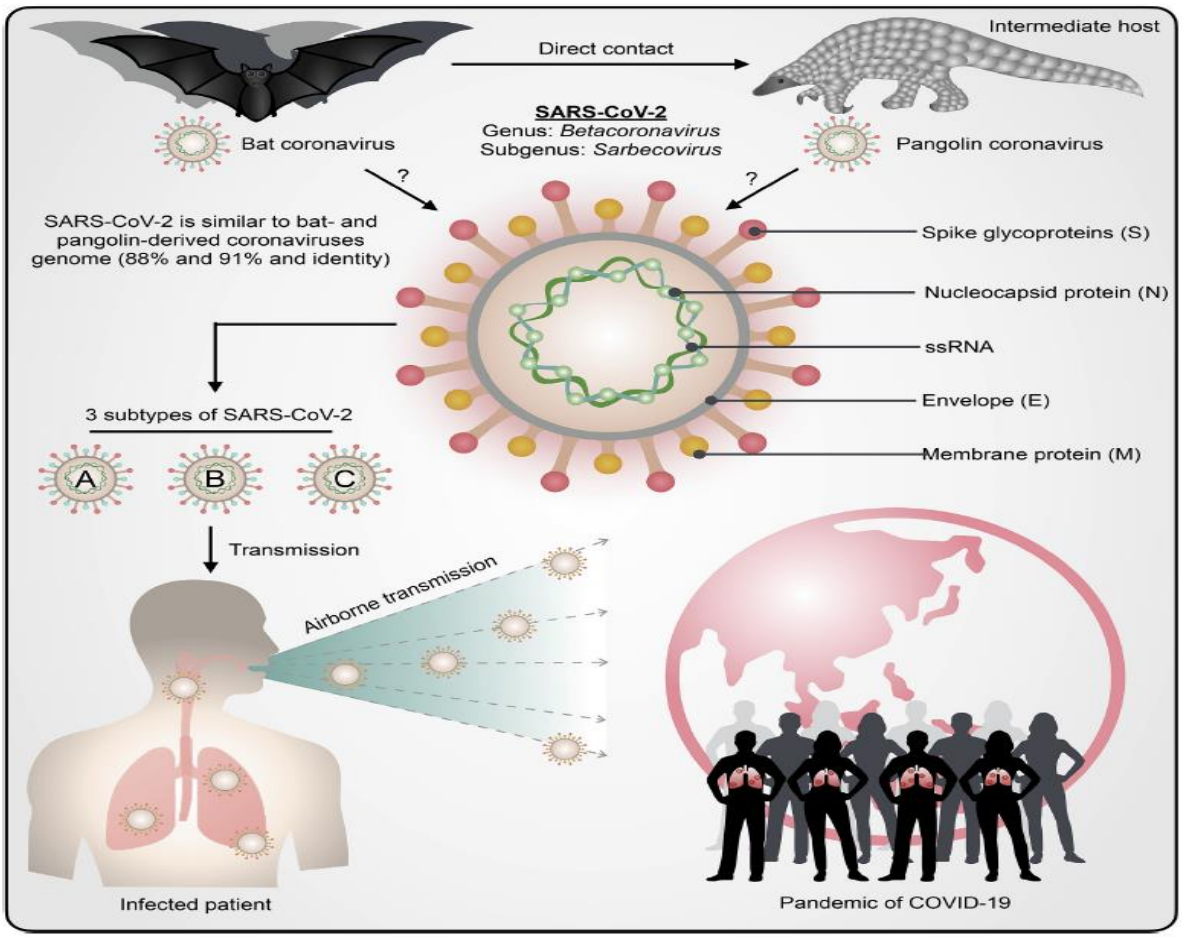

Figure 1: Structure, Etiology, and transmission cycle of the COVID-19

[*Source:* Panyod et al. (2020)]

2.2 Transmission

The emergence of COVID-19 was thought to be associated with a seafood market in China precisely in Wuhan, the particularity of this market is the trade of wild animals dead or alive like snakes, bats, and many others. Studies have shown that the genome of current SARS-CoV-2 may have its origin in the Rhinolophus bat family. The epidemiologic report showed what many of the previous patients had in common was to have been in that market, suggesting that the market was the starting point of transmission which was probably zoonotic. In the course of this epidemic

growing, it has become apparent that the route of transmission was person to person (Dhama et al., 2020; Mcintosh, 2021; Park, 2020).

As seen in other respiratory viruses, human-to-human transmission of COVID-19 happens mainly by close exposure to the respiratory secretion like droplets from an infected person symptomatic or asymptomatic while talking, coughing, sneezing, and shaking hands. It may also occur by direct contact with contaminated inanimate surfaces on which droplets have been deposited and then the person touches his mucous membrane (Mcintosh, 2021; Wiersinga et al., 2020). SARS-CoV-2 has been reported to be presented in other samples than the respiratory secretion like stool, blood, and semen; however, the possibility of infection through these routes appears to be less significant in the course of the infection (Mcintosh, 2021).

The effective transmission of COVID-19, maybe due to the fact that the viral shedding is higher during the beginning of the infection, while the infected persons do not display a sign of infection and they are unaware of how infectious they can be (Dhama et al., 2020; Mcintosh, 2021). It is important to note that people are at risk of transmission or secondary infection while being in some environments which are susceptible to help in the spread of the disease like hospital settings, especially for health care workers, social gatherings like church, work, any other events where individuals display close contact among them, possibly during talking or hugging (Mcintosh, 2021).

2.3 Pathogenesis

The SARS-CoV-2 found in the respiratory droplet once deposited on the epithelium cells lining the nasal cavity attaches to the ACE2 receptor on the host cell, then entry will be facilitated by the priming of the spike protein by the transmembrane serine protease. From there a local replication occurs, which will then propagate along the ciliated epithelial cell lining the airways conduct. At this point, the infected individuals are mostly asymptomatic and very infectious contributing to the shedding of the virus. This phase lasts a couple of days and in most individuals, the infection can be limited to the nasal cavity (Parasher, 2021; Stratton et al., 2021). From the nasal cavity through the epithelial cell lining the airway conduct, the virus invades the upper lung, we assist in an immune response involving the interferon and the motif chemokine ligand. Infected individuals

present with mild symptoms like fatigue, fever, and dry cough. Around 80% will be able to stop the evolution of the infection within 10-14 days (Lin et al., 2021; Parasher, 2021).

In Around 20% of patients, the disease will progress to the lower respiratory airways, infecting the type 2 pneumocytes. The viral replication increases leading to cell apoptosis with the production of new virions which then infect the surrounding cells. The infected cell releases many inflammatory mediators and cytokines like Interleukin (IL 1, 6, 8,12), tumor necrosis factor-alpha, interferons gamma and beta, and macrophages creating a cytokines storm. The cytokines storm then attract other inflammatory cells the neutrophils, the CD4 the CD8. As a consequence of this acute inflammatory reaction, there will be diffuse alveolar damage, intravascular thrombi formation due to the action of the virus on the vascular endothelial, and fluid leakage with impaired air exchange. The ending result of all this damage will be respiratory distress syndrome (Lin et al., 2021; Parasher, 2021; Stratton et al., 2021). Apart from affecting the lung mainly, the SARS-CoV disseminates to affect other organs, especially via viremia. the lesions observed vary according to the organ involved. Multifocal hepatic necrosis, sinusoidal dilation, and steatosis are seen in the liver. Myocardial hypertrophy, focal fibrosis, Arrhythmias, and acute coronary syndrome are observed in the heart. As observed in the lung, endothelial cell infection is also seen in the kidney, the affection of the endothelial cell is responsible for microthrombi formation and clotting disorder (Esakandari et al., 2020; Stratton et al., 2021).

2.4 Clinical Presentation

2.4.1 Overview of Clinical Presentation

Data have shown that the incubation period for SARS-CoV-2 virus infection is about 2-14 days, with a median of 5 days. The clinical manifestations differ from one individual to another, vacillating from asymptomatic to severe or critical illness (Macera et al., 2020; Park, 2020; Pascarella et al., 2020; Thevarajan et al., 2020; Wiersinga et al., 2020). The proportion of individuals asymptomatic or with mild manifestations accounts for around 80% with a mild flu-like symptom, about 14% will develop a severe form defined as severe pneumonia, while 5% will develop a critical condition including a respiratory failure and a multi-organ failure (Pascarella et al., 2020; Thevarajan et al., 2020; Wiersinga et al., 2020). Being a respiratory virus, SARS-CoV-2 symptomatology predominates mostly as a respiratory infection syndrome. But extrapulmonary

manifestations are also present (Macera et al., 2020; Thevarajan et al., 2020). The typical clinical symptoms observe are fever, cough, dyspnea, fatigue, anorexia, anosmia, and myalgia. However, symptoms like nasal congestion, rhinorrhea, and sore throat were reported to be relatively rare (Macera et al., 2020; Park, 2020; Pascarella et al., 2020; Thevarajan et al., 2020).

The non-classical or atypical manifestations involved other organs than the pulmonary system. In the gastrointestinal, the symptoms observed are diarrhea, nausea, and vomiting. Rarely we can have abdominal pain and hemorrhagic intestinal. Liver injury has been reported (Macera et al., 2020; Mehta et al., 2021). The cardiac manifestations include myocarditis, arrhythmias, hypotension, atrial fibrillation, heart failure, and elevated cardiac troponin suggestive of a cardiac injury (Macera et al., 2020; Mehta et al., 2021). Ocular involvements include conjunctivitis, chemosis, tearing, and a sensation of a foreign body in the eye (Macera et al., 2020). As observed in other viruses, the COVID-19 infection can present with some cutaneous manifestations, like maculopapular rash, urticaria, red papules, and livedo reticularis. The lesions are observed mostly on the trunks and some on the limbs (Macera et al., 2020; Mehta et al., 2021). Apart from myalgia or arthralgia which were observed at the beginning of the disease, some other musculoskeletal signs were observed such as rhabdomyolysis, and myositis. In a few individuals, acute arthritis was observed (Mehta et al., 2021). Neurological manifestations have been observed mostly without an association with respiratory manifestation. The symptoms are observed most of the time at the beginning of the infection, the most commonly observed are confusion, headache, dysgeusia, ataxia seizures, hypoxic-ischemic brain injury, loss of smell and taste, other symptoms were present like acute necrotizing encephalopathy, Guillain barre syndrome (Health Organization, 2021; Macera et al., 2020; Mehta et al., 2021).

2.4.2 Clinical presentation in specific population groups

2.4.2.1 In Children

Children, just like adults, are prone to get infected with the SARS-CoV-2 virus. However, children develop milder symptoms than seen in an adult. It consists mostly of fever, cough, erythema, purpuric skin lesions, and poor feeding. In lower cases gastrointestinal symptoms nausea and vomiting are present. Although the manifestations are milder, we can observe a complication the multisystem inflammatory syndrome (MIS) (Health Organization, 2021; Mehta et al., 2021; Rajapakse & Dixit, 2021; Zimmermann, 2020).

2.4.2.2 In a pregnant woman

Although pregnant women seem to be less symptomatic, symptoms like fever, cough, sore throat, dyspnea, nasal congestion, malaise, myalgia, and diarrhea have been observed. Vertical transmission in the fetus has not been proved (Health Organization, 2021; Mehta et al., 2021).

2.4.2.3 In the immunocompromised

Even though immunocompromised individuals infected with SARS-CoV-2 seem to be at risk to develop severe form because of their altered immune response as compared to immunocompetent individuals, it has been observed that their impaired immunity could lessen an overexpression of the immune system which spare them to develop the severe or critical form of the disease. The symptoms observed do not differ from those seen in immunocompetent individuals such as fever, cough, myalgia, and gastrointestinal manifestations (Mehta et al., 2021).

2.5 Risk factors associated with the severity

It has been observed that around 15% of COVID-19 patients present with a severe form of the disease, while 5 % end up developing the critical form of the disease (Health Organization, 2021). The risk factors associated with COVID-19 like older age and underlying comorbidities increase the susceptibility to getting the infection, developing complications, and dying (Health Organization, 2021). However, every individual of any age with prevailing health conditions is also at risk. The principal health conditions associated with COVID-19 are hypertension, cardiovascular diseases, diabetes, cerebrovascular diseases, chronic kidney diseases, chronic respiratory diseases, immunosuppression, cancer, obesity, and smokers (Health Organization, 2021; Jakhmola et al., 2020; Sanyaolu et al., 2020). Pregnant women with chronic diseases like gestational diabetes, with pre-eclampsia, are at higher risk of death (Health Organization, 2021). The classification of the disease severity is listed in Appendix 2

2.6 Case Definition

The symptoms of SARS-CoV-2 appear to be often atypical resembling other diseases which may be confusing. The case definition as set by the WHO includes individuals who can be classified as a suspected case, a probable, and a confirmed case (World Health Organization, 2020). The criteria of a case definition are given in Appendix 1.

2.7 Diagnosis

SARS-CoV-2 preferred diagnosis test is the polymerase chain reaction (PCR), however in case PCR is lacking other tests can be considered such as SARS-CoV-2 antigen detection, laboratory, imaging, and clinical examination which may assist in making a diagnosis (Lin et al., 2021; Ministry of Health - Kenya, 2021).

2.7.1 Specimens

The specimens can be collected from the upper respiratory tract through nasal and oral swabs, or they can be collected from the lower respiratory through the bronchoalveolar lavage and the expectorated sputum (Ministry of Health - Kenya, 2021; Parasher, 2021).

2.7.2 Molecular test

Detection of the viral nucleic acid from respiratory samples mostly the nasopharyngeal and oropharyngeal swabs using the RT-PCR is considered the gold standard for the confirmation of COVID-19 diagnosis (Dhama et al., 2020; Sreepadmanabh et al., 2020; Wiersinga et al., 2020). The process encompasses the synthesis of double-strand DNA fragments (Parasher, 2021). The specificity of this test appears to be high; the sensitivity varies according to the time of collection or exposure and the source of the specimen. It ranges from 66 to 80%(Pascarella et al., 2020; Wiersinga et al., 2020). It is advised in order to be precise in the diagnosis, to repeat the swab (Dhama et al., 2020; Parasher, 2021).

2.7.3 Laboratory findings

Laboratories abnormalities seen in COVID-19 are more specific to pneumonia, and the persistence of these abnormalities will be associated with worsening of the infection. The abnormalities include leukocytosis, lymphopenia, increased levels of alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase C-reactive protein, and reduced procalcitonin levels. Coagulopathy was seen with an increase in prothrombin time, thrombocytopenia, and elevated D-dimer levels. Elevated troponin is a great indicator of death (Parasher, 2021; Pascarella et al., 2020; Wiersinga et al., 2020).

2.7.4 Imaging

A variety of radiological techniques have been used to help in the clinical diagnosis of COVID-19. The chest Computed Tomography (CT) scan is an important tool and method to assist in diagnosing SARS-CoV-2 pneumonia, the image findings include, a patchy infiltration which turns later to multifocal ground-glass opacities affecting both lung and mostly the lower lobes, later we have a septal thickening, pleural effusion, air bronchograms, masses, cavitations, and lymphadenopathies (Parasher, 2021; Pascarella et al., 2020; Sreepadmanabh et al., 2020; Wiersinga et al., 2020). Additionally, the CT scan is a valuable tool in the evaluation of the disease progression, the occurrence of complications, and treatment efficacy (Sreepadmanabh et al., 2020). The sensitivity of a chest X-ray is inferior compared to the CT scan, and it is not conclusive of the changes in the early-stage manifestations (Dhama et al., 2020; Parasher, 2021). However, in the course of the disease, the observed features include bilateral multifocal alveolar opacities and signs of pleural effusions (Parasher, 2021). The use of ultrasound has been so limited since it has a low specificity with a sensitivity of around 75%. The observed features are isolated or confluent B lines, subpleural consolidation, and air bronchogram. It helps in monitoring the evolution of the disease (Pascarella et al., 2020).

2.7.5 Other diagnostic methods

Reverse Transcriptional Loop-Mediated Isothermal Amplification (RT-LAMP) is a new technique for SARS-CoV-2 detection. It is a rapid and simple low-cost method that doesn’t require a trained healthcare worker to run the test (Dhama et al., 2020; Sreepadmanabh et al., 2020). It allows the amplification of a nucleic acid at a given temperature via colorimetric detection using a fluorescent calcein or a cresol red (Sreepadmanabh et al., 2020). Some emerging techniques have been proposed also, like a polymer-grafter using an antibody to detect the RNA but it lacks specificity which exposes the results to an elevated probability of false positives (Sreepadmanabh et al., 2020). Another one is the CRISPR-based technique to detect a viral nucleic acid (Dhama et al., 2020; Sreepadmanabh et al., 2020). It works by activating a Cas variant by attaching to the suitable target and then degrading the adjacent RNA. By use of fluorophen, there will be a fluorescence signaling the release of the desired sequence. It helps to detect rapidly the viral RNA samples (Sreepadmanabh et al., 2020).

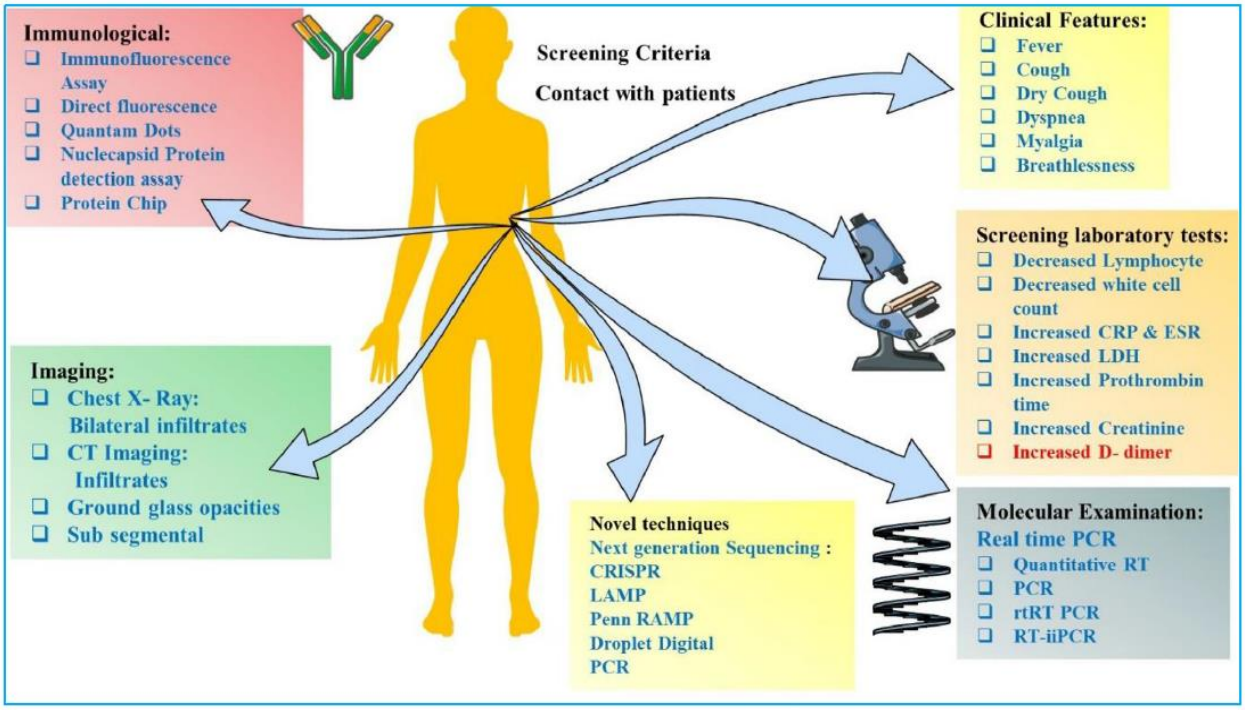

Figure 2: Diagnostics methods employed for SARS-CoC-2

[Source: Tiwari et al. (2021)*]*

2.8 Management of COVID-19

The management of COVID-19-positive individuals starts with an assessment to find out if they present signs of a severe illness and the risk factors which may expose them to develop a severe illness. It will further determine the environments where infected persons will be managed, which are at home or in hospital (Thevarajan et al., 2020). COVID-19 management lies in different approaches which consist of treating the symptoms, preventing or correcting respiratory failure, and use of different types of the drug such as antiviral, inflammatory inhibitors, immunoglobulins, and low molecular weight heparins (Pascarella et al., 2020; Stasi et al., 2020). In the early phase of the disease antiviral will be more suitable by decreasing the viral load and preventing the evolution of the infection, while in the pulmonary stage apart from the antivirals, oxygen is recommended as supportive respiratory therapy and anti-inflammatory drugs. In the critical stage additionally to anti-inflammatory, intubation is needed due to acute respiratory syndrome (Stratton et al., 2021).

2.8.1 Supportive and respiratory care management

Oxygen therapy is considered to be a vital tool in the management of COVID-19. Once the oxygen saturation (SaO2) level is under 90%, a supplementation in oxygen is highly required (Pascarella et al., 2020; Stratton et al., 2021; Thevarajan et al., 2020). This will be delivered as a low-flow oxygen therapy using a prong or Hudson mask or a non-rebreather mask (Stratton et al., 2021; Thevarajan et al., 2020). If patients keep not improving and persisting in hypoxemia or in case the desired level of SaO2 >90% is not met, high flow oxygen (HFO) should be considered using a nasal cannula or a face mask (Pascarella et al., 2020; Stratton et al., 2021; Thevarajan et al., 2020; Wiersinga et al., 2020). Precautions need to be observed since this process generates a lot of aerosols and the patient should be treated in an isolated room (Pascarella et al., 2020; Wiersinga et al., 2020). In a study done in Wuhan China, HFO showed to improve oxygenation in 61,9% of patients (Hu et al., 2020). Another study in Poland showed an effectiveness of 46% in patients with severe respiratory failure (Rorat et al., 2021). For the infected individuals who do not respond to high flow oxygen, mechanical ventilation using endotracheal intubation will be vital (Pascarella et al., 2020; Stratton et al., 2021; Wiersinga et al., 2020).

Oxygen therapy should be coupled with some techniques to help improve oxygenation such as raising the bed head and moving the patient correctly in bed or out of bed (Thevarajan et al., 2020). During ventilation some other practices should be applied, like ventilation with a limited volume, a positive end-expiratory pressure, use of a muscle relaxant, and a prone position which not only improves oxygenation but also facilitates alveolar ventilation (Pascarella et al., 2020; Stratton et al., 2021; Wiersinga et al., 2020).

2.8.2. Specific Therapies

2.8.2.1 Antiviral Agents

Different antivirals have been proposed in the treatment of COVID-19 depending on their mechanism of action. An antiviral agent is more suited to be given in the early stage of the infection in virtue to reduce the viral load (Stratton et al., 2021).

Remdesivir is a nucleotide analog and broad-spectrum antiviral with success against many RNA viruses, it acts by inhibiting the RNA-dependent polymerase which then causes a chain termination leading to a reduction in viral production (Gavriatopoulou et al., 2021; Maciorowski et al., 2020;

Pascarella et al., 2020; Trivedi et al., 2020; Uzunova et al., 2020). It was first tested to treat the Ebola virus but also showed efficacy in vitro against some coronaviruses like SARS-CoV and MERS-CoV, which then suggest its use against SARS-Cov-2 infection (Stasi et al., 2020; Tiwari et al., 2021; Uzunova et al., 2020). It is mostly used in patients with moderate or severe infection, but better in combination with other therapies. It is administered in course of five to ten days, intravenously starting with 200mg the first day and then 100mg the following days (Parasher, 2021; Stratton et al., 2021). It should be avoided in children, pregnant women, and people with elevated liver and renal disorders (Maciorowski et al., 2020; Parasher, 2021). A study that collected information on clinical outcomes of the use of remdesivir in different countries in patients with severe COVID-19, showed improvement of oxygen in 68% of patients and 13% of mortality (Grein et al., 2020). However, a study done in China showed no significant difference in time of clinical improvement and mortality rate among the treatment group and the placebo group(Wang et al., 2020)

Lopinavir/Ritonavir is a protease inhibitor, used in HIV infection (Gavriatopoulou et al., 2021). It was used during the SARS-Cov and MERS epidemics, which has motivated its use for COVID-19 as an emergency alternative drug for patients presenting mild symptoms (Parasher, 2021; Stasi et al., 2020). However, an open-label study conducted in China made the conclusion that there was no profit with the drug compared to the standard of care (Thevarajan et al., 2020; Trivedi et al., 2020; Wiersinga et al., 2020).

Favipiravir is a purine nucleic acid analog; it has broad antiviral activity against RNA viruses. It acts by inhibiting RNA-dependent RNA polymerase. It has been used against the influenza virus in Japan, and as an alternative against Ebola. It has shown effectiveness against SARS-Cov-2 in vitro, and it has been shown to decrease the viral load. It was given at a dose of 1800 mg two times a day on the first days followed by 800 mg two times a day for 14 days (Parasher, 2021; Stratton et al., 2021; Trivedi et al., 2020). A study done in China found that patients treated with favipiravir showed better viral clearance and better changes in chest CT, with an improvement in the disease progression (Cai et al., 2020).

2.8.2.2 Immunomodulatory Drugs

Tocilizumab is a recombinant monoclonal antibody of IgG1, initially used in the management of rheumatoid arthritis as well juvenile arthritis. It acts by inhibiting the binding of IL-6 to its receptor,

which will lessen the cytokine syndrome release, the reason why it has been used as an option in the management of COVID-19 infection (Parasher, 2021; Thevarajan et al., 2020; Trivedi et al., 2020). It has been associated with a decreased risk of invasive mechanical ventilation and death mostly in severe patients with elevated inflammatory markers and elevated oxygen demand. It is administered at a dosage of 8mg/kg in 100ml normal saline (Parasher, 2021; Stasi et al., 2020). A retrospective study done on 21 critical patients in China, showed a change in symptoms and CT opacity improving after treatment with tocilizumab, and patients were discharged on an average of 15 days (Xu et al., 2020).

Chloroquine (CQ) and hydroxychloroquine (HCQ), are aminoquinoline drugs used in the treatment of malaria (Maciorowski et al., 2020; Parasher, 2021; Pascarella et al., 2020). They have an anti-inflammatory effect in the treatment of rheumatic disorder and SLE (Maciorowski et al., 2020). It has been observed to have activity against many viruses such as influenza virus, Dengue virus, and coronavirus (Parasher, 2021; Pascarella et al., 2020; Stratton et al., 2021). Their antiviral mechanism is explained as they are bases, they increase the pH endosomal which damage some enzyme and inhibit the posttranslational change of the synthesized proteins (Maciorowski et al., 2020). They deplete the glycosylation of the ACE2 receptor preventing the binding of the virus (Maciorowski et al., 2020; Stasi et al., 2020). As an immunomodulatory effect, they can suppress the disproportionate immune response as they interfere with the secretion of cytokines (Maciorowski et al., 2020; Parasher, 2021). It was observed to reduce the aggravation of COVID-19 pneumonia and also enhance viral clearance (Parasher, 2021). However, a lot of observations from different studies show that HCQ does not show enough benefit in SARS-Cov-2 patients (Stratton et al., 2021). A study done in France on the efficacy of HCQ and Azithromycin showed a decreased risk of transfer to ICU or death, a decreased risk of hospitalization, and a shorter duration of viral shedding; QTc prolongation was observed in 0.67% of the patients (Lagier et al., 2020). However, another study done internationally in various center analyses which were later retracted, showed that chloroquine or hydroxychloroquine with or without the combination of antibiotics were associated with an increased risk of cardiac complications (ventricular arrhythmias) and death (Mehra et al., 2020).

2.8.2.3 Corticosteroids

The value of corticosteroids as an anti-inflammatory in the management of viral pneumonia has raised a lot of controversies. Seen the role of the host immune in the pathophysiology of COVID-19, a theory has been made suggesting that corticosteroids could have an impact on pulmonary inflammation (Gavriatopoulou et al., 2021).

Dexamethasone act by inhibiting TSST-1 induced cytokine formation and T cell proliferation (Stratton et al., 2021; Trivedi et al., 2020). A randomized control study where patients were given dexamethasone 6mg per day for ten days showed that dexamethasone reduced the incidence of 28 days mortality rate by 1/3 in ventilated patients and 1/5 in oxygenated patients as compared to the control group which was higher (Horby et al., 2021). The WHO advises the use of low-dose dexamethasone in severe COVID-19 patients in requirement of a supplement in oxygen (Stasi et al., 2020).

2.8.2.4 Passive Immunotherapy

Convalescent plasma (CP) from infected individuals has shown the ability to neutralize viruses obtain after a bronchoalveolar lavage in critical patients (Parasher, 2021). The elevated antibody titers taken from the CP of three healed patients have been shown to reduce mortality in critical patients (Stasi et al., 2020; Stratton et al., 2021; Trivedi et al., 2020). This may be explained by the fact that the antibodies from the CP prevent the binding of spike protein and entry into the cell which then limits viremia, it prevents the complement cascade which then diminishes the pulmonary inflammatory reaction (Gavriatopoulou et al., 2021; Stratton et al., 2021). The treatment needs to be started early and consideration is given to critically ill patients, the elderly, and those with comorbidities (Gavriatopoulou et al., 2021; Parasher, 2021; Stratton et al., 2021). It is given at a dose of 4-13 mL/kg or 200 mL for 2 hours (Parasher, 2021). A study done in the U.S assessing the efficacy of CP in 20,000 COVID-19 patients, confirmed its safety with a 7 days mortality rate of 8.6%, however, this rate was 10.5% in critically ill patients admitted to the ICU and 12.1% in patients who needed mechanical ventilation (Joyner et al., 2020).

2.8.2.5 Anticoagulants

Low Molecular Weight Heparin (LMWH) at the dose of 40 mg SC is the desired and considered anticoagulant therapeutic option in COVID-19 patients with risk or complication of venous

thromboembolism and coagulation (Gavriatopoulou et al., 2021; Parasher, 2021; Stasi et al., 2020; Stratton et al., 2021). It has been shown to be associated with a decrease in mortality rate (Gavriatopoulou et al., 2021). Some blood markers should be considered such as elevated D-dimer, elevated prothrombin time, and reduced fibrinogen, in order to detect those in need of the anticoagulant (Stratton et al., 2021). A study in China that compared the 28-day mortality between two groups - the first who received heparin 30.3% and the second who did not receive 29.7% - showed no statistically significant difference. However, in a group of sepsis-induced coagulopathy patients, there was noted a difference in the 28 days mortality with 40.0% in those we received compared to those who did not receive 64.2% (Tang et al., 2020).

2.8.2.6 Herbal medicine

Different herbs have been shown to have antiviral and immunomodulatory actions and have been considered alternative options for therapy against COVID-19 disease. In Asia, it has been observed the use of traditional medicine to face COVID-19 using the same plants which were used during the SARS-CoV outbreak (Esakandari et al., 2020; Trivedi et al., 2020).

The herbs used in Asia including *Astragalus membranaceus*, rhizoma, and Re-Du-Ning have an immunosuppressive action as they reduce the level of cytokines. The Qingfei Paidu can control the immune pathway and lessen the inflammation in the lung. Ginseng controls the action of immune cells. Ginger has many properties such as being an anti-inflammatory, antioxidant, and analgesic agent (Esakandari et al., 2020). Others like aloe vera, *Angelica gigas*, *Astragalus membranaceus*, and *Scutellaria baicalensis* have an immunomodulatory effect due to the fact they activate lymphocytes, elevate the NK cells count, and stimulate macrophage action. Due to their immunomodulatory effect, these herbs can boost the immune system and help the organism fight the SARS-CoV-2 infection (Panyod et al., 2020). A meta-analysis review by Ang L et al, comparing the efficacy of combined therapy of herbal medicine and western medicine to western medicine alone found a significant effect of the combined therapy showing its potential role in treating COVID-19 (Ang et al., 2020).

2.8.3 Preventive and Control Measures

Applying preventive measures has shown to be one of the effective ways to interfere with the spread of new infections. Depending on the environment, different approaches have been used

which can be summarized as personal actions, case identification, regulatory actions, and borders regulations measures

2.8.3.1 In Community

Several actions have been taken to avoid transmission. This includes physical or social distancing to reduce individual interactions since the transmission occurs through respiratory droplets, observing a certain distance of two meters from one to another is considered, avoid crowding places as a way to limit transmission. These other measures should be taken and put mandatory in an environment at higher risk of community transmission such as closure or restriction of the number of people in workplaces, educational institutions, public transport, in mass gathering places. Where possible work from home should be encouraged (Güner et al., 2020; Mcintosh, 2021; Wiersinga et al., 2020).

Observance of hand hygiene, regularly washing hands especially after touching various surfaces, and using soap or alcohol-based sanitizer can help reduce transmission from person to person (Dhama et al., 2020; Mcintosh, 2021; Pradhan et al., 2020).

Personal protective equipment, people should observe the use of face masks while in public environments such as in shops, in public transport, in closed spaces, or in any other places which expose to physical proximity to others. This is to prevent from getting the aerosol and also to spread respiratory droplets since many individuals are asymptomatic. Once the mask is removed, it is advised to avoid touching the face, and when sneezing cover using the elbow fold (Dhama et al., 2020; Güner et al., 2020; Mcintosh, 2021).

Quarantine measure is the best way to reduce the number of infections and mortality. Recommendations have been made that anyone who turns out to be SARS-CoV-2 positive and is asymptomatic or has mild symptoms and any individuals who had close contact with a positive patient, should isolate themselves for 14 days avoiding contact with other individuals and wearing a mask at all the times. Quarantined individuals will be actively monitored until they turn negative and the symptoms subside (Güner et al., 2020; Mcintosh, 2021).

2.8.3.2 In Health Care Setting

All the health care workers should be trained on the Infection and Prevention Control (IPC) measures, make a triage area for an early diagnosis of all infected individuals, and put them in an

isolation room facility located away from the rest of the hospital consisting of 3 different zones, provide all the patients with a mask (Islam et al., 2020; Ministry of Health - Kenya, 2021).

The health worker should observe the PPE measures, which consist of a mask, gown, gloves, goggles face shields, anytime they are in contact with the patients. Observe all the transmission and standard precautions while interacting with patients, and while handling a dead body (Islam et al., 2020; Ministry of Health - Kenya, 2021).

All touched surfaces and those soiled by body fluid should be continuously cleaned and disinfected. Different solutions are used according to the surface. Soap and enzymatic detergent, 0.5 % chlorine for disinfection. Always use disposable gloves while cleaning or disinfecting (Güner et al., 2020; Ministry of Health - Kenya, 2021).

2.8.3.3 Vaccination

In the fight to get an appropriate treatment against COVID-19, many efforts have been made to develop vaccines against the SARS-CoV-2 infection. This has led to a reduced time for the vaccine development to one year due to the emergency situation of this pandemic (Ghasemiyeh et al., 2021; Kaur & Gupta, 2020). Different types of technology vaccines were under development such as nucleic acid vaccine (Moderna, Pfizer), viral vector vaccine (AstraZeneca, Janssen, Sputnik V), inactivated vaccine (Sinovac), protein-based (Novavax) (Ghasemiyeh et al., 2021; Kashte et al., 2021). In December 2020, the United Kingdom was the first country to approve the use of a COVID-19 vaccine the Pfizer vaccine, followed by the WHO for emergency use (Kashte et al., 2021). More details are summarized in Appendix 4

CHAPTER THREE: MATERIALS AND METHODS

3.1 Study area

This study was conducted at various health facilities located in Nairobi County, that is, Kenyatta National Hospital (Public) and Mater Misericordiae Hospital (Private), and in Mombasa County, that is, Coast General Teaching Hospital (Public). The study regions were selected because they have well-equipped facilities with isolation rooms for the management of COVID-19 patients. Besides, Nairobi County and Mombasa County recorded some of the highest cases of SARS-CoV-2 infections since the pandemic started (Ministry of Health - Kenya, 2021).

3.2 Study design

This was a retrospective cross-sectional study involving COVID-19 positive patients admitted into the healthcare facilities of interest in Kenya, since the first case was reported on 13th March 2020 until 31st December 2021.

3.3 Study population

The study enrolled 408 patients with a confirmed positive laboratory test for COVID-19 who were admitted and treated in the selected hospitals during the study period, regardless of their severity classification or their sociodemographic variations. The source of data was the patient files obtained from the medical record departments of the hospitals of interest.

3.4 Eligibility Criteria

3.4.1 Inclusion Criteria

The following were the inclusion criteria for enrolling patients into the study:

i. Confirmation of COVID-19 positive test based on the fulfillment of the criteria of the confirmed case definition of SARS-CoV-2 (Appendix 1).
ii. The patient was established to be manifesting with mild to critical COVID-19 infection based on the national guideline for COVID-19 severity classification (Appendix 2).

iii. The patient was admitted to the hospitals of interest during the specified study period (13th March 2020 to 31st December 2021).

3.4.2 Exclusion Criteria

The following were the exclusion criteria for the study:

i. The patient was not within the study period
ii. The patient was not established to have a positive COVID-19 infection test
iii. The patient was not treated for COVID-19 at all due to various issues like declining treatment.

3.5 Variables

3.5.1 Dependent Variables

The dependent variable in this study was the treatment outcomes, that is, whether a person improves or deteriorates his disease conditions further after being administered with a treatment modality for COVID-19 as specified in the national guideline for the management of COVID-19 or otherwise.

3.5.2 Independent Variables

The independent variable in this study was the treatment modalities/therapeutic options. This is because the method of treatment for COVID-19 used in a given patient has been hypothesized in this study to affect their treatment outcomes.

3.5.3 Intervening variables

Intervening variable influence how the independent variables relate to the dependent variables. In this study, it was theorized that other variables like co-morbidities, age, sex, immune depression, pregnancy, and hospital category (i.e., private/public) could moderate the relationship between treatment and outcome.

3.5.4 Outcome definition

In this study, two outcomes of interest were considered, that is, discharge or death.

3.6 Sample Size Determination

The formula used for sample size determination was the Cochran formula (Cochran, 1977):

$$n = \frac{Z^2 P(1-P)}{e^2}$$

Where:

n: The required sample size

Z: Value corresponding with the chosen confidence interval (At 1.96 for 95% CI)

e: The confidence level of precision expressed (at 0.05) margin of error for 95%

P: The proportion of the estimated prevalence; is assumed to be 50% (made especially if the exact prevalence is not known).

$$n = \frac{1.96^2 x 0.5(1-0.5)}{0.05^2}$$

$n = 384.16 \approx 384$ patients

Cochran, W. G. (Cochran, 1977) recommends that for a population size above 10,000, the minimum sample size should be 384, while for a population size less than 10,000, there is a moderating formula further used to adjust the minimum required sample size. Since the population of COVID-19 positive individuals in Kenya during the study period had reached 267,571 people (World Health Organization, 2022) between March 2020 and December 2021, which is above the 10,000 thresholds, this study shall maintain the sample size at a minimum of 384 patients. However, more data samples exceeding 384 can be collected, if possible, to improve the generalizability of the findings. Out of the minimum of 384 samples targeted for enrollment in the study, our study enrolled 408 patient files, giving an enrollment rate of 106.3%.

3.7 Sampling Procedure: Sampling frame and sampling method

The sampling frame for this study included the hospitals of interest, that is from Nairobi County – Kenyatta National Hospital (Public) and Mater Misericordiae Hospital (Private); and Mombasa County – Coast General Hospital (Public).

Table 1: The hospitals and the minimum number of samples to be obtained from each

Hospital	No. of samples to be taken
Kenyatta National Hospital (KNH)	194 patients
Mater Misericordiae Hospital (MMH)	111 patients
Coast General Hospital (CGH)	103 patients

For this study, a simple random sampling method was used to obtain the required sample size among each of the clusters, that is, every hospital. This method ensured that all hospitalized COVID-19 patients had an equal chance of being selected for the study. To achieve this, a lottery method was used to randomly pick the data samples using a Microsoft Excel software functionality (=RANDBETWEEN) whereby random numbers between 1 and 10 were generated. The principal investigator then picked the records that got an odd number until the desired sample size was obtained.

3.8 Data collection

Data were collected using the Research Electronic Data Capture (REDCap) software, which is a web-based data management software. The variables that were collected included sociodemographic information such as age and gender; clinical information such as symptoms, comorbidities or underlying diseases, pharmacological treatments administered, laboratory parameters such as WBC, ALT, and AST, and clinical outcomes, that is, discharge or death. The full detail of the variables is in the Data Collection Sheet (Appendix 5).

3.9 Data Analysis

Data analysis was done using the Statistical Package for Social Science (SPSS) version 25 (IBM Corp., 2017). IN general, the analysis was done to obtain descriptive statistics such frequency, mean, mode, and median, and inferential statistics such as Chi-square. All hypotheses were tested at a 95% confidence interval with the significance level (alpha) set at 0.05. The results were presented in form of tables and charts. The detailed analysis of the results section is delineated below:

3.9.1 Sociodemographic and clinical characteristics

For hospital category, sex, severity of COVID-19, presence of a comorbidity, and common comorbidities present, frequency and proportion were determined followed by a crosstabulation with outcome (death or discharge). Bivariate analysis was done with Chi-Square to obtain p-values showing significance of the association, if any, between the sociodemographic/clinical variables and outcome. For age, mean and standard deviation were determined in addition to frequency and proportions. Crosstabulation was also done with outcome, giving Chi-square p-values for association between age and the outcome of COVID-19 treatment. For the outcome variable, further analysis was done to obtain the 95% confidence interval of proportions using the Clopper-Pearson method.

3.9.2 Management of COVID-19

First, a variable called "Regimen group" was created by considering the treatment modalities specified in the Kenyan national guidelines for the management of COVID-19 used among the patients whereby regimen 1 comprised paracetamol and/or antihistamine; regimen 2 comprised regimen 1 elements, Enoxaparin and/or oxygen; regimen 3 comprised regimen 2 elements plus oxygen, dexamethasone, and/or proning; regimen 4 consisted of regimen 3 elements, mechanical ventilation, and/or dexamethasone. Second, the drugs Tociluzimab +/ Baricitinib +/ Remdesivir were classified as "other therapy". The regimen groups were done according to the level of COVID-19 severity. Third, the other non-COVID-19-treatment-related drugs used among the patients were captured as supplementary drugs, which were further reclassified into their drug types, for instance, antibiotics, anticoagulants, etc. Fourth, supportive therapy included the use of oxygen and ventilation, which were also constituents of the regimen groups already mentioned. For the treatment modalities, frequency and proportions were determined followed by bivariate analysis for association with outcome by the use of Chi-square test.

3.9.3 Adherence to treatment guidelines for COVID-19

Adherence was analyzed in terms of the performing of laboratory tests, some of which were baseline tests stipulated in the national guideline, e.g., HIV test and random blood sugar; and the use of recommended treatment modalities. For laboratory tests, frequency and proportions and proportions were determined, followed by bivariate analysis for association between the various

laboratory tests and outcome by the use of Chi-square p-value. The overall outcome of assessment of adherence to the national guidelines for the management of Covid-19 based on disease severity was also commented on by the individual gathering data based on the patterns observed in general. Adherence or non-adherence was reported using frequency and proportions followed by bivariate analysis using Chi-square for the association between adherence and outcome. Furthermore, the particular instances of non-adherence were documented and reported.

3.9.4 Relationship between clinico-sociodemographic characteristics and treatment outcomes

Multivariable binary logistics regression was used to model the predictors of discharge. This was in three phases – phase 1, regression for sociodemographic and clinical characteristics on the discharge; phase 2, regression for the influence of the commonly encountered underlying co-morbidities on clinical outcomes (discharge) during the management of COVID-19; and phase 3, regression for the influence of treatment modality on clinical outcomes (discharge) during the management of COVID-19. For phase 1, both crude odds ratios and adjusted odds ratios were obtained with their 95% confidence intervals and associated p-values. For phases 2 and 3, beta coefficients were obtained and used to rank the variable with only the adjusted odds ratios being computed.

3.10 Ethical considerations

The study obtained ethical approval from the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee (KNH-ERC/A/299), and license from the National Commission for science and Technology (NACOSTI/P/22/20482). We sought further approval to access records from Coast General Teaching Hospital & Referral Hospital Ethics and Research Committee (Ref. ERC-CGH/Msc/VOL. I, 29th March, 2023), and Mater Misericordiae Hospital Research Committee as well (Appendix 6, Appendix 7, Appendix 8, and Appendix 9).

3.11 Dissemination of study findings

The study findings will be presented to the University of Nairobi Faculty of Health Sciences Department of Medical Microbiology and Immunology. A manuscript will be developed in

consideration for publishing in a reputable journal. Conferences presentations of the study findings will also be explored.

CHAPTER FOUR: RESULTS

4.1 Sociodemographic and clinical characteristics of the study participants

Of the 408 study participants, 312 (76.5% [95% CI: 72.8%, 79.9%]) were treated and discharged while 96 (23.5% [95% CI: 19.5%, 28.0%]) died (Figure 2). This difference was observed to be statistically significant by Chi-square test, $\chi 2$ (1) = 114.353, p <0.001 (Figure 3).

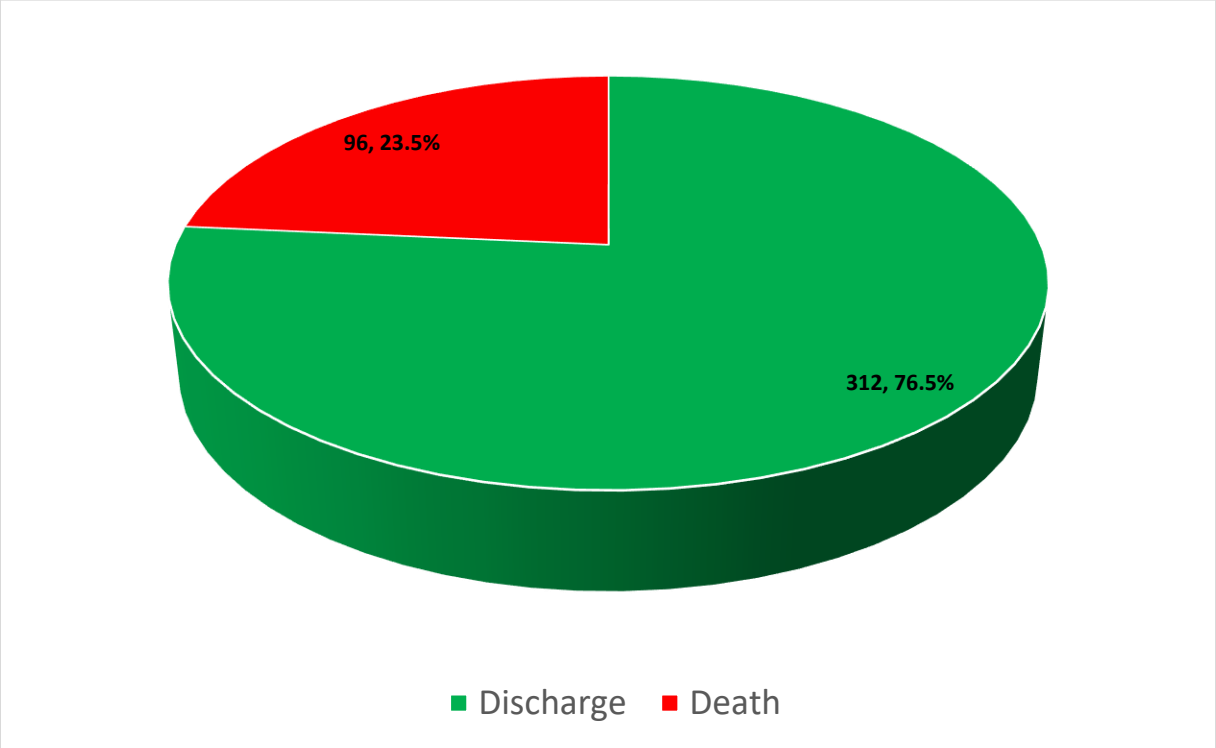

Figure 3: The clinical outcome of treatment among COVID-19 patients in general

The sociodemographic characteristics of study participants are depicted in table 2. In private hospitals participants were 111 (27.2%), and 297 participants (72.8%) were in public hospitals. There was a significant difference in outcomes between private and public hospitals (p < 0.001). A higher proportion of patients in private hospitals 102 (91.9%) were discharged compared to those in public hospitals 210 (70.7%). Concerning age, majority of the study participants were aged 50 years and above (209, 51.2%). The mean age of the study participants was 50.46 (SD = 16.00) years with a higher mean age for those who died (58.77 years, SD =16.25 years) compared to those who were discharged (47.90 years, SD = 15.05 years). The youngest and oldest study participants were aged 8 years and 92 years, respectively. Younger patients (<= 30 years) had a

higher proportion of discharge (87.2%) compared to older age groups. There was a statistically significant difference in outcomes across different age groups ($p < 0.001$). Patients with mild and moderate disease severity had a very higher percentage of discharge (96.3%) and (92.2%) respectively compared to the other groups. Among those classified as severe, only (69.0%) were discharged. The critical group had the least number of participants, only (4.5%) was discharged, and a substantial number of participants (95.5%) in the critical category did not survive. This group had the highest mortality rate. There was a strong association between disease severity and the outcome ($p < 0.001$). Table 2 below shows a significant association between the presence of comorbidities and the outcomes ($p < 0.002$). Only 193 (47.3%) participants had no known comorbidity and 215 (52.7%) participants had at least one comorbidity. Majority of discharged cases were observed in patient with no comorbidity (89.6%) compared to those with underlying comorbidities (64.7%). Information on specific comorbidities and their association with the outcome are also provided in Table 2 below and it shows a statistically significant association ($p = 0.002$). The more prominent comorbidities were hypertension, diabetes mellitus and end-stage renal disease/chronic kidney disease (ESRD/CKD).

Table 2: The distribution of the study participants by sociodemographic and clinical characteristic

Variables and categories	Overall	Outcome		p-value[a]
		Discharge	Death	
	n (%)	n (%)	n (%)	
Hospital category				
Private	111 (27.2)	102 (91.9)	9 (8.1)	<0.001*
Public	297 (72.8)	210 (70.7)	87 (29.3)	
Total	408 (100.0)	312 (76.5)	96 (23.5)	
Age				
<=30 years	47 (11.5)	41 (87.2)	6 (12.8)	<0.001*
31 - 49 years	152 (37.3)	130 (85.5)	22 (14.5)	
>=50 years	209 (51.2)	141 (67.5)	68 (32.5)	
Total	408 (100.0)	312 (76.5)	96 (23.5)	
Mean (SD), years	50.46 (16.00)	47.90 (15.05)	58.77 (16.25)	
Sex				
Male	248 (60.8)	185 (74.6)	63 (25.4)	0.27
Female	160 (39.2)	127 (79.4)	33 (20.6)	
Total	408 (100.0)	312 (76.5)	96 (23.5)	
Severity				

Mild	54 (13.2)	52 (96.3)	2 (3.7)	<0.001*
Moderate	129 (31.6)	119 (92.2)	10 (7.8)	
Severe	203 (49.8)	140 (69.0)	63 (31.0)	
Critical	22 (5.4)	1 (4.5)	21 (95.5)	
Total	408 (100.0)	312 (76.5)	96 (23.5)	
Presence of a comorbidity				
No	193 (47.3)	173 (89.6)	20 (10.4)	<0.002*
Yes	215 (52.7)	139 (64.7)	76 (35.3)	
Total	408 (100.0)	312 (76.5)	96 (23.5)	
Common comorbidities				
Hypertension	147 (69.3)	97 (66.0)	50 (34.0)	0.002*
Diabetes mellitus	101 (47.6)	68 (67.3)	33 (32.7)	
End-stage renal disease/chronic kidney disease (ESRD/CKD)	39 (18.4)	23 (59.0)	16 (41.0)	
Acute kidney injury	27 (12.7)	10 (37.0)	17 (63.0)	
Congestive cardiac failure	17 (8.0)	11 (64.7)	6 (35.3)	
Cancer	12 (5.7)	5 (41.7)	7 (58.3)	
Diabetic ketoacidosis	8 (3.8)	3 (37.5)	5 (62.5)	
Acute decompensated heart failure (ADHF)	4 (1.9)	2 (50.0)	2 (50.0)	
Deep vein thrombosis	4 (1.9)	0 (0.0)	4 (100.0)	
Cerebrovascular accident/hypoxic brain injury	3 (1.4)	1 (33.3)	2 (66.7)	
Total	212 (100.0)	138 (65.1)	74 (34.9)	

Note:
[a]Chi-square test; SD, standard deviation; *Statistically significant at 95% confidence interval

4.2 Management

4.2.1 Pharmacological Treatment and supportive treatment

Regimen 1 appeared to be associated with a higher discharge percentage (94.1%), while Regimen 4 was associated with a higher mortality percentage (89.3%). Those who did not use other therapy (Tocilizumab/Baricitinib/Remdesivir) were also associated with a better outcome in terms of discharge (78.8%). The p-values indicated a statistical significance of these associations for regimen group ($p < 0.001$) and other therapy ($p = 0.01$). Table 3 below shows that, there was a significant association between the outcome and the use of oxygen and ventilation with p-values of < 0.001 each. The proportion of discharge was lower in those who received oxygen (68.9%) compared to those who did not receive (95.0%). The use of oxygen appeared to be associated with a higher risk of death. Among those who received oxygen, a significantly higher proportion died

(31.1%) compared to those who did not receive oxygen (5.0%). Out of the 408 participants, (6.9%) received ventilation. Among those who received ventilation, (10.7%) were discharged, while a significantly higher proportion (89.3%), died. The vast majority (93.1%) did not receive ventilation, with (81.3%) being discharged, and (18.7%) dying (Table 3).

Table 3: The pharmacological treatment modalities used among the study participants

Variables and categories	**Overall**	**Outcome**		**p-value[a]**
		Discharge	**Death**	
	n (%)	**n (%)**	**n (%)**	
Regimen group				
Regimen 1[b]	68 (16.7)	64 (94.1)	4 (5.9)	<0.001*
Regimen 2[c]	2 (0.5)	2 (100.0)	0 (0.0)	
Regimen 3[d]	310 (76.0)	243 (78.4)	67 (21.6)	
Regimen 4[e]	28 (6.9)	3 (10.7)	25 (89.3)	
Total	408 (100.0)	312 (76.5)	96 (23.5)	
Other therapy[f]				
No	344 (84.3)	271 (78.8)	73 (21.2)	0.01*
Yes	64 (15.7)	41 (64.1)	23 (35.9)	
Total	408 (100.0)	312 (76.5)	96 (23.5)	
Other therapy: Tocilizumab				
Yes	12 (2.9)	3 (25.0)	9 (75.0)	<0.001*
No	396 (97.1)	309 (78.0)	87 (22.0)	
Total	408 (100)	312 (76.5)	96 (23.5)	
Other therapy: Baricitinib				
Yes	14 (3.4)	7 (50.0)	7 (50.0)	0.02*
No	394 (96.6)	305 (77.4)	89 (22.6)	
Total	408 (100)	312 (76.5)	96 (23.5)	
Other therapy: Remdesivir				
Yes	59 (14.5)	38 (64.4)	21 (35.6)	0.02*
No	349 (85.5)	274 (78.5)	75 (21.5)	
Total	408 (100)	312 (76.5)	96 (23.5)	
Oxygen				
Yes	289 (70.8)	199 (68.9)	90 (31.1)	<0.001*
No	119 (29.2)	113 (95.0)	6 (5.0)	
Total	408 (100.0)	312 (76.5)	96 (23.5)	
Ventilation				
Yes	28 (6.9)	3 (10.7)	25 (89.3)	<0.001*
No	380 (93.1)	309 (81.3)	71 (18.7)	
Total	408 (100.0)	312 (76.5)	96 (23.5)	
Note:				

[a]Chi-square test; [b]Regimen 1 = Paracetamol +/ Antihistamine; [c]Regimen 2= Regimen 1 + Enoxaparin +/ Oxygen; [d]Regimen 3 = Regimen 2 + Oxygen + Dexamethasone +/ Proning; [e]Regimen 4 = Regimen 3 +/ mechanical ventilation +/ Dexamethasone; [f]Tociluzimab +/ Baricitinib +/ Remdesivir; *Statistically significant at 95% confidence interval

4.2.2 Supplementary drug

Overall, table 4 showed a statistically significant association (p = 0.002) between the supplementary treatment and the outcomes whereby the most commonly used supplementary treatment was antibiotics 255 (66.4%). Most of those who used antibiotics were discharged (177, 69.4%). More details are listed in Table 4 below.

Table 4: The types of supplementary drugs commonly used among the study participants

Drug type[b]	Overall	Outcome		p-value[a]
		Discharge	Death	
	n (%)	n (%)	n (%)	
Antibiotics	255 (66.4)	177 (69.4)	78 (30.6)	0.002*
Anticoagulants	244 (63.5)	187 (76.6)	57 (23.4)	
Antihypertensives	204 (53.1)	151 (74.0)	53 (26.0)	
Antacids	171 (44.5)	131 (76.6)	40 (23.4)	
Antidiabetics	119 (31.0)	90 (75.6)	29 (24.4)	
Mineral supplements	117 (30.5)	89 (76.1)	28 (23.9)	
Vitamin supplements	95 (24.7)	78 (82.1)	17 (17.9)	
Bronchodilators	68 (17.7)	49 (72.1)	19 (27.9)	
Expectorants	53 (13.8)	45 (84.9)	8 (15.1)	
Antihypertensive/anti-heart failure agents	47 (12.2)	32 (68.1)	15 (31.9)	
Total	384 (100.0)	292 (76.0)	92 (24.0)	

Note:
[a]Chi-square test; *Statistically significant at 95% confidence interval; [b]The top 10 drug types out of 66 drug types reported to be used among the study participants

4.3 Adherence to treatment guidelines for COVID-19

4.3.1 Laboratory and radiological tests done

The laboratory tests with p < 0.05 (e.g., Full Blood Count, Hepatic Function Tests, Random Blood Sugar Test, Inflammatory Markers, X-ray, and Coagulopathy: Prothrombin) were considered to have a significant association with the outcomes as opposed to tests with p > 0.05 (e.g., Renal Function Tests, HIV Test, Cardiac Function, CT-scan, and MRI), which are not considered to have a significant association with the outcomes as detailed in table 5 below.

Table 5: The laboratory and radiological tests done for the study participants during COVID-19 management

Laboratory test	If done	Overall	Outcome		p-value[a]
			Discharge	Death	
		n (%)	n (%)	n (%)	
Full blood count	Yes	398 (97.5)	307 (77.1)	91 (22.9)	0.05
	No	10 (2.5)	5 (50.0)	5 (50.0)	
	Total	408 (100.0)	312 (76.5)	96 (23.5)	
Hepatic function tests	Yes	363 (89.0)	272 (74.9)	91 (25.1)	0.04*
	No	45 (11.0)	40 (88.9)	5 (11.1)	
	Total	408 (100.0)	312 (76.5)	96 (23.5)	
Renal function tests	Yes	389 (95.3)	295 (75.8)	94 (24.2)	0.17
	No	19 (4.7)	17 (89.5)	2 (10.5)	
	Total	408 (100.0)	312 (76.5)	96 (23.5)	
HIV test	Yes	195 (47.8)	144 (73.8)	51 (26.2)	0.23
	No	213 (52.2)	168 (78.9)	45 (21.1)	
	Total	408 (100.0)	312 (76.5)	96 (23.5)	
Random blood sugar test	Yes	327 (80.1)	237 (72.5)	90 (27.5)	<0.001*
	No	81 (19.9)	75 (92.6)	6 (7.4)	
	Total	408 (100.0)	312 (76.5)	96 (23.5)	
Inflammatory markers	Yes	322 (78.9)	236 (73.3)	86 (26.7)	0.003*
	No	86 (21.1)	76 (88.4)	10 (11.6)	
	Total	408 (100.0)	312 (76.5)	96 (23.5)	
Coagulopathy: Prothrombin	Yes	156 (38.2)	104 (66.7)	52 (33.3)	<0.001*
	No	252 (61.8)	208 (82.5)	44 (17.5)	
	Total	408 (100.0)	312 (76.5)	96 (23.5)	
Cardiac function	Yes	120 (29.4)	86 (71.7)	34 (28.3)	0.14
	No	288 (70.6)	226 (78.5)	62 (21.5)	
	Total	408 (100.0)	306 (76.9)	96 (23.5)	
X-ray	Yes	205 (50.2)	148 (72.2)	57 (27.8)	0.04*
	No	203 (49.8)	164 (80.8)	39 (19.2)	
	Total	408 (100.0)	312 (76.5)	96 (23.5)	
CT-scan	Yes	138 (33.8)	105 (76.1)	33 (23.9)	0.90
	No	270 (66.2)	207 (76.7)	63 (23.3)	
	Total	408 (100.0)	312 (76.5)	96 (23.5)	
Ultrasound	Yes	0 (0.0)	0 (0.0)	0 (0.0)	N/A
	No	408 (100.0)	312 (76.5)	96 (23.5)	
	Total	408 (100.0)	312 (76.5)	96 (23.5)	
MRI	Yes	1 (0.2)	0 (0.0)	1 (100.0)	0.07
	No	407 (99.8)	312 (76.7)	95 (23.3)	
	Total	408 (100.0)	312 (76.5)	96 (23.5)	

Note:
[a]Chi-square test; N/A, not applicable; *Statistically significant at 95% confidence interval; CT, computed tomography; MRI, magnetic resonance imaging

4.3.2 Adherence to the national guidelines for the management of Covid-19 based on disease severity

Table 6 shows that overall, majority of healthcare workers followed the directives of the national guidelines, as observed on 326 (79.9%) records. For the files where the national guidelines were strictly adhered to, the majority of the patient 260 (79.8%) had a favorable outcome (discharged) which is higher compared to the records which did not show a complete adherence to the guidelines 52 (63.4%). Conversely, a higher percentage of patients who did not receive the treatment following the national guidelines 30 (36.6%) died compared to those who did 66 (20.2%). There was a significant association between adherence to the guidelines and patient outcomes (p = 0.002). Following the guidelines was associated with a higher rate of discharge and a lower rate of death.

Table 6: The overall outcome of assessment of adherence to the national guidelines for the management of Covid-19 based on disease severity

Adherence status	Overall	Outcome		p-value[a]
		Discharge	Death	
	n (%)	n (%)	n (%)	
Yes	326 (79.9)	260 (79.8)	66 (20.2)	
No	82 (20.1)	52 (63.4)	30 (36.6)	0.002*
Total	408 (100.0)	312 (76.5)	96 (23.5)	

Note:
[a]Chi-square test; *Statistically significant at 95% confidence interval

4.3.3 Identified non-adherence instances

Non-adherence instances had a significant association with outcome, p = 0.002. Of those who did not receive baseline HIV tests (52, 63.4), 34 (65.4%) were discharged while 18 (34.6%) died. Among patients who did not receive dexamethasone/prednisolone, 12 (52.2%) died while 11 (47.8%) were discharged. For the patients whose RBS (random blood sugar) tests were nor ordered, 18 (85.7%) were discharged and 3 (14.3%) died among those who didn't receive the test. For those whose VTE prophylaxis enoxaparin/clexane were not administered 6 (54.5%) died and 5 (45.5%) were discharged (Table 7).

Table 7: The particular non-adherence instances identified

Non-adherence instance[b]	Overall	Outcome		p-value[a]
		Discharge	Death	
	n (%)	n (%)	n (%)	
Baseline tests not ordered: HIV	52 (63.4)	34 (65.4)	18 (34.6)	0.002*
Dexamethasone/prednisone not administered	23 (28.0)	11 (47.8)	12 (52.2)	
Baseline tests not ordered: RBS	21 (25.6)	18 (85.7)	3 (14.3)	
VTE prophylaxis enoxaparin/clexane not administered.	11 (13.4)	5 (45.5)	6 (54.5)	
Radiological findings not documented	11 (13.4)	7 (63.6)	4 (36.4)	
No ICU admission and/or mechanical ventilation	6 (7.3)	0 (0.0)	6 (100.0)	
Some tests were not performed as required by the guidelines	6 (7.3)	4 (66.7)	2 (33.3)	
Baseline tests not ordered: LFTs	5 (6.1)	4 (80.0)	1 (20.0)	
No ICU admission; due to lack of bed	5 (6.1)	1 (20.0)	4 (80.0)	
No demonstrated self-proning or oxygen supplementation	4 (4.9)	1 (25.0)	3 (75.0)	
Baseline tests not ordered	1 (1.2)	0 (0.0)	1 (100.0)	
No imaging suggestive of pneumonia	1 (1.2)	1 (100.0)	0 (0.0)	
No intubation or ventilation to remedy respiratory failure	1 (1.2)	0 (0.0)	1 (100.0)	
No oxygen supplementation	1 (1.2)	0 (0.0)	1 (100.0)	
Prophylactic (dexamethasone and enoxaparin/clexane) not administered	1 (1.2)	0 (0.0)	1 (100.0)	
Renal function tests	1 (1.2)	1 (100.0)	0 (0.0)	
The treatment not done as advised per the national guideline	1 (1.2)	1 (100.0)	0 (0.0)	
Total	82 (100.0)	52 (63.4)	30 (36.6)	

Note:
[a]Chi-square test; *Statistically significant at 95% confidence interval; [b]The 17 types of non-adherence instances observed regarding the management of the COVID-19 patients based on the national guidelines; HIV, human immunodeficiency virus; RBS, random blood sugar; VTE, venous thromboembolism; ICU, intensive care unit; LFTs, liver function tests

4.4 Relationship between clinico-sociodemographic characteristics and treatment outcomes

Patients in private hospitals had a higher likelihood (aOR = 10.166, p <0.001) of being discharged compared to patients in public hospitals, and this difference was statistically significant. Female patients were more likely to be discharged (aOR = 2.073, p = 0.01) compared to male patients. The more severe the disease was at admission the lower the odds of discharge were (adjusted OR = 0.214, p < 0.001). For each unit increase in disease severity, the odds of discharge decreased to 21.4% of the previous odds. Similarly, an increase in the level of regimen group was associated

with a significant decrease in the odds of getting discharge (aOR = 0.297, p = 0.007). Patients with comorbidities had lower odds of discharge (adjusted OR = 0.281, p < 0.001) compared to those without comorbidities. The use of Tocilizumab was significantly associated with outcome from COVID-19 (aOR = 0.169, p = 0.04) but was not an indicator of discharge. Other independent variables used in the model such as age (aOR = 0.987, p =0.46), age of >60 years (aOR = 0.955, p = 0.93), Baricitinib (aOR = 0.979, p = 0.98), Remdesivir (aOR = 0.518, p = 0.19), supplementary drugs (aOR = 3.979, p =0.16), other supportive treatment (aOR = 1.655, p = 0.10), adherence to national guidelines (aOR = 1.011, p = 0.98) were not significant predictors of discharge (Table 8).

Table 8: Multivariable binary logistic regression for sociodemographic and clinical characteristics in predicting discharge as a clinical outcome

Variable	Categories	Crude OR [95% CI]	p-value[a]	Adjusted OR [95% CI]	p-value[a]
Hospital category	Public	Reference		Reference	
	Private	4.695 [2.272, 9.703]	<0.001*	10.166 [3.195, 32.345]	<0.001*
Age	Continuous	0.955 [0.940, 0.971]	<0.001*	0.987 [0.955, 1.021]	0.46
Age>60 years	No	Reference		Reference	
	Yes	0.281 [0.172, 0.459]	<0.001*	0.955 [0.345, 2.644]	0.93
Sex	Male	Reference		Reference	
	Female	1.311 [0.813, 2.114]	0.27	1.688 [0.913, 3.123]	0.01*
Disease severity at admission	Continuous	0.145 [0.086, 0.246]	<0.001*	0.214 [0.113, 0.405]	<0.001*
Presence of a comorbidity	No	Reference		Reference	
	Yes	0.211 [0.123, 0.363]	<0.001*	0.281 [0.145, 0.545]	<0.001*
Regimen group	Continuous	0.172 [0.088, 0.334]	<0.001*	0.297 [0.124, 0.713]	0.007*
Tocilizumab	No	Reference		Reference	
	Yes	0.094 [0.025, 0.354]	<0.001*	0.169 [0.032, 0.899]	0.04*
Baricitinib	No	Reference		Reference	
	Yes	0.292 [0.100, 0.854]	0.03*	0.979 [0.218, 4.393]	0.98
Remdesivir	No	Reference		Reference	
	Yes	0.495 [0.274, 0.894]	0.02*	0.518 [0.195, 1.375]	0.19
Supplementary drugs	No	Reference		Reference	
	Yes	0.754 [0.248, 2.299]	0.62	3.979 [0.591, 26.796]	0.16
Other supportive treatment	No	Reference		Reference	
	Yes	0.962 [0.608, 1.523]	0.87	1.655 [0.908, 3.017]	0.10
Adherence to national guidelines	No	Reference		Reference	
	Yes	2.273 [1.345, 3.839]	0.002*	1.011 [0.504, 2.029]	0.98

Note:
[a]Wald Chi-square test; *Statistically significant at 95% confidence interval; OR, odds ratio; CI, confidence interval

Among the top ten comorbidities, having cancer was associated with the worst outcome, that is, a significantly decreased odds of discharge (B = -1.826, aOR = 0.161, p < 0.001) compared to the other comorbidities. This suggests that individuals with cancer were less likely to be discharged during the management of COVID-19 compared to those with other comorbidities or those without any comorbidities. AKI (Acute Kidney Disease) was also associated with a significantly decreased odds of discharge (aOR = 0.172, p < 0.001), indicating that individuals with AKI were less likely to be discharged. HTN (Hypertension) was associated with a significantly decreased odds of discharge (aOR = 0.433, p = 0.003). Individuals with hypertension were less likely to be discharged. ESRD/CKD (End-Stage Renal Disease/Chronic Kidney Disease) had a negative effect on discharge (aOR = 0.499, p = 0.06) indicating a decrease in discharge likelihood, though not statistically significant. This means that the effect of ESRD/CKD on discharge outcomes is not as clear-cut as the other comorbidities. DM (Diabetes Mellitus) diabetes mellitus did not have a significant effect on discharge odds (Odds Ratio = 0.806, p = 0.46). CCF also did not have a significant effect on discharge odds (Odds Ratio = 0.992, p = 0.99). It does not appear to influence discharge outcomes significantly (Table 9).

Table 9: The influence of the commonly encountered underlying co-morbidities on clinical outcomes (discharge) during the management of COVID-19

Comorbidity	Categories	B	S.E.	Adjusted Odds Ratio [95% CI]	p-value[a]
Cancer	No	Reference			
	Yes	-1.826	0.633	0.161 [0.047, 0.556]	0.004*
AKI	No	Reference			
	Yes	-1.758	0.437	0.172 [0.073, 0.406]	<0.001*
HTN	No	Reference			
	Yes	-0.837	0.279	0.433 [0.251, 0.748]	0.003*
ESRD/CKD	No	Reference			
	Yes	-0.695	0.376	0.499 [0.239, 1.042]	0.06
DM	No	Reference			
	Yes	-0.216	0.294	0.806 [0.453, 1.432]	0.46
CCF	No	Reference			
	Yes	-0.008	0.573	0.992 [0.323, 3.049]	0.99

Note:

[a]Wald Chi-square test; *Statistically significant at 95% confidence interval; CI, confidence interval; B, unadjusted beta coefficient (log odds); S.E, standard error for the unadjusted beta coefficient; AKI, acute kidney disease; HTN, hypertension; ESRD/CKD, end-stage renal disease/chronic kidney disease; DM, diabetes mellitus; CCF, congestive cardiac failure

Among the treatment modalities used for COVID-19 patients, tocilizumab (B = 1.712, aOR = 5.542, p = 0.024) emerged the most significant predictor of discharge compared to the other treatment modalities. This was followed by supplementary drugs (B = 0.801, aOR = 2.228, p = 0.285), other supportive treatment (B = 0.321, aOR = 1.378, p = 0.222), Baricitinib (B = 0.043, aOR = 0.732, p = 1.044), Remdesivir (B = 0.006, aOR = 1.006, p = 0.99), regimen group (B = -1.691, aOR = 0.184, p < 0.001) (Table 10).

Table 10: The influence of treatment modality on clinical outcomes (discharge) during the management of COVID-19

Treatment modality	**Categories**	**B**	**S.E.**	**Adjusted Odds Ratio [95% CI]**	**p-value[a]**
Tocilizumab	No	Reference			
	Yes	1.712	0.759	5.542 [1.253, 4.511]	0.024*
Supplementary drugs[c]	No	Reference			
	Yes	0.801	0.749	2.228 [0.513, 9.672]	0.285
Other supportive treatment[b]	Ordinal	0.321	0.263:	1.378 [0.824, 2.306]	0.222
Baricitinib	No	Reference			
	Yes	0.043	0.732	1.044 [0.249, 4.385]	0.95
Remdesivir	No	Reference			
	Yes	0.006	0.367	1.006 [0.490, 2.063]	0.99
Regimen group	No	Reference			
	Yes	-1.691	0.344	0.184 [0.094, 0.362]	<0.001*

Note:
[a]Wald Chi-square test; *Statistically significant at 95% confidence interval; CI, confidence interval; B, unadjusted beta coefficient (log odds); S.E, standard error for the unadjusted beta coefficient; [b]The use of at least 1 component of the "other supportive therapy" regimens; [c]The use of at least 1 supplementary drug

CHAPTER FIVE: DISCUSSION, CONCLUSION, AND RECOMMENDATIONS

5.1 Discussion

5.1.1 Clinical outcomes of the treatment strategies used in the management of COVID-19 patients in Kenya

This study sought to describe the outcomes of treatment strategies used in the management of COVID-19 patients in Kenya. We have found that, of the 408 patients' records, 76.5% of patients had a favorable outcome (discharged), private hospitals had a higher percentage of discharged patients compared to public hospitals, and younger patients (<=30 years) were the most discharged group compared to their older counterparts.

The observation that 23.5% of patients had died was higher than the findings from other studies in Kenya (Ombajo et al., 2020) and DRC (Nachega et al., 2020) whereby the COVID-related mortality rates were 13.5% and 13.2%, respectively. On the contrary, our study outcome was consistent with that of Belgium (de Meester et al., 2021) and China (Zhou et al., 2020) which had closer mortality rates compared our findings. These disparities may be due to the study time frame, and sample size. The observation that there was a higher likelihood of being discharged among the younger individuals than their older counterparts is in accordance with the findings of studies from Ethiopia (Kaso et al., 2022), and Kenya (Ombajo et al., 2020). This may be explained by the fact that older persons tend to have a deteriorating immune system, and have various underlying comorbidities and chronic diseases(Esakandari et al., 2020)

The observation that there were better treatment outcomes among the patients in private hospitals compared to those in public hospitals (aOR = 10.166, $p < 0.001$) is consistent with another study done in Brazil that reported similar findings among COVID-19 patients (Marcolino et al., 2021). The mortality rate in this present study was 8.1% in private hospitals versus 29.3% in public hospitals. This compares well with the findings of Marcolino and colleages where the mortality rate was 10.8% in private hospitals compared to 24.7% in public hospitals (Marcolino et al., 2021).

This study showed that patients under regimens 1 and 2 had a favorable outcome as compared to those under regimens 3 and 4. A multivariable binary logistic regression showed that the more a molecule was added to the treatment, the poorer outcomes were. This could be due to the fact that

the regimen groups were aligned to the level of disease severity whereby the more severe the disease the higher the regimen group the patient was assigned to. The use of corticosteroids such as dexamethasone or prednisolone in regimen 3, as directed by the Kenyan national guidelines (12), was observed in our study to lead to better outcomes whereby 78.4% of those under regimen 3 had a favorable outcome. This is similar to the findings of a study in Germany which found that 69.4% of patients were discharged after treatment with dexamethasone (Marx et al., 2023). The overall death of patients under dexamethasone was 21.6% similar to the finding from a study in the United Kingdom 22.9% (Horby et al., 2021). Corticosteroids (dexamethasone) were largely prescribed to 82.9% (regimen 3 and regimen 4) of patients. This is because the majority of our enrolled patients had severe disease at admission. This is very much in accordance with the WHO guidelines that strongly recommends not to use corticosteroids in non-severe COVID-19-positive patients (World Health Organization, 2020).

A small number of patients 59 (14%) in our study received Remdesivir, and clinical improvement was found in 64.4% of them. Similar observations were seen in a small cohort analysis on the use of Remdesivir whereby the results showed clinical improvement in 68% of the patients treated with Remdesivir (Grein et al., 2020). A randomized controlled trial conducted on 1063 patients, showed that patients assigned remdesivir treatment had an average hospitalization time of 11 days, compared to 15 days on placebos, with a mortality estimate of 7.1% compared to 11.9%, in Remdesivir-treated patients and placebos, respectively. The conclusion based on the results of that study, suggests starting remdesivir treatment early before lung disease progresses to the level requiring mechanical ventilation (Beigel et al., 2020).

Our finding showed that Tocilizumab was administered to a small number of patients (12, 2.9%) and 75% of them had a poor outcome. A retrospective observational cohort study comparing the efficacy of Tocilizumab in addition to usual care versus standard treatment in COVID-19 severe patients, concluded that administration of Tocilizumab may be able to reduce the risk of invasive mechanical ventilation or death in patients with severe COVID-19 pneumonia (Guaraldi et al., 2020). However, a multi-center, open-label study that evaluated the effectiveness of the early administration of Tocilizumab in patients with COVID-19 concluded that the early administration of tocilizumab in patients with COVID-19 pneumonia does not provide any relevant clinical benefit for patients (Stasi et al., 2020). Baricitinib was suggested as a probable treatment for COVID-19 infection (Richardson et al., 2020). Our results showed that 14 (3.4%) of the patient

received Baricitinib, and favorable outcome was found in 50% of them. A longitudinal multi-center retrospective study that assessed the effectiveness and safety of baricitinib plus antivirals compared to the standard of care found that the 2-week case fatality rate was significantly lower in patients treated with Baricitinib compared with the controls (Cantini et al., 2020). In light of these facts, our findings show that Remdesivir, Tocilizumab, and Baricitinib were not associated with improvement in outcome discharge. The potential explanation for these observations is that only a few patients were administered with these drugs. This is probably because due to the lack of availability of the drugs and lack of affordability, only a few patients, particularly in private hospital, could get access to these drugs.

5.1.2 Adherence to treatment guidelines with reference to drug contraindications among COVID-19 patients in Kenya

Regarding compliance of doctors to the COVID-19 national guidelines, few studies have attempted to address the question. A multicenter hospital-based cross-sectional survey in Ethiopia found poor compliance with COVID-19 preventive measures by healthcare workers (Etafa et al., 2021), while findings from another study in Saudi Arabia established that Health Care Workers have an acceptable level of adherence to COVID-19 preventive measures during the pandemic (Albeladi et al., 2021). This gives an impression of varied levels of compliance to preventive measures against COVID-19 in particular, and by extension, its treatment and management. One particular study in India that considered adherence to treatment guidelines, found that Indian doctors were largely (76.15%) following the scientific guidance provided by Indian National Task Force for COVID-19 (Gangopadhyay et al., 2020). This finding is similar to our study which found that in 326 (79.9%) patient files, the health care professions adhered to the Kenyan national guidelines recommended by the Ministry of Health to combat COVID-19.

5.1.3 The influence of underlying co-morbidities on the clinical outcomes of the various treatment strategies used in the management of COVID-19 in Kenya.

The presence of comorbidity was associated with an increased risk of poor outcome (aOR = 0.281; 95% CI [0.145, 0.545]). This finding is similar to those of another study done in Kenya (Ombajo et al., 2020), HR = 2.34 (95% CI: 1.69, 3.25), and a study from China with HR = 1.79 (95% CI: 1.16, 2.77) among patients with at least one comorbidity and HR = 2.59 (95% CI:1.61, 4.17) among patients with two or more comorbidities (Wei-jie et al., 2020). In all these studies,

comorbidities led to poor outcomes. Our results were also consistent with data from an observational study from various countries in Europe which showed an association between at least one comorbidity with death (Jakhmola et al., 2020) We found in our study that patients admitted with severe and critical conditions were highly predisposed to the outcome of death compared to patients with moderate and mild conditions at admission. These results are consistent with those reported in Ethiopia (Kaso et al., 2022) and DRC (Nachega et al., 2020). The reason for that may be because people with these severe conditions were older patients with higher probability of underlying comorbidities, which our study has shown to be a strong predictor of in-hospital mortality.

5.1.4 Limitations of the study

A few limitations, however, encumbered this study. For instance, being that this was a retrospective observational study, many files had incompleteness in the data of interest. This limitation was addressed by considering as many patient files as possible so that the sample size is not adversely affected. The study design being a cross-sectional study as opposed to a randomized control trial, made it impossible to elucidate the cause-and -effect relationship between dependent and independent variables. The study was conducted in two counties and 3 hospitals with only one private hospital which limits the generalizability of our findings to other settings.

5.2 Conclusion

In accordance with the specific objectives of this study, it can be concluded that around three-quarters of COVID-19 patients had a favorable treatment outcome (discharged). Patients treated in private hospitals were more likely to be discharged compared to patients in public hospitals. Patients treated with mild and moderate disease severity had better treatment compared to those with severe and critical disease. As disease severity increases from mild to critical, the likelihood of discharge decreases, and the likelihood of death increases. The overall treatment strategies used in Kenya were not a strong predictor of a favorable outcome (discharge). The presence of a comorbidity was shown to reduce the chances of getting discharged whereby patients with cancer, acute kidney injury (AKI), and hypertension (HTN) were the most likely to have the poorest outcome. For the majority of the patient files, it was observed that the directives of national guidelines were adhered to. This leads to the conclusion that there was a well-above-average level

of adherence to the national guidelines regarding the treatment of COVID-19 in Kenya among the patients treated for COVID-19 between the 13th of March 2020 and 31st of December 2021.

5.3 Recommendations

The following recommendations can be made based on the present study findings:

5.3.1 Recommendations for policy and practice

1. The treatment strategies used so far have not been shown to significantly influence discharge. Therefore, there is a need to make improvements by incorporating new molecules into the guidelines and also making drugs available, accessible, affordable.
2. There should be a routine training for health care professionals on any updates of the guidelines every time there is new input.
3. Health workers should endeavor to adhere to the national guidelines for COVID-19 management.

5.3.2 Recommendations for future studies

1. More research is needed to evaluate the efficacy of the drugs used in the management of COVID-19 in Kenya
2. Future studies should consider larger sample sizes and incorporate several health centers in order to improve the generalizability of study findings.

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7.0 APPENDICES

Appendix 1: National Guideline Covid-19 case definition

A suspected case of SARS-CoV-2 infection

1. A person who meets the clinical AND epidemiological criteria:
Clinical criteria:
- Acute onset cough AND fever; OR
- Acute onset of ANY TWO OR MORE of the following signs or symptoms: Cough, fever, loss of taste or smell, difficulty breathing, sore throat, running nose, chest pain, fatigue/general weakness, headache, diarrhea, altered mental status (Children may present with atypical symptoms)
AND
Epidemiologic criteria:
- Residing, working or traveling (within the last 14 days) to an area with a high risk of transmission of the virus (In Kenya, this will be as reported by the Ministry of Health
- Where there is widespread community transmission in several regions of the country, then all patients will be considered to have met epidemiologic criteria
- Working in a healthcare facility
- International travel in the last 14 days

2. A patient with severe acute respiratory illness (SARI)
(SARI: Acute respiratory infection with or without fever; and cough; with onset within the last 10 days; and requires hospitalization)

A probable case of SARS-CoV-2 infection

- A patient who meets clinical criteria above AND is a contact of a probable or confirmed case, or linked to a COVID-19 cluster
- A suspected case with chest imaging showing findings suggestive of COVID-19 disease
- Recent onset loss of taste or loss of smell with no other identified cause (Common imaging findings include bilateral peripheral opacities with lower lung distribution. Opacities usually ground-glass opacities that may progress to consolidations)
- Unexplained death in an adult with SARI prior to death AND had contact with a probable or confirmed case or linked to a COVID-19 cluster

Confirmed case of SARS-CoV-2 infection
- A person with a positive SARS-CoV-2 PCR test
- A person with a positive SARS-CoV-2 Antigen RDT AND meeting criteria for either suspected or probable case; OR has contact with a probable or confirmed case.

Multisystem Inflammatory Syndrome in Children (MIS-C)

- Preliminary case definition: Children and adolescents 0–19 years of age with fever > 3 days AND
- Two of the following: rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands, or feet); hypotension or shock; features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities; evidence of Coagulopathy, acute gastrointestinal problems; AND
- No other obvious microbial cause of inflammation AND
- Evidence of COVID-19 (RT-PCR, antigen test, or serology positive), or likely contact with patients with COVID-19

Appendix 2: National Guideline Covid-19 severity classification

A. Adult and Adolescent	
Category	Features
1. Mild illness	Fever, cough, sore throat, malaise, headache, muscle pain, BUT **No dyspnoea (shortness of breath**) and **No abnormalities on chest imaging**
2. Moderate illness	Clinical features of pneumonia (fever, cough, **dyspnoea**) AND/OR **radiological features of pneumonia,** BUT **Oxygen saturations (SPO2) greater than or equal to 94% on room air**
3. Severe illness	Clinical and radiological features of pneumonia, tachypnea with RR>30 AND **oxygen saturation (SPO2) less than 94% on room air**
4. Critical illness	Features of severe illness AND Any of the following: • respiratory failure • sepsis/septic shock • multiorgan dysfunction • acute thrombosis
B. Children	
1. Mild illness	Fever, cough, sore throat, malaise, headache, muscle pain **BUT** No dyspnoea (shortness of breath and No abnormalities on chest imaging
2. Moderate illness	Clinical signs of non-severe pneumonia (cough or difficulty breathing) **AND** Fast breathing* **AND/OR** chest indrawing *Fast breathing (in breaths/min): <2months: 360; 2-11months: 350; 1-5years: 340
3. Severe illness	Child with clinical signs of pneumonia (cough or difficulty in breathing) + at least one of the following: • Central cyanosis or SPO2 <90%; • Severe respiratory distress (e.g., fast breathing*, grunting, very severe chest indrawing); • General danger sign: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions *Fast breathing (breaths/min): <2months: ³60; 2-11months: ³50; 1-5years: ³40

4. Critical illness	Features of severe illness AND Any of the following: • Acute respiratory distress syndrome • Respiratory failure requiring mechanical ventilation • Sepsis/Septic shock • Other organ failure requiring ICU care
5. MIS-C	Preliminary case definition: Children and adolescents 0–19 years of age with fever > 3 days **AND** Two/more of the following: • Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands or feet); • Hypotension or shock; • Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities; • Evidence of coagulopathy, • Acute gastrointestinal problems; **AND** No other obvious microbial cause of inflammation **AND** Evidence of COVID-19 (RT-PCR, antigen test, or serology positive), or likely contact with patients with COVID-19

Appendix 3: National Guideline management of Covid-19 based on disease severity

Asymptomatic or mild illness	**Assess for eligibility for home-based care** Patient qualifies if they have no risk factors for disease progression or poor outcomes (see below) and a suitable space is available at home (separate room with separate bathroom), has resources to access basic PPE for family members e.g., face masks and gloves, no house members who are increased risk of severe illness if exposed e.g., see below **Risk factors for poor outcome:** Age >60, coronary artery disease, stroke, diabetes, hypertension, cancer, chronic lung disease, frailty, pregnancy, immunosuppression, chronic kidney disease **Management** Symptomatic treatment for mild disease (paracetamol, antihistamines). **Steroids should NOT be used for patients with asymptomatic, mild or moderate disease.** (Isolation precautions as outlined in the IPC section)
Moderate Illness	• Baseline tests - blood count, renal and liver function, HIV test, random blood sugar. • symptomatic treatment: -Fever - Paracetamol -Sore throat - gargles -cough, nasal congestion - antihistamine • VTE prophylaxis with Enoxaparin 40mg once a day if admitted to a health facility -Where enoxaparin is not available, use low dose unfractionated heparin at 5000units subcutaneous BD) -Where patient unable to use standard anticoagulation therapy, consider use of direct-acting anticoagulants -Consider prophylaxis for children older than 5 years with comorbidities and not ambulant. Refer to BNF for dosage guidelines for pediatrics Where there is pressure for space for isolation of patients, the following patients with moderate illness can be managed at home: • Young <60 years • Oxygen saturations >94% on room air • No comorbidities • Have easy access to a health facility in case of worsening of symptoms • Physically active
Severe illness	• Baseline Tests (Total blood count, renal and liver function, HIV test, random blood sugar) • Symptomatic treatment • Oxygen supplementation to maintain SPO2s above 90% and above 92% in pregnant women (oxygen supplementation can be via nasal prongs, masks, non-rebreather masks or high flow nasal cannula - see below) • Dexamethasone 6mg per day for up to 10 days (where dexamethasone is not available, consider using prednisone 40 mg OD or methyl prednisone 32mg OD. This short duration of dosing does not require tapering); For children - Dexamethasone 0.15mg/kg iv/PO OD to a maximum of 6mg or prednisolone 1mg/kg OD maximum 40mg OD, methylprednisolone 0.8 mg/kg IV OD maximum 32mg OD • VTE prophylaxis Enoxaparin 40mg OD once a day for the duration of hospitalization (Where enoxaparin is not available, use low dose unfractionated heparin at 5000units subcutaneous BD) • Self proning for 12 to 16 hours a day (see self-proning guide below) as tolerated
Critical Illness	• Baseline tests- total blood count, renal and liver function tests, HIV test, random bold sugar • Symptomatic treatment

	• Admit to a **Critical Care Unit.** • Mechanical Ventilation if no improvement in oxygenation with maximal oxygen flows with other modalities - see guide to noninvasive ventilation, tracheal intubation and ventilation below • Prone for 12 to 16 hours per day • Conservative fluid management i.e., give IV fluid only if hypovolemic • Closed suctioning of secretions where available • Give Dexamethasone 6 mg per day for up to 10 days (where dexamethasone is not available, consider using prednisone 40 mg OD or methylprednisolone 32mg OD. This short duration of dosing does not require tapering); For children - Dexamethasone 0.15mg/kg iv/ PO OD to a maximum of 6mg or prednisolone 1mg/kg OD maximum 40mg OD, methylprednisolone 0.8 mg/kg IV OD maximum 32mg OD • VTE prophylaxis 40mg Enoxaparin OD SC (Where enoxaparin is not available, use low dose unfractionated heparin at 5000units subcutaneous BD) **Where possible, document advance directives for all patients e.g., do not resuscitate for patients who are unlikely to do well or have another terminal condition**

Appendix 4: Covid-19 Vaccines

Innovator company	Technology	Dosage	Number Of shots	interval	Storage	Efficacy	Common Adverse reaction	Adverses reactions
Pfizer/ BioNTech	RNA vaccine	0.3 mL (30 µg nucleosid-modified mRNA) IM	2	21 days	-70 ˚C	95%	Pain, swelling, redness, fever, fatigue, headache, chills, vomiting, diarrhea, muscle pain, joint pain, lymphadenopathy, shoulder injury, right axillary lymphadenopathy, and right leg paresthesia.	including anaphylaxis, paroxysmal ventricular arrhythmia, and syncope. Multisystem inflammatory syndrome (MIS).
Moderna	RNA vaccine	0.5 mL (100 µg mRNA) IM	2	28 days	- 20 ˚C	94.5%	Pain, swelling redness at the site of injection, fever, fatigue, headache, chills, vomiting, arthralgia, myalgia, urticaria. (These clinical symptoms were mild to moderate after the first dose of vaccine and	Allergic reactions including anaphylaxis, facial swelling, and Bell's palsy

							moderate to severe after the second dose of vaccine).	
Astrazeneca	Adenovirus-vectored vaccines	0.5 mL (5 × 1010 viral particles) IM	2	4-12 weeks	2–8 ˚C	70%	Headache, nausea, vomiting, diarrhea, myalgia, arthralgia,, injection site tenderness, pain, warmness, pruritus, bruising, swelling, and erythema, fatigue, malaise, chills, and fever	Thrombosis with thrombocytopenia syndrome (TTS), Guillain-Barr´e syndrome, capillary leak syndrome (CLS), cerebral venous sinus thrombosis (CVST) without thrombocytopenia.
Johnson & Johnson	Adenovirus-vectored vaccines	0.5 mL (5 × 1010 viral particles) IM	1		2–8 ˚C	66.3%	fever	Venous thromboembolism
Gamaleya Research Institute	Adenovirus-vectored vaccines	0.5 mL (1 × 1011 viral particles rAd26-S, followed by 1 × 1011 viral	2	21 days	-18 ˚C	92%	Flu-like illness, injection site pain, headache, and asthenia.	Renal colic, deep vein thrombosis, and extremity abscess was observed in patients older than 60 years old. But no association was found between

		particles rAd5-S) IM						serious adverse events and COVID- 19 vaccine administration.
CanSino	Adenovirus-vectored vaccines	0.5 mL (5 × 1010 viral particles) IM	1		-20 ˚C	65.7%	Injection site pain, soreness, fatigue, and mild fever.	No serious adverse events reported
Novavax	Protein-subunit vaccine	0.5 mL (5 µg SARS-CoV-2 rS/50 µg Matrix-M1 adjuvant) IM	2	21 days	-20 ˚C	89.3%	Headache, fatigue and malaise.	No serious adverse events reported.
Sinopharm (Beijing)	Inactivated vaccine	0.5 mL (4 µg in aluminum adjuvant) IM	2	21-28 days	2–8 ˚C	79%	Pain and fever	No serious adverse events reported.
Sinovac Biotech	Inactivated vaccine	0.5 mL (3 µg in aluminum adjuvant) IM	2	28 days	2–8 ˚C	81%	Injection site pain, fever, fatigue, nausea, and vomiting.	No serious adverse events reported.

Appendix 5: Data collection sheet

Code No: _____

Part 1: Hospital Information

1. Hospital name:
    a) Kenyatta National Hospital
    b) Mater Hospital
    c) Coast General Hospital
2. Hospital category:
    a) Private
    b) Public

Part 2: Patient Clinico-Sociodemographics

3. Patient hospital ID: ……..
4. Date of admission: ……..
5. Age: …….. (years)
6. Sex
    a) Male
    b) Female
7. Had the patient been vaccinated against covid-19?
    a) Yes
    b) No
    c) Unknown
8. Clinical symptoms at admissions into hospital:
    ……
    ……
    ……
    ……
9. Diagnosis: …….
10. Disease severity at admission:
    a) Mild
    b) Moderate
    c) Severe
    d) Critical
11. Co-morbidities

……
……
……
……

12. Complications, if any

……
……
……
……

13. What was the hospital duration stay?

14. What was the outcome (ticks as appropriate)?

    a) Discharge

    b) Death

15. If discharge, then specify if with full recovery or disability?

    a) Full recovery

    b) With disability

Part 3: Adherence to covid-19 management guidelines

16. Laboratory findings

a) Full Blood count: Yes [ ] No [ ]

b) Hepatic Function: Yes [ ] No [ ]

c) Renal Function: Yes [ ] No [ ]

d) HIV test: Yes [ ] No [ ]

e) Random blood sugar test: Yes [ ] No [ ]

f) Inflammatory Markers: Yes [ ] No [ ]

g) Coagulopathy: Prothrombin: Yes [ ] No [ ]

h) Cardiac function: Yes [ ] No [ ]

17. If imaging findings are suggestive of pneumonia:

a) X-ray: Yes [ ] No [ ]

b) CT-scan: Yes [ ] No [ ]

c) Ultrasound: Yes [ ] No [ ]

d) MRI: Yes [ ] No [ ]

18. Patient management

A. Pharmacological Treatment

a) Paracetamol: Yes [ ] No [ ]; If yes, dosage: …… Duration: ……

b) Antihistamine: Yes [ ] No [ ]; If yes, dosage: …… Duration: ……

c) HCQ/CQ: Yes [ ] No [ ]; If yes, dosage: …… Duration: ……

d) Azithromycin: Yes [ ] No [ ]; If yes, dosage: …… Duration: ……

e) Enoxaparin: Yes [ ] No [ ]; If yes, dosage: …… Duration: ……

f) Dexamethasone: Yes [ ] No [ ]; If yes, dosage: …… Duration: ……

g) Tocilizumab: Yes [ ] No [ ]; If yes, dosage: …… Duration: ……

h) Baricitinib: Yes [ ] No [ ]; If yes, dosage: …… Duration: ……

i) Lpr/Rtr: Yes [ ] No [ ]; If yes, dosage: …… Duration: ……

j) Remdesivir: Yes [ ] No [ ]; If yes, dosage: …… Duration: ……

B. Supportive Treatment

a) Oxygen: Yes [ ] No [ ]; If yes, duration: …….

b) Ventilation: Yes [ ] No [ ]; If yes, duration: …….

c) If other: specify ……..…….

C. Non-conventional treatment

List of non-conventional treatments (if used/recorded): ……..

19. Adherence pattern: Based on the management of the patient, is there proper adherence to the national guidelines for the management of Covid-19 based on disease severity?

    Yes [ ] No [ ]

Appendix 6: KNH-UoN ERC Approval

UNIVERSITY OF NAIROBI
FACULTY OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
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KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
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Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/299

29th July, 2022

Glory Kalobe Mulenda
Reg. No W64/33117/2019
Institute of Tropical & Infectious Diseases (UNITID)
Faculty of Health Sciences
University of Nairobi

KENYATTA NATIONAL HOSPITAL APPROVED 29 JUL 2022 KNH/UoN-ERC P.O. Box 20723 - 00202, NAIROBI

Dear Glory,

RESEARCH PROPOSAL: CLINICAL OUTCOMES OF TREATMENT STRATEGIES USED IN THE MANAGEMENT OF COVID-19 PATIENTS IN KENYA; POTENTIALLY EFFECTIVE THERAPY OPTIONS (P279/04/2022)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P279/04/2022.** The approval period is 29th July 2022 – 28th July 2023.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Appendix 7: Ethical Approval from Coast General Hospital

COUNTY GOVERNMENT OF MOMBASA
DEPARTMENT OF HEALTH SERVICES
COAST GENERAL TEACHING & REFERRAL HOSPITAL

Phone : 2314202/5, 2222148,2225845
Mobile No : 0722207868
Fax : 2220161, Mombasa
Email : ceocgtrh@yahoo.com
When replying please quote :

P O Box 90231 – 80100
Mzizima Street
MOMBASA

Ref. ERC-CGH/MSc/VOL.I

Date: 29th March, 2023

Dr. Glory Kalobo Mulenda

RE: CLINICAL OUTCOMES OF TREATMENT STRATEGIES USED IN THE MANAGEMENT OF COVID-19 PATIENTS IN KENYA; POTENTIALLY EFFECTIVE THERAPY OPTIONS.

This is to inform you that the Ethics Review Committee reviewed the proposal you submitted for review in a meeting held on 15th March, 2023.

The study is granted approval for implementation effective from the date of this letter. Please note that authorization to conduct this study will automatically expire on the 15th March, 2024. If you plan to continue with data collection and analysis beyond this date, please submit an application for continuing approval to the ethical Review Committee-Coast General Hospital in appropriate time.

Any unanticipated changes/problem resulting from the implementation of this protocol should be brought to the attention of the ERC-CGH. You are also required to submit any changes to this protocol to the ERC- CGH.

The ERC-CGH looks forward to receiving a summary of the research findings upon completion of the study to be part of the data base to be consulted when processing related researches to minimize duplication.

DR. WANJIRU-KORIR M.N.
SECRETARY ERC-CGH

COAST GENERAL TEACHING & REFERRAL HOSPITAL
29 MAR 2023
P. O. Box 90231
MOMBASA

Appendix 8: Research Committee Approval from Mater Hospital

Mater Misericordiae Hospital
Under the Sisters of Mercy

P. O. Box 30325 - 00100
Dunga Road, Nairobi, Kenya
Telephone: (254) (020) 6903000
Mobile Lines: 0719 - 073000, 0732 - 163000
Fax: (254) (020) 6534289
Email:inform@materkenya.com
Website: www.materkenya.com

26th October 2022

Dr. Glory Mulenda Kalobo
Glorykalobo24@gmail.com
0715956523

Dear Dr. Glory

RE: CLINICAL OUTCOMES OF TREATMENT STRATEGIES USED IN THE MANAGEMENT OF COVID-19 PATIENTS IN KENYA; POTENTIALLY EFFECTIVE THERAPY OPTIONS (P27/04/2022)

The Mater Misericordiae Hospital is in receipt of your proposal submitted to the Research Office. The Research Committee Has Reviewed And Approved Your Project On **Clinical Outcomes Of Treatment Strategies Used In The Management Of Covid-19 Patients In Kenya; Potentially Effective Therapy Options (P27/04/2022).** You are authorised to conduct this study from 31st October 2022. This approval is valid until 31st October 2023 and is subject to compliance with the following requirements:

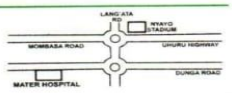
1. The conduct of the study shall be governed at all times by all applicable rules and regulations communicated to you by the Mater Misericordiae Hospital Research Committee and you should notify the committee of any changes that may affect your research project (amendments, deviations and violations).
2. You must provide an interim progress report form, 60 days before expiration of the validity of this approval and request extension if additional time is required for study completion. You must advise the Research Committee when this study is complete and a final report submitted to the Research Office for record purposes. You must also advice the research committee in the event you discontinue the research.
3. Please see the attached comments following the ethical review.
4. You are required to pay the Nominal Research Fee of Kes. 10,000.00. as per Proforma Invoice No. MMH02/10 already sent to you.

If you have any questions, please contact the Research Office on 0732163211 or 0732163373.

We wish you all the best in your study.

Yours sincerely

Dr. Andrew Ndonga
MMH Research Committee Chair



Appendix 9: NACOSTI Approval

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Ref No: **251138**

Date of Issue: **17/October/2022**

RESEARCH LICENSE

This is to Certify that Dr.. glory Mulenda kalobo of University of Nairobi, has been licensed to conduct research as per the provision of the Science, Technology and Innovation Act, 2013 (Rev.2014) in Mombasa, Nairobi on the topic: clinical outcomes of treatment strategies used in the management of Covid-19 patients in Kenya: potentially effective therapy options for the period ending : 17/October/2023.

License No: **NACOSTI/P/22/20482**

251138

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Verification QR Code

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See overleaf for conditions

Appendix 10: Turnitin Originality Report

Turnitin Originality Report

Clinical outcomes of treatment strategies used in the management of COVID-19 patients in Kenya: Potentially effective therapy options by Glory Kalobo from the University of Nairobi

From d3 (09oi)

- Processed on 08-Dec-2023 8:41 AM EST
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