EVALUATING MANAGEMENT AND CLINICAL OUTCOMES OF PATIENTS ADMITTED WITH COVID-19 ASSOCIATED ACUTE RESPIRATORY DISTRESS SYNDROME AT THE AGA KHAN UNIVERSITY HOSPITAL

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List of abbreviations

APACHE-	Acute physiology and chronic health evaluation 11 score
ARDS-	acute respiratory distress syndrome

CARDS-	Covid -19 associated ARDS
Covid-19 -	Coronavirus disease of 2019
CPR-	Cardiopulmonary resuscitation
ECMO;	Extracorporeal membrane oxygenation
$FIO_{2;}$	Fraction of inspired oxygen
HDU	High dependency Unit
HFNO	High flow nasal oxygen
ICU	Intensive care unit
IHCA	In-hospital cardiac arrest
JCIA	Joint commission international accreditation
MOD	Multi-organ dysfunction
NIPPV	Noninvasive positive pressure ventilation
Pao_2	Arterial partial pressure of oxygen
RT-PCR-	Real time reverse transaction polymerase chain reaction
RCT`S	Randomized controlled trials
SARS-COV-2-	severe acute respiratory syndrome corona 2 virus
SOFA	Sequential organ function Assessment

Operational definitions

ARDS- This referred to a respiratory condition that had an onset within 1 week, presenting with the presence of hypoxia, bilateral opacifications not fully explained by effusions, lobar or lung collapse not related to heart failure of fluid overload with

oxygenation PAO2/FIO2 ratio of less than 200, with PEEP requirement greater than 5cmH_2O.

Critically ill Patient: This referred to any patient with respiratory distress, cardiovascular derangement needing support in the critical care unit.

CARDS: was defined as a positive Covid test and features of ARDS

High Flow Nasal Cannula oxygenation was defined as a noninvasive technique that delivered warmed humidified oxygen with a fraction of inspired oxygen (FIO2) of 1.0 and a maximum flow rate of 60l/min

Covid test- This referred to the use Polymerase chain reaction (PCR) to detect the presence of the Corona virus in either a nasal or pharyngeal swab, which was considered as the gold standard of Covid testing.

Outcome: This was defined as survival or death from CARDS

Sars-Cov-2-severe acute respiratory syndrome coronavirus 2-a Novel coronavirus, an enveloped positive single stranded RNA which binds to the host cell receptors Angiotensin converting enzyme

Treatment modalities: Referred to the various methods used by a health professional to treat patients including pharmacological and non-pharmacological interventions

ABSTRACT

Study Background: The Covid 19- pandemic has seen a surge of patients with ARDS across many intensive care units globally. While most people with Covid 19 infections develop only mild or uncomplicated disease, the World Health Organization (WHO) reports that 14 % develop severe disease requiring hospitalization and are in need of oxygen support, and 5% develop ARDS and do need admission into ICU for respiratory support.

Broad objective: To evaluate the management and clinical outcomes of patients admitted with Covid 19 Associated Acute Respiratory Distress Syndrome at the Aga Khan University Hospital Intensive Care Unit

Expected benefits of the study/utility of the study: The study was meant to provide information regarding different outcomes in relation to the management methods used in treating patients with varying severity of Covid-19 ARDS.

Methodology: The study was a retrospective descriptive cohort study that was done at the Aga Khan University Hospital Nairobi at the intensive care unit. Census was done on all the 201 patient files admitted with severe Covid -19 pneumonia who developed ARDS, from March 2020 to December 2020. A Data extraction tool was used to extract data from medical records. Data collected included initial assessment, demographics, severity score on admission, diagnostic test results, mode of mechanical ventilation, length of ICU stay and discharge status. Descriptive analysis was done through the use of percentages and standard deviation while inferential analysis included the tests of association between mortality rates and mode of mechanical ventilation.

The study findings: The demographic factors; age and gender had a significant association with disease outcomes among the CARDS Patients. Male patients tended to have worse outcomes and so did older patients. The Sequential Organ Failure Assessment (SOFA) score on admission had quite a significant association with patient outcomes: ($r=368$, $P< .05$) Acute Physiology and Chronic Health Disease Classification System II (APACHE) score on the other hand did not have a significant association with disease outcome: ($r=.014$, $P>.873$)

The study findings indicated both non-invasive and invasive treatment modalities significantly influenced outcomes among COVID 19 associated ARDS. Additionally the findings established a high probability of survival of patients on non-invasive ventilation, 56.7%, compared to invasive mechanical ventilation with a 43.3% survival rate. Also, results indicate Pearson Chi-Square ($X2$, 33.419; $P<.000$); which showed that there was a significance difference in the outcome.

Study Recommendations: While invasive and non-invasive methods remain the effective methods in the treatment of CARDS, there is need for to consider the best method of treatment that can reduce the percentage of possible deaths given that the highest death outcomes were with the Invasive mechanical ventilation. There is currently no specific tool for evaluating COVID 19 infections, and the medical team continues to use the existing tools of SOFA score and APACHE score as heighted by Attaway et al. (2021), therefore there is need for more research on better tools for better prediction of the patients with COVID-19 associated acute respiratory distress syndrome.

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CHAPTER 1: INTRODUCTION

1.1 Introduction

In this chapter, the background of the study, problem statement, and significance of the study, research questions/objectives, and hypotheses are presented. The COVID-19 pandemic has seen a surge of patients with Acute Respiratory Distress Syndrome (ARDS) across many intensive care units globally. While most people with Covid-19 infections develop only mild or uncomplicated disease, the World Health Organization (WHO) reports that 14 % develop severe disease requiring hospitalization and oxygen support, while 5% develop ARDS necessitating admission into ICU for respiratory support. COVD- 19 ARDS occurs as a result of an acute inflammatory response, caused by insults to the lungs either directly or indirectly (Zhou et al., 2021).The number of deaths resulting from COVID-19 infection inducing this severe form of respiratory failure is significantly high. (Badraoui et al., 2020).Advanced age, comorbid diseases, higher sequential organ failure assessment score and D-Dimmers greater than one, are associated risk factors for developing severe disease and higher mortality. In children with COVID-19 infections the symptoms are usually less severe than in adult populations, and mainly present with cough and fever. (WHO, 2020)

In Kenya more than 220,000 cases of COVD-19 infection with at least 4,300 deaths had been reported (WHO-DASHBOARD, 2021). The characteristics and risk factors for severe outcomes are not fully understood and documented.

1.1.1 Background of the study

The COVID-19 virus was first reported in 2019 and declared a pandemic by the World Health Organization in March 2020, (WHO, 2020). This decision was informed by the increasing number of cases in nearly all parts of the world. United States had the highest Covid-19 cases totaling 34.3 million and million deaths by mid-June 2021 It was estimated that by November 22, 2021, the number of confirmed COVID-19 cases in Africa was to 8,664,388 which represented around 3.35 % of global infections, with By December 2021, 322,946 infections and 5,639 coronavirus-related deaths were already reported in Kenya since the pandemic began (WHO, 2021).

Covid-19 associated pneumonia was regarded as a medical emergency with enormous impact on society, global health care systems, families and affected individuals (Pfortmueller, 2020). The pathological process of severe Covid-19 pneumonia is an inflammation reaction characterized by the destruction of the deep airway and alveoli. It is argued that the lung injury is not only associated with the direct virus–induced damage but also by immune responses triggered by Covid -19 virus that led to the activation of immune cells to release a large number of pro and anti-inflammatory cytokines (Wang et al., 2020). Histological examination has shown diffuse alveolar damage and mucinous exudate, which is similar to acute respiratory distress syndrome. Aggravation of symptoms occur during 5–7 days after onset of the disease in patients with Covid-19 pneumonia and severe cases progress rapidly to acute respiratory failure. The outcomes of patients with severe COVID-19 ARDS admitted into ICU remain uncertain but have generally been poor. Grasselli et al, (2020), in a retrospective case series of 1591 patients admitted into Lombardy ICU Network in one of the ICUs of 72 hospitals in Italy reported that, of the 1300 who developed CARDS 1287 needed mechanical ventilation, 137 non-invasive mechanical ventilation. A high number of 405(61.3%) died in ICU while only 256(38.7%) were discharged from ICU.

Similarly, Roedl *et al.* (2021) in a multi-center retrospective observational cohort study of 15 hospitals in Germany, established that in a total of 223 critically ill patients admitted into ICU with CARDS,167(74%) needed mechanical ventilation,31(14%) hand non-invasive ventilation 26(12%) had High-Flow Nasal Cannula (HFNC). ICU mortality was 35% and 44 % among mechanically ventilated patients. In contrast Ombajo *et al.*, (2020) who carried out a retrospective multicenter cohort study in Kenya reported a mortality rate of 107(14 %) in a sample size of 787 patients and 90 (11%) required ICU admission while 52(7%) required mechanical ventilation.

In Kenya there is limited data on clinical outcomes of CARDS, but anecdotal reports indicate high mortality. According to Lee (2020) some patients are asymptomatic while others suffer from acute respiratory distress syndrome (ARDS) It is considered present if the patient has hypoxic respiratory failure with pulmonary infiltrates in the presence of a positive Covid test and no other explanation (Pfortmueller *et al.*, (2020) ARDS causes diffuse alveolar damage in the

lungs with hyaline formation occurring in the acute phase followed by interstitial widening and alveolar edema, and finally fibroblast proliferation in the organization stage. The patient is dyspneic, fatigued, agitated and fine crackles develop as respiratory failure sets in. The partial pressure of oxygen falls despite supplemental oxygen (refractory hypoxemia). (Pfortmueller 2020).

Respiratory acidosis ensues as a result of tissue hypoxia and anaerobic respirations and if not adequately managed, leads to coma and death. According to Gibson, (2020) ARDS develops in 42% of patients presenting with COVID–19 pneumonias and 61-81% will require ICU care. CARDS are a predictable serious complication of Covid -19 pneumonia that requires early recognition and comprehensive management (Gibson *et al*., 2020). The current treatment modalities include high flow oxygen with 20-60litres of oxygen progressing to assisted ventilation in patients who remain hypoxic despite oxygen therapy. Extracorporeal Membrane Oxygenation (ECMO) has also been recommended and has shown better outcomes if initiated early (Dreier *et al.,* 2021).

1.2 Statement of the problem

Acute respiratory distress syndrome associated with COVID-19 disease is part of the continuum of COVID-19 infection. Patients who develop severe disease often require admission to the ICU for intensive monitoring and advanced care. Survival from severe COVID associated Pneumonia is dependent on several factors. Advance age of the patient has been associated with poor outcomes. According to Prado (2020) mortality of 67% was of patients above 80 years of age. Similarly, Alharbi.et.al (2020) also found that children infected with Covid -19 are less likely to develop severe forms of disease.

Non–invasive delivery of oxygen via high flow nasal cannula has been associated with better outcomes. Dobler, (2020) reported that in patients where intubation was avoided and patients put on non-invasive ventilation (NIV) Bipap mode, they had a shorter ICU stay compared to intubated patients. Similar outcomes were associated with the use of Continuous Positive Airway Pressure (CPAP) helmets. NIPPV is supported in patients with Covid -19 acute hypoxic respiratory failure (Dobler, 2020). However, Wilcox (2020) reported that arguments for and against early intubation are not yet resolved due to lack of enough evidence. Those that suggest early intubation noted that the high death rates reported among intubated patients, thought that

ventilator induced lung injury was a contributing factor. Lee (2020) established that survival did not improve with delay in intubation and mechanical ventilation. This could be attributed to the severity of the disease at admission based on severity assessment scores.

Severe COVID -10 associated Pneumonia is still poorly understood and there is hardly any documented evidence in Kenya on the outcomes among patients admitted in ICU. An understanding of the determinants of these outcomes is necessary in informing quality care among these patients. The purpose of this study therefore was to describe the outcomes and management of patients admitted with severe covid-19 pneumonia at Aga Khan University hospital Nairobi between March 2020 and December 2020.

Research Objectives

1. To describe the management and the clinical outcomes of patients admitted with CARDS at the Aga Khan University hospital ICU?
2. To establish the association between severity of disease at admission and outcome.
3. To compare patients outcomes on non-invasive and invasive mechanical ventilatory support

1.3 Research Questions

1. What is the management and the clinical outcomes of patients admitted with CARDS at the Aga Khan University hospital ICU?
2. Is there a correlation between severity score on admission and patient outcome?
3. How do treatment modalities influence patient outcomes?

1.4 Research Hypothesis

Ho_1: There is no relationship between management and clinical outcomes of patients admitted with CARDS at the Aga Khan University hospital ICU.

Ha_1: There is a relationship between management and clinical outcomes of patients admitted with CARDS at the Aga Khan University hospital ICU

Ho_2: There is no correlation between severity score on admission and outcomes in patients admitted with CARDS at the Aga Khan University hospital ICU

Ha_2: There is a correlation between severity score on admission and patient outcome of patients admitted with CARDS at the Aga Khan University hospital ICU

Ho_3: Treatment modality has no influence on the outcome of patients with Covid 19 associated with ARDS.

Ha_3: Treatment modality has an influence on the outcome of patients with Covid 19 associated with ARDS.

1.5 Study justification

There is very minimal data in Kenya on clinical outcomes of Covid 19 associated ARDS hence the study will document the study findings which may inform care of patients admitted with CARDS. Ombajo et al. (2020) documented that the characteristics and risk factors for Covid 19 associated ARDS in Kenyan setting have not been described yet. As an evolving disease this study is going to act as a steppingstone for more research in areas where data is not complete. As a Kenyan research paper, the recommendations that have been offered in this paper provide a uniquely relevant source of data for implementation of guidelines in the Kenyan health care setup.

1.6 The Significance of the study

The study's significance is to understand determinants of these outcomes which were necessary in informing quality of care among the patients with CARDS. This study generated knowledge that helped in identifying those patients at greatest risk of deterioration and guided in decision making in management of patients with severe Covid-19 pneumonias.

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

The purpose of this study is to evaluate the clinical outcomes of patients admitted with CARDS. In this chapter a review of the relevant literature is done. The researcher searched several databases including PubMed, Cochrane, and Google scholar. The key words used in this search were Covid -19, SARS-Cov-2 virus, Covid -19 associated ARDS, clinical outcomes. The study sought to establish the management and clinical outcomes of patients with Covid 19 associated acute respiratory distress syndrome at Aga Khan University Hospital ICU.

This chapter summarizes the findings as per the objectives which include to identify the clinical characteristics of patients admitted with CARDS, to establish the correlation between severity of disease at admission and outcome of the patients and finally, to compare outcomes of noninvasive versus invasive ventilatory support in patients with CARDS admitted in ICU.

2.2 Clinical characteristics of patients admitted with Covid-19 associated ARDS

Covid -19 is a novel disease whose clinical course is still poorly understood. However, from observations, what is clear is that it has affected different categories of people in the population with varying degrees of severity. Jin *et al.* (2020) reported that patients younger than 50 years of age experience less severe form of disease while patients with advanced age with Commodities experience severe form of disease and high Mortality. Another study by. Muñoz-Rodríguez et al. (2021) also reported that some of the clinical characteristics that increased the probability of developing CARDS and death included Male sex, age above 50 years, obesity, cardiac disease, fever, dyspnea, pulmonary infiltrates, lymphopenia, D-Dimers above1000ng/dl and mechanical ventilation both invasive and non-invasive.

Hao *et al.*, (2020) reported that being male, having diabetes mellitus, cloudy chest x-rays findings, derangement of some laboratory results were among the most important risk factors for progression to CARDS and requiring Mechanical ventilation. Severity of disease on admission is a strong predictor of mortality have also been associated with other factors apart from gender,

where more men are affected by the disease than women. Comparably, also the patients with a body mass index of 28 and above have also been observed to suffer from CARDS.

Additionally, mortality has also been observed to be significantly high among that requiring hospital admission. (Huang *et al.,* 2020a) in a study done in Wuhan China, out of 41 patients admitted with Laboratory confirmed Covid 19 infections,73 % were men, all of them had pneumonia and abnormal findings on CT scan of the chest,55% had dyspnoea,32% were admitted into ICU and 29 % developed Covid 19 associated ARDS and 15% died. Those who progressed to CARDS, median age was reported to be 49 years, commodities like diabetes, hypertension and other acute cardiac injury were reported to be present The Centers for disease control and prevention also includes immunosuppression, liver disease as potential risk factors for progression to CARDS in patients with Covid 19 infections (Revzin *et al.,* 2020). These characteristics are discussed below.

2.3 Socio demographic characteristics

2.3.1 Age of the Patients

Internationally it is now recognized that Covid -19 has affected adults more than children with the mortality increasing with age. Prado *et al.* (2020), noted that patients aged above 80 years had a mortality of 16% when compared to those aged less than 50 years (<50%). This data shows variation in the number of patients admitted to the hospital. These findings compare with those of Wang et al. (2020) who reported that Covid -19 related deaths were more common among those aged above 65 years. Alharbi *et al,* (2020), also found that the median age of patients infected with SARS-COV-2 was 75 months, yet they did not develop severe disease.

Zhou et al., (2021) similarly reported among the factors associated with poor outcome of Covid 19 ARDS is age above 65 years. World Health Organization, (2020) also reported older age as one of the risk factors that lead to severe disease and higher mortality. Similarly, (Muñoz-Rodríguez et al., 2021) reported that the risk factors that increased the probability of death in the CARDS was age above 50 years. Oliveira *et al.,* (2021) in a retrospective cohort study in Central Florida observed that out of 1283 of patients with Covid 19 infections131 patients required ICU

admission due to CARDS and the median age of the patients admitted into the ICU was 61 years. The deceased patients were older with a median age of 71.5 years.

According to the world journal of research and Review Basavarajegowda *et al.,* (2020), reported age as one of the strongest risk factors for severe disease and death in Covid -19 infections. He also reported that 80% of the people who died by 5th February 2020 were over 60 years of age. Grasselli *et al.,* (2020) too reported that older patients above 64 years of age mortality were higher than those under 63 years of age.

2.3.2 Gender of the Patients

There has been scanty data on the incidence of CARDS among gender. Initial reports from China revealed the early evidence of increased male mortality associated with Covid -19. Arentz et al., (2020) reported 52% of the patients admitted in the ICU with CARDS to be males

In a case series study done in Seattle from February 2020 to March 2020. Bhatraju et al., (2020) reported that out of 24 critically ill patients 67 % were men. Yang et al., (2020) reported that out of 710 patients, 52 who developed CARDS 67% were men. Similarly, (Huang et al., 2020b) in a retrospective cohort study, in a sample of 41 patients with severe COVID19 pneumonia who developed CARDS 73% (30 patients) were men Grasselli *et al*., (2020) made similar observations, in a sample size of 1591 of patients admitted into ICUs 1304(82%) were males. It is understood that females have a stronger immune system and therefore are more likely to survive and get less severe disease (Souyris et al., 2018). However, (Jin *et al.,* 2020) found that age was comparable between men and women in all data sets.

2.4 Comorbidities

Generally, hospitalized patients tend to be older and have comorbid conditions like hypertension and diabetes mellitus. Whether these diseases confer a disadvantage to the patient infected with Covid -19 has been a matter of debate since the data is still scanty. Atkins *et al. (*2020) found that chronic kidney disease and Asthma were risk factors for Covid -19 hospitalization in men and not women. The research was carried out among geriatrics patients often have comorbidities. The findings compare with those of Yang *et al.* (2020) who assessed the prevalence of comorbidities in the Covid -19 patients and found that hypertension, respiratory disease and

cardiovascular disease conferred a greater risk in patients with severe disease compared to those with mild disease. Baradaran *et al.* (2020) also reported that severe disease was more common with advancing age, which is often associated with comorbidities. Pfortmueller *et al.* (2020) Reported key prevalent comorbidities of Covid infected patients as hypertension, diabetes mellitus and acute kidney disease.

Those that underwent in-hospital cardiac arrest and died 48.7% were male, had elevated plasma levels of D-Dimers, serum creatinine, creatinine kinase, lactate dehydrogenase, lower percentage of lymphocytes, low platelet counts and low albumin levels.60% received corticosteroids,51% received IV immunoglobulin infusions,44% were on non-invasive ventilation,19% were invasively intubated. Comorbidities were identified in 101(64%) with hypertension, cardiovascular diseases, diabetes being the most common ones (Aggarwal *et al.,* 2020). Suleyman *et al.,* (2020) reported similar findings in a retrospective study of 463 patients admitted with Covid 19 infections 33% developed CARDS. Among them 94% had at least 1 comorbidity, 63% had hypertension, 39.3% had chronic kidney disease, 38.4% had diabetic mellitus.26% had a body mass index of above 30.

2.5 The Relationship between severity of disease at admission and outcome

2.5 .1 Severity of CARDS

The severity of the disease at admission is a strong predictor of survival. In critically ill Covid 19 patients early medical interventions to reduce mortality depends on early and effective accurate assessment on admission. There are no special tools available tool for evaluating Covid 19 infections but rely on the existing tools currently used for other conditions (Attaway *et al.,* 2021).

One of the methods used to assess and predict a patient's outcome is sequential organ failure assessment (SOFA) and quick sequential organ failure assessment (qSOFA) scoring systems. SOFA score and qSOFA scoring systems have widespread application to screen patients with life-threatening conditions in both emergency and critical care units. SOFA score describes conditions of multiorgan dysfunction using several parameters. Pao2/fio2, Glasgow coma scale, creatinine levels, platelets, bilirubin, mean arterial pressure, the function of each organ is scored

0-4. total score is 0-24, The score of 0-6 mortality is <10%, score of 7-9 mortality is 15-20%, score of 10-12 is 40-50%, and score of 13-14 mortality of 50-60% (Suleyman *et al,*2020).

Wang *et al.,* (2020) looked at the survivability of patients admitted with severe COVID 19 pneumonia in the ICU and found that those who had a high SOFA score had poorer outcome. (SOFA) scores above 4 (OR=5.16, 95% CI=1.29– 20.55) had a high risk of mortality. Zou, et al., (2020) documented similar findings using APACHE 11 score. Score greater than or equal to 17 mortalities was higher for those admitted in ICU. In his study 33.7% of those who died had APACHE score of 23.23 +- 6.05 while the survivors had a score of 10.87+- 4.40. Most of the severity assessment scores use data on organ function to predict outcome (Zou *et al.,* 2020). Patients with poor presentation tend to have poor survivability.

In a prospective multicenter and cohort study that included 30 ICUs in Spain and Andorra with a total of 663 patients. Ferrando *et al* (2020) reported an overall mortality of 31%. Among the non survivors SOFA score of 7 and APACHE 11 score of 17 on admission to ICU.APACHE score – acute physiology and chronic Health disease classification system 11 looks at patients' temperature, mean arterial pressure, respiratory rate, arterial pao2/fio2 serum sodium and Potassium, hematocrit white blood cells Glasgow coma scale and Age. Each component is given a score between 0-4. Total score of 71. A score of 25 predicts a mortality rate of 50% while a score of 30 and above a mortality rate of 80%.

2.5.2 Radiological Presentation

Different radiological patterns are observed at different times throughout the course of the Covid 19 infection. Pure type glass ground opacification which is the most commonly observed pattern usually develop between day 0-4 days after onset of symptoms, peaking at 6-13 days (Revzin *et al.,* 2020). The main finding in CARDS on chest computerized tomography scan is glass ground opacities, consolidation. Pleural effusions, lung cavitation's and pneumothorax are rare findings in COVID associated ARDS and other causes of inflammation should be investigated (Revzin et al., 2020). The distribution of lesions is said to be peripheral, asymmetric, and a lot of lung involvement. A study done in China retrospectively reviewed CT scans of 101 patients and found that 87% had typical glass ground images and 53% had this finding together with consolidation (Ortiz-Prado *et al*., 2020).

Shi *et al.,* (2020) in a retrospective Cohort study done in Wuhan China, reported that among 81 patients admitted into ICU with CARDS, the predominant pattern of abnormality in their CT chest was bilateral, peripheral ill-defined glass ground opacification in 65% of the patients and lesions quickly evolving to diffuse bilateral grass ground opacification in 90% of the patients.
Ombajo *et al.,* (2020) in a multicenter retrospective study done in Kenya, she reported the commonest radiological findings were ground grass opacities in 83%, mixed ground glass opacities and consolidation in 58% and interlobular septal thickening in 48% while another study by Revzin *et al.,* (2020) reported that patients with ground glass opacities(GGOs) in 2 lung zones are more likely to require hospitalization while those with GGOs in three Lung zones required hospitalization, intubation and mechanical ventilation.

2.5.3 Laboratory investigations

Common Laboratory findings in CARDS patients hospitalized in ICU include lymphopenia, elevated aminotransaminase levels, elevated lactate dehydrogenase levels, elevated inflammatory markers like ferritin, C- Reactive protein, procalcitonin levels, erythrocyte sedimentation rate (ESR) and abnormalities in coagulation tests. Ibrahim et al., 2021 in a retrospective cohort study done in Saudi Arabia reported that out of the 132 patients admitted with COVID 19 infections,25 % who were admitted into the ICU with CARDS all patients had elevated neutrophils, decreased lymphocytes, C-reactive protein (CRP) was elevated in 48,5% of patients-dimers in 43.2% ESR elevated in 40.9%.

WHO (2020) has listed real time quantitative polymerase chain reaction (RT-qPCR) as a diagnostic protocol as a guide to detect presence of SARS-COV-2. This involves taking a nasal or throat swab and checking these swabs for the genetic footprint of the virus. Other markers found in patients with CARDS are Lymphopenia, increased neutrophil-lymphocyte ratio, decreased percentage of basophils, eosinophils and monocytes, thrombocytopenia, elevated lactate dehydrogenase (LDH), elevated D-Dimer, elevated ferritin and elevated interleukin 6.(Ortiz-Prado et al., 2020).Oliveira *et al.,* (2021) reported median ferritin levels 0f 848ng/ml upper normal limit being 336ng/ml ,D-Dimers of 1.4ug/ml upper normal limit 0.8ug/ml,interleukin -6 level 18pg/ml upper limit being 2 pg./ml .Nugroho *et al.,* (2021) In a meta-analysis involving 29 studies 4328 patients revealed a higher mean D-dimers levels on

admission and were associated with an increased risk of disease severity and mortality in patients with CARDS

2.6. Comparisons of outcomes between invasive intubation and non- invasive mechanical ventilation

Covid 19 is the most recent cause of Adult Acute Respiratory syndrome. The risk benefit evaluation of invasive versus non-invasive ventilation should take into account complications that are associated with invasive intubation and mechanical ventilation including ventilation induced lung injury, ventilation acquired pneumonia, and difficult weaning from mechanical ventilation (Rahmanzade *et al.*, 2020)

The role of Non-Invasive mechanical ventilation (NIV) in management of acute lung injury and severe ARDS remains highly controversial. The current approach of maintaining low threshold for endotracheal intubation in patients with COVID associated ARDS is being followed by clinicians globally (Rahmanzade *et al.*, 2020).

Use of NIV in patients with mild hypoxic respiratory failure has demonstrated that intubation can be avoided in up to 70% of patients with COVID associated ARDS.In a retrospective study Zhou et al reported that the mortality was higher in the intubated group 96% than the NIV group where mortality was 92%. In a similar study Yang et al (2020) reported a mortality rate of 86% in the intubated group and 57%mortality in the NIV group. Casella, et al (2020) showed a favorable outcome of NIV outcome in patients with COVID-19 respiratory failure (Singh, 2020).

Zuccon *et al* (2021) in a retrospective cohort study observed 54 patients admitted into ICU due to Covid 19 associated ARDS.48 patients were intubated while 6 patients were treated with noninvasive mechanical ventilation. General reference was spo2 less than 92, RR >28b/min, p/f ratio <300.Among the intubated, 21 died while there was no mortality reported among the 6 that were treated with non-invasive mechanical ventilation. For those who died complications that occurred in the course of their ICU stay included renal failure in 16 patients, liver failure in 7 patients, and sepsis in 6 patients.

2.7. Treatment modalities

2.7.1 High flow nasal oxygen

The target range of oxygen saturations is 90-96%measured by pulse oximetry. High flow nasal cannula is one of the modalities used in management of Covid 19 acute respiratory distress syndrome. This therapy involves delivery of heated and humidified oxygen at high flows at 20-60l/min titrated to a precise fraction of inspired oxygen. Attaway *et al*., (2021) reported that High Flow oxygen reduce the risk of intubation and invasive intubation by 15% but use of HFNC requires intensive monitoring for signs of impending respiratory failure. However according to WHO (2020) patients with hypercapnia, exacerbation of obstructive lung disease, cardiogenic edema, hemodynamic instability, multiorgan failure, abnormal mental status should generally not receive HFNO.

Noninvasive ventilation is another treatment modality which is done via facemask, or a helmet placed on patients face or head. NIV use in acute severe respiratory illness can avoid intubation in 70%of patients with mild ARDS. Zhou, et al (2020) reported the mortality being higher in the intubated group 96% than in the NIV group by 92%. A similar study on Covid 19 patients by Yang et al (2020) revealed a mortality rate of 86 % and 57%in the intubated group and in the NIV group respectively. Cascella *et al* (2020) showed a favorable outcome of NIV in Covid 19 patients with non-severe respiratory failure.

2.7.2 Proning

Proning is yet another treatment modality. It has been shown to be one of the most effective adjuvant therapies in Covid associated ARDS and is associated with increased survival. Placing a person in a prone position promotes more homogeneous aeration of the lungs and has been shown to improve oxygenation (Gibson *et al*, 2020). Early prone position of patients with moderate to severe Covid ARDS with P/F ratio of less than 150 is recommended for a period of 16 hours. Longer periods of up to 36 hours have had a more substantial impact on oxygenation than 16 hours. PRONA-COVID Group et al., 2021 reported that patients with CARDS who were mechanically ventilated, majority improved their oxygenation on prone position, and this could have been attributed to a better ventilation perfusion matching. However, safety and efficacy remain to be determined in large RCT

2.7.3 Invasive ventilation

Invasive intubation is another modality of treatment. According to WHO guidelines patients with severe hypoxic respiratory failure failing to respond to oxygen standard therapy like in Covid 19 ARDS should receive advanced oxygen administration and ventilatory support. Hypoxemic respiratory failure in ARDS commonly results from intrapulmonary ventilation perfusion mismatch and patients will require intubation and mechanical ventilation (World Health Organization, 2020).

ECMO is another treatment modality. Venous –venous extracorporeal oxygenation has been seen to reduce mortality and morbidity. A recent analysis showed a similar mortality of 40% in ARDS patients with venous-venous ECMO than in Covid ARDS patients with ECMO suggesting that patients with COVID -19 ARDS benefited from ECMO just like any other patient with ARDS. Specific pharmacologic treatment includes Antiviral treatment with remdesivir, hydroxychloroquine, lopinavir and interferon. Many patients with Covid 19 ARDS receive antiviral and immunosuppressive therapy. Their full effects are not conclusive yet, but anecdotal observations report that they have contributed to reduced mortality. Corticosteroids use the evidence is still scarce and are recommended for patients with concomitant shock not responsive to vasopressors. Analgesics are used to manage pain, minimize sedations whenever possible. Neuromuscular blocking agents are a rescue therapy reserved for patients with severe hypoxemia and inability to achieve adequate ventilation (Pfortmueller, 2020).

2.8 Association between treatment modalities and outcomes

Clinical manifestations of Covid 19 infections particularly in younger populations without comorbidities mostly include mild symptoms such as fever, cough, dyspnea, and malaise/fatigue. These populations have reported better outcomes with symptom management and supplemental oxygen. Oxygen administration being titrated basically to avoid hyperoxemia and hypoxemia. These mild symptoms are observed in a majority of cases 85%.5% will develop critical illness and will require intensive care because of hypoxemic respiratory failure.

According to Attaway *et al* (2021) patients with Pao2/Fio2>200 before commencing HFNS treatment and had reduction of respiratory rate of less than 35 b/minute within the first hour had very good outcomes and significantly reduced need for intubation, however intensive monitoring

was key to note signs of impending respiratory failure as delayed intervention had worse outcomes. He also reported NIV to be superior to HFNC but patients with severe hypoxemia with Pao2/Fio2<100 need intubation and mechanical ventilation, and such have poorer outcomes Prone position has been shown to reduce mortality in severe corvid associated ARDS and there is emerging evidence that Non-Invasive positive ventilation can be provided for these patients in prone position in a ward set up, Dobler *et al.,* (2020) prone position is associated with a 28-day reduction in mortality.

Neuromuscular blockade in early Covid associated ARDS potentially reduces lung strain by eliminating spontaneous breathing activity. ECMO treatment is considered for patients with CARDS with profound respiratory failure despite optimized conventional care.Dreiler.et al (2020) reported that high SOFA score and prolonged pre ECMO ventilation is an indicator of higher mortality, but when ECMO was initiated early by experienced personnel with SOFA score less than 3 patients had better outcomes. Jozwiak *et al.* (2020) also reported that patients with CARDS, ECMO were a rescue therapy that allowed ultra-protective ventilation and improved patient oxygenation. However, because of the poor prognosis of these patients and limited ECMO services, COVID-19 patients with severe ARDS eligible for ECMO should be selected in the light of benefit/risk balance.

2.9 Survival rates

COVID-19 ARDS seems to have worse outcomes when compared with ARDS from other causes. The intensive care unit and hospital mortality rate from atypical was estimated to be 35.5% and 40.0% respectively. Covid 19 associated ARDS mortality ranged between 26%-61.5%. Those who received mechanical ventilation mortality ranged between 65.7% and 94%. Death from Covid- 19 ARDS was mainly due to respiratory failure at 53% (Gibson *et al.,* 2020). Similarly, Stawicki *et al*., (2020) reported mortality rate ranging from 14-66% among the patients admitted into the ICU and this depended on patient specific factors.

The most characteristic clinical course of severe COVID-19 patients is the development of CARDS. Pathophysiologically the lungs suffer from cytokine storm that damages the lung tissue interfering with oxygenation, leading to hypoxemia and multiorgan failure and 40% of the patients do not survive (Machhi et *al.,* 2020). In a study done in Seattle area Hospitals in March

2020, Bhatraju *et al.,* (2020) reported that out of 24 patients with CARDS half of the patients died between day 1 and 18 days of admission. Of the 12 surviving patients 5 of them were discharged home, 4 were discharged from ICU but remained within the hospital, 3 remained in ICU on mechanical ventilation by the end of study period.

According to Tzotzos *et al,* (2020), she reported that among patients the Covid-19 patients transferred to ICU 75 % of patients had ARDS mortality rate in Covid -19 associated ARDS was 45% and incidences of ARDS among non-survivors of Covid-19 was 90%. The outcomes of patients with severe Covid-19 infections admitted into ICU have been poor generally and mortality has been reported to be high despite being closely monitored and resuscitation being commenced immediately. According to Shao, et al, (2020) in a retrospective study, reported that out of 136 patients with 19 admissions,119(87.5%) had cardiac arrests due to respiratory causes and an overall mortality rate of 19.2%. In Wuhan the mortality rate was 62% among the critically ill while in the USA Washington mortality rate was 67%.

2.10. Outcome

2.10.1 Death

2.10.2 Discharged/Discharged with complications

2.11 Theoretical Framework

This study will apply the Faye Abdellah's 21 nursing problems theory that is a patient centered Theory. It is considered a human need. The theory has categorized the needs of patients into four categories. The basic needs, sustenal care needs, remedial care needs and restorative care needs. The basic needs are to help maintain good hygiene and physical comfort such as prevention of spread of infections, exercise, rest and sleep. In terms of Covid-19, WHO guidelines have outlined activities that individuals need to undertake in order to remain healthy and if infected measures to prevent spread of infection. This include wearing of face masks, hand hygiene with alcohol-based sanitizer or washing hands with soap and water, avoid overcrowding, quarantine for those infected with the Coronavirus.

The sustenal care needs facilitate maintenance of a supply of oxygen to all body cells, facilitate maintenance of nutrition of all body cells elimination, and maintenance of fluid and electrolyte

balance as well as recognize the physiological responses of the body to disease conditions. CARDS is a respiratory disease and patients present with hypoxemia needing supplemental oxygen. The needs for oxygen supplementation and respiratory support are key to the survival of the patient. Maintenance of nutrition will be achieved parentally since patients with severe hypoxemia will not be able to feed themselves and so will the maintenance of fluid and electrolyte balance. Elimination needs will include catheterizing patients and monitor intake and output and also ensure the patient is adequately opening bowels.

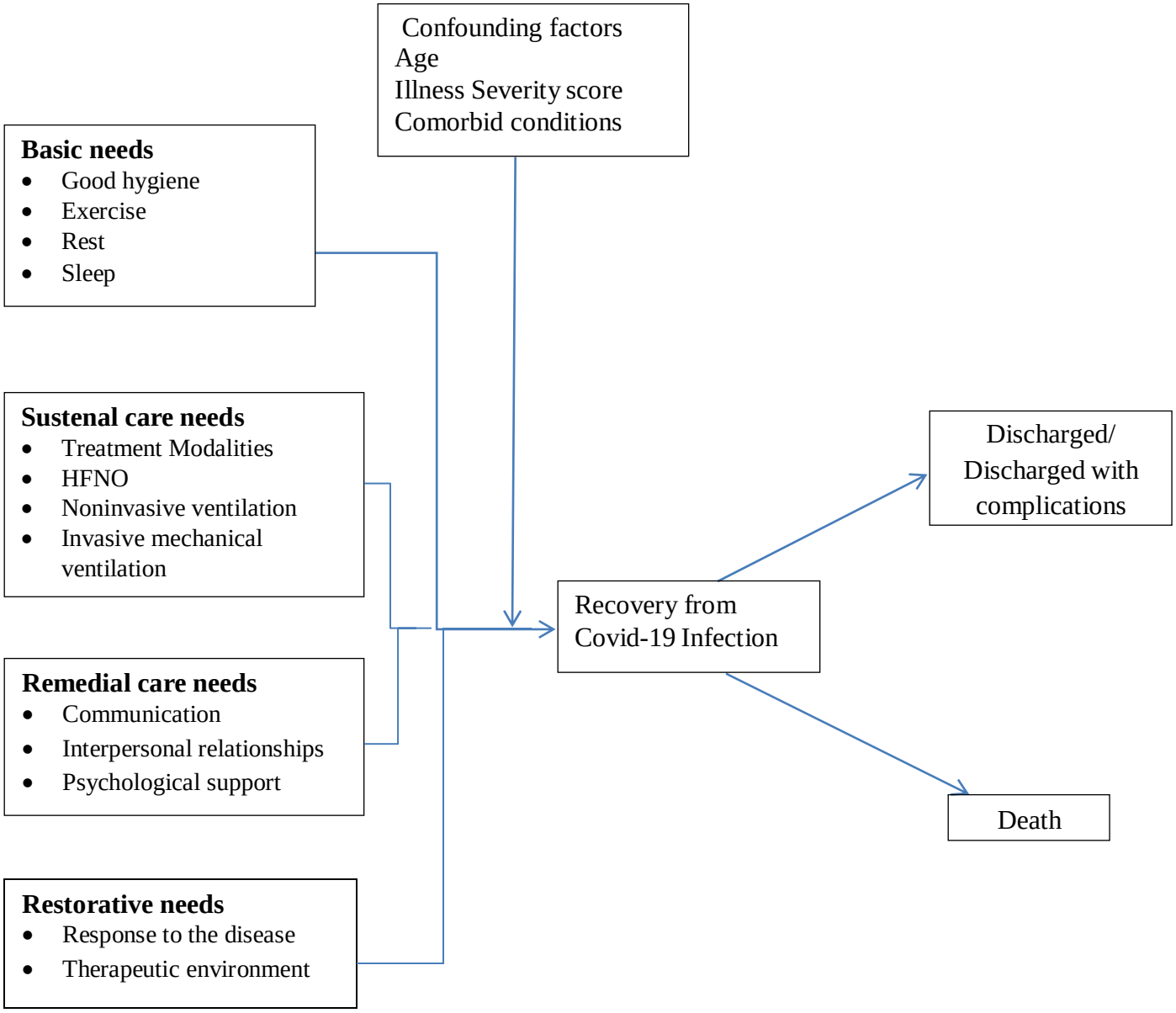
The Remedial needs to identify and accept interrelatedness of emotions and organic illness and facilitate effective verbal and non-verbal communication. Patients with Covid-19 infection are usually nursed Isolated with no relatives visiting them and also have fear of death and stigmatization. Those with CARDS might be unable to communicate verbally because they are intubated and if not intubated, they have masks on, hence the clinicians need to identify these needs and address them as much as possible. Psychological support and counselling is key in addressing these issues.

Restorative care needs involve assessing patient limitations and acceptance of optimum possible goals in both physical and emotional limitations, use of community resources as an aid to resolve problems that arise from illness. As patients with CARDS improve, assessment of what they are able to do is key and setting up goals of what the patient is able to achieve. Support from the family, community and health members is encouraged even as health protocols are observed.

2.12 Conceptual framework

Conceptual framework depicts relationships between variables.

Figure 1 Conceptual Framework



CHAPTER 3: METHODOLOGY

3.1 Introduction

This chapter describes the study design used to conduct the study, the target population, description of the study area, the methods used to collect data, sample size and sample size determination, inclusion and exclusion criteria, data analysis, data dissemination and presentation.

3.2 Study design

This was retrospective cross section study. This design helps to assess histories of exposures and outcomes over a specified time period. The study focused on a group of patients who had CARDS and following up on the outcomes of this patient retrospectively. The study described the outcomes of patients who were managed using invasive versus noninvasive mechanical ventilation. It was the best design to help the researcher describe exposure to COVID -19 virus, progression to CARDS and outcome

3.3 Study area description

The study was carried out at The Aga Khan University hospital. This is a premier, tertiary, teaching and referral hospital located in the Parklands area of Nairobi about 6.8 km from Nairobi city Centre. It has a capacity of 290 beds, 11 ICU beds and 16 HDU beds. The nurse patient ratio is 1; 1 in ICU and 2; 1 in HDU and this is internationally acceptable as per Canadian staffing ratio standards. (The Canadian association of critical care nurses (CACCN 2015). The ICU has a total number of 50 nurses and 6 intensivists. The Unit has admission criteria which includes any patient in need of respiratory support, and support of more than 1 organ among other factors. The institution is Joint Commission International accreditation (JCIA) accredited and is dedicated to identifying and finding solutions to the health and medical challenges of sub-Saharan Africa community. Hence, it is one of the hospitals that has been receiving significantly high numbers of patients with COVID- 19 infection from East Africa and beyond.

3.4 Target population

The study included all patients admitted into adult critical care units (ICU and HDU) from March 2020 to December,

3.5 Eligibility criteria

3.5.1 Inclusion criteria

Study subjects had to fulfill the following inclusion criteria.

1. Patients diagnosed with severe /critical Covid -19 ARDS as per the definition
2. Adults above 18 years of age since they are the ones who experience severe form of disease
3. Admission into critical care units within the study period from March 2020 to December 2020

3.5.2 Exclusion Criteria

Patient with missing data

Patient with ARDS from other causes

3.6 Sample size determination

3.6.1 Sampling and sample size determination

The census method was used to identify those to be included in the sample. The researcher used all the 201 files of patients admitted into ICU/HDU with Covid 19 severe pneumonia. The files of all patients who met the criteria of inclusion from March to December 2020 were included in the study.

3.6.2 Study instrument

Data were collected using a data abstraction tool. (Appendix 1) The tool has four sections: Socio-demographic characteristics, such as age, gender. Marital status, Clinical characteristics, treatment modality, and outcome of care. Experts in the field to ensure completeness reviewed the tools. These included the ICU nurse manager and ICU intensivist consultant well versed with management of patient with ARDS including COVID-19 associated ARDS. The data that was collected comprised of triage data, demographics, length of ICU stay (was determined by date of admission and date of discharge), mortality, mechanical ventilation, laboratory and radiological studies, discharge status. This was amalgated in four sections on demographic data, clinical characteristics: comorbidities, severity assessment score, disease progression, treatment modalities, outcome (Appendix 1).

3.6.3 Reliability and validity of study instruments

Reliability assesses the extent of reproducibility of measurements if different observers use the same instrument for the study, they would be able to produce the same results.

Validity of a research tool depicts accuracy of what the tool is supposed to measure. Internal validity of a study is important when assessing causation. It refers to whether the observed effect of a variable under investigation can be attributed to the hypothesized cause. Internal validity is only related to a specific study. External validity is related to whether the results of research can be generalized to a larger population (Kirkwood, (2006). The reliability and validity of the data abstraction tool was pretested at the Aga Khan University Hospital before data collection commenced. The pilot study registered a Cronbach score of more than .70 which was considered adequate for the study.

3.7 Study procedures

3.7.1 Participants' recruitment and selection

Upon clearance from KNH-UON ERC and Aga Khan University hospital ERC and researcher sought permission from Aga Khan University administration and ICU/HDU administration to carry out this study. The researcher went to the medical records manager and sought permission to use the medical records to obtain data for the study

3.7.2 Consent procedure

Since the researcher did not deal with human subjects directly, consent to carry out the study was obtained from hospital administration and waiver of consent form.

3.7.3 Data collection process

Data collection commenced after getting a waiver of consent. Data was collected using a data abstraction tool. After obtaining permission to access the records, the researcher visited the ICU and accessed the admission book which has a list of all the patients admitted in the ICU. Using the inclusion criteria, the researchers identified those who qualified to be included in the study (Patients admitted from March 2020 to December 2020). The researchers' information did not include names of patients but only medical records. Using the data abstraction tool, the researcher collected the data from 192 files out of the total 201 patients admitted in the facility

from March to December 2020. 9 files with incomplete information were not included in the study.

3.8 Data management

Data was entered in an excel sheet. Data cleaning was done by inspecting the entire checklist, every case had an allocated checklist and those found incomplete were not included in the analysis. A standard entry of information was done to prevent duplication. The data was then entered in SPSS for effective storage and subsequent analysis.

3.8.1 Data Analysis and presentation

Data was analyzed using the statistical package for social sciences (SPSS IBM) software version 27. Frequencies and percentages were used to describe categorical data. The outcome was determined as a percentage of the whole sample. Cross tabulation was done to assess the relationship between the categorical variables. Binary logistic regression was used to determine the relationship between the method of treatment (invasive and non-invasive mechanical ventilation) and the outcome. The level of significance was set at critical level or $P< 0.05$ at a significance level of 95%. Data was presented through tables and pie chart.

3.9 Ethical Considerations

The researcher received ethical approval from the KNH-UON research and Ethics number ERC/A/350 and Aga Khan University Hospital research number Ref.2021/IERC=160 and Ethics committee and. The research was conducted as per the University of Nairobi guidelines. Anonymity of the files selected was ensured by ensuring no names of patients was included and serializing the checklist used, Data was stored in a cabinet that was locked and only accessible to the researcher and in a password locked computer known by the researcher to ensure confidentiality. Data were coded in a manner that source of data is not identifiable to the source to ensure anonymity. The files were searched by the medical records staff and after abstracting the data the information was removed from the system. The checklists will be kept for a period of 5 years after which they will be destroyed. The researcher will not mention the name of the hospital nor the names of the patient in any publication.

3.10 Study Limitations

This study was done in a private hospital which had adequate resources. The study findings have generalizability, in regard to both public and private institutions. For the former, there needs to be adjustment for certain factors such as resource allocation. The irrelevant and incomplete data was not included in the study. To overcome this, the researcher used only files that had complete information. Additionally, this is a new area of study and studies are still ongoing so there is limited data particularly on large scale RCTS as well as minimal data published locally. The researcher also reviewed any anecdotal evidence that has not been published yet in order to get a comprehensive outlook.

3.11 Dissemination plan

Research findings are important as they contribute to the body of knowledge and help to improve practice. The researcher will provide the research findings to the research supervisor panel at the University of Nairobi and thereafter will submit a copy of the research findings to the UON Nursing department as well as to the administration of The Aga khan University hospital. The researcher will also publish in a peer-reviewed journal and if possible present the findings in the critical care conference.

CHAPTER FOUR: RESULTS

4.1 Introduction

The purpose of this study was to evaluate the management and clinical outcomes of patients with Covid 19 associated ARDS at Aga Khan University Hospital ICU. This chapter therefore presents results of the study from the data collected using the data abstraction tool; whereby the researcher looked at patients' medical records to evaluate the management and clinical outcomes of patients with Covid 19 associated acute respiratory distress syndrome at Aga Khan University Hospital ICU.

The chapter presents the findings in frequency tables and percentages with clear discussions of each finding.

The study sought to meet out the following objectives,

1. To describe the management and the clinical outcomes of patients admitted with CARDS at the Aga Khan University hospital ICU?
2. To establish the association between severity of disease at admission and outcome.
3. To compare outcomes of non-invasive and invasive mechanical ventilatory support

4.2 Document Validity Rate

The study intended to collect data from all the 201 patients that were admitted between March 2020 to December 2020 and among these only 192 files were complete and hence included in this study.

4.3 Characteristics of the CARDs Patients

4.3.1 Socio-Demographic Information of the CARDs Patients

The study had sought to establish the socio-demographic information of the patients that were covered by the study. The follow were the findings.

Table 1 Gender of the Patients

Category	n	(%)
Gender		
Male	140	72.9
Female	52	27.1
Total	192	100,0

The results indicated that 72.9 %(n=140) were male patients compared to 27.1 %(52) that were female. This indicated that most of the patients with CARDs that were admitted at Aga Khan University Hospital were male.

Table 2 Age of the Patients

Category	n	(%)
Age		
18-29	4	2.1
30-39	4	2.1
50-59	20	10.4
60-69	76	39.6
70-79	64	33.3
80 and above	24	12.5
Total	**192**	**100.0**

The results indicated that 4.2%(n=8) 39 years old and below , 10.4%(n=20) were 50-59 years old , 72.9%(n=140) were between ages 60 to 79 while only 12.5%(24) were 80 years old and above . This indicated that most of the patients with CARDs that were between ages 60 to 79 years old.

Table 3 Employment status of the Patients

Category	n	(%)
Employment status		
Employed	36	18.7
Self Employed	84	43.8
Unemployed	72	37.5
Total	192	100

The results indicated that 18.7 %(36) of the CARDs patients were employed, 43.8 %(84) were self-employed while 37.5(72) were unemployed. This indicated that most of the CARDs patients were running their own business.

4.3.2 Clinical Characteristics of Patients with CARDs admitted to the ICU

The study had also sought to establish the Clinical Characteristics of Patients with CARDs admitted to the ICU and the response was as follows.

Table 4 Comorbid conditions and Disease outcome

Comorbid condition	Disease Outcome	
	Died	**Discharged**
Hypertension	59.5%(n=78)	40.5%(n=30)
Diabetes	60.0%(n=48)	40.0%(n=32)
Chronic obstructive pulmonary disease	58.1%(n=92)	41.9%(n=66)
Asthma	55.6%(n=15)	44.4%(n=12)

Since the emergence of COVID 19 infection, the patients have presented with varied signs and symptoms. In this study, 35% (n=.67) presented with multiple symptoms while the rest presented only with a cough (43.8%), dyspnea (22.9%), fever (20.8 %) and fatigue (12.5%). In terms of comorbid conditions, 108(68.8 %) were hypertensive, 120 (62.5%) were diabetic and 40 (20.8%) had COPD, only 24 (12.8%) were asthmatic. Upon analysis, the mortality rate among the participants with comorbid conditions is summarized as shown in table 4.5

Table 5 X-ray and laboratory results

Laboratory values			
D-dimers	**High (>500 ng/ml)**	**Normal(>220,<500 ng/mL)**	**Low (<220 ng/mL)**
	83.3% (n=76)	16.7%(n=15)	0%
Ferritin levels	**High(>336µg/l)**	**Normal (24-336 µg/l)**	**Low (<30 µg/l)**
	93.2%(n=84)	6.8%(n=12)	0%
Lymphocyte count	**High (>45%)**	**Normal (18-45%)**	**Low (<18%)**
	6.3%(n=2)	39.6% (n=13)	54.2%(n=17)

Chest X-RAY results		
Category	**Findings**	**Percentage**
Abnormal X Ray with glass ground opacities	Yes	98.4
	No	1.6

In the study, radiological findings were analyzed by looking at the chest X-rays. The results in Table 4.6 indicated that all the X-rays analyzed were abnormal with most (98.4%, n= 188.) having the characteristic bilateral glass opacity appearance. The laboratory findings were analyzed by looking at the d-dimer levels, ferritin levels, and lymphocyte count. 83.3% had high d-dimer levels, 93.2% had high ferritin levels 54.2 had low lymphocyte count. Further analysis also indicated that comparatively the odds of dying with a high lymphocytic count were higher

with 61.4 % dying compared to 64.1% of those with high ferritin levels and 65% of those with -dimer levels.

The researcher sought to establish the percentage of the patients who developed complications resulting in organ failure. Results as indicated on figure 4.1 showed that acute kidney injury was the commonest complication at 41.7% (n=80) requiring renal replacement therapy, 30.7% developed neurological deficits while the rest (21.4%) did not develop any complications. Of those who developed acute kidney injury, 92.5% died compared to 37.0% of those who developed neurological complications.

Figure 2 Patients Complications

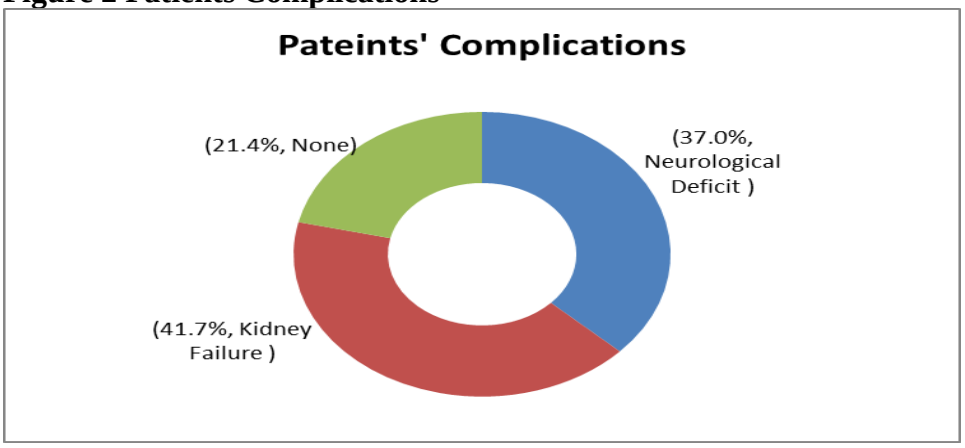


Table 6 Day in ICU and Disease Outcome

Disease Outcome	Day in ICU					Sig.
	1-10	11-20	21-30	31-40	51 and above	
Died	56	32	11	0	0	0.012
Discharged	55	14	6	3	3	
Total	111	46	17	3	3	

Most of the participants were in ICU for less than ten days (n=111) and this is when most deaths occurred (n=56) compared to those who were in ICU for more than 10 days (69) and 11 deaths

were recorded. Only six patients were in the ICU for more than 30 days and all were discharged home. The results also indicated a high positive significance relationship *(P*<.012*)* between the number of days in ICU and the disease outcome

4.4 Management of Patients with CARDs and their outcomes

There are different approaches that are instituted for the patients with CARDS. The study sought to establish the various methods applied in the management of patients with CARDS admitted at ICU at Aga Khan University Hospital.

Table 7 Treatment modalities for participants with CARDS

Modality	**Duration in days**		
High flow oxygen nasal cannula	0-10	11-20	21-30
	n=56	n=0	n=0
Noninvasive mechanical ventilation	0-10	11-20	21-20
Continuous Positive Airway Pressure (CPAP)	n=24	n=12	n=8
Bi-level Positive Airway Pressure (BIPAP)	n=44	n=8	n=0
	Duration in days		
Invasive mechanical ventilation	Less than 5 Days	Between 5-10	>10 days
Bi-level	n=8	n=8	n=12
AC/VC APRV	n=0 n=4	n=8 n=0	n=8 n=12
AC- Assist Control/VC- Volume Control; CARDS: COVID associated acute respiratory distress syndrome ; APRV:			

The results showed that high flow oxygen, noninvasive ventilation and invasive methods were used among the patients. Patients with spo2 of 90-92% and were commenced on High flow nasal cannula, and if hypoxemia persisted they were put on Noninvasive mode of ventilation and progressively graduated to invasive mode of mechanical ventilation. Patients with signs of impending respiratory failure were first put on noninvasive mode of mechanical ventilation.

Out of the 192 patients all were initially started on High flow nasal oxygen, and with persistent hypoxemia 152 required Noninvasive mechanical ventilation while 40 of them who developed signs of impending respiratory failure required intubation and invasive mechanical ventilation. Self Proning was also encouraged for those patients on high flow oxygen and those on noninvasive mode on ventilation. Due to lack of sufficient human resources to prone patients on invasive mechanical ventilation, this was minimally utilized. Patients on different modes of ventilation spent varying duration of days in the ICU, with those critically ill spending an average of 12 days.

Table 8 Treatment modalities for participants with CARDS and their outcome

Treatment Modalities	**Disease Outcome**	
	Death	Discharge
High flow oxygen nasal cannula	52.3%(n=52)	47.7 (n=42)
Noninvasive mechanical ventilation		
Continuous Positive Airway Pressure (CPAP)	62.5& (n=20)	37.5% (n=12)
Bi-level Positive Airway Pressure (BIPAP)	60% (n=39)	40% (n=26)
Invasive mechanical ventilation		
Bi-level	63.8%(n=30)	36.2%(n=17)
AC/VC	81.5% (n=31)	18.5%(n=7)

The study had also sought to establish that 52.3% the patients that were on High flow oxygen nasal cannula died, 62.5% on Continuous Positive Airway Pressure (CPAP) also died with another 60% patients that were on the Bi-level Positive Airway Pressure (BIPAP) treatment also died. The results also indicated that 63.8% on Bi-level treatment also died with the highest percentage at 81.5% died. The results indicated that the highest death outcomes were with the Invasive mechanical ventilation treatment methods of CARDS.

4.5 Correlation between severity of Diseases at admission and treatment outcomes

The second objective was to establish the Correlation between severity of Diseases at admission and treatment outcomes. A multi-variate analysis was done to establish the association between the independent variables (Commordities, Clinical Presentation, SOFA score on Admission and APACHE score on admission) and the dependent variable (disease outcomes).

Table 9 Correlation Analysis

		Y	SOFA score on admission	APACHE score	clinical presentation	X4
Disease Outcome	Pearson Correlation	1				
	Sig. (2-tailed)					
	N	192				
SOFA score on Admission	Pearson Correlation	.368**	1			
	Sig. (2-tailed)	.000				
	N	189	189			
APACHE score on admission	Pearson Correlation	.014	.271**	1		
	Sig. (2-tailed)	.873	.001			
	N	135	135	135		
Comorbidities	Pearson Correlation	.122	.090	.095	1	
	Sig. (2-tailed)	.096	.220	.276		
	N	189	186	135	189	
Clinical Presentation	Pearson Correlation	.170*	.181*	.062	.239**	1
	Sig. (2-tailed)	.019	.013	.472	.001	
	N	192	189	135	189	192
**. Correlation is significant at the 0.01 level (2-tailed).						
*. Correlation is significant at the 0.05 level (2-tailed).						

The aim of the study was to establish whether there was an association between SOFA score on Admission and disease outcomes of patients with Covid 19 associated acute respiratory distress syndrome. The findings of the study showed that SOFA score on Admission (X1) had a low but a + positive significant association (r=.368, P< .000) with the disease outcomes of the patients with Covid 19 associated acute respiratory distress syndrome at Aga Khan University Hospital ICU. This indicated that SOFA score on admission would determine whether the patients of COVID 19 pneumonia treatment died or not.

The study had first sought to establish whether there was an association between APACHE scores on admission and disease outcomes of the patients with Covid 19 associated acute respiratory distress syndrome at Aga Khan University Hospital ICU. The findings of the study showed that APACHE score on admission (X2) had a low but a + positive non-significant association (r=.014, P> .873) with disease outcomes of patients with Covid 19 associated acute respiratory distress syndrome at Aga Khan University Hospital ICU. This suggests that APACHE score on admission was less likely to determine whether the patient died or not. This

contradicts the findings by Ferrando *et al* (2020) that reported an overall mortality of 31% for APACHE score of 17 on admission to ICU.

The study also sought to establish whether there was an association between comorbidities and disease outcomes of patients with Covid 19 associated acute respiratory distress syndrome. The findings of the study showed that commodities (X4) had a very low but a + positive non-significant association (r=.122, P> .096) with disease outcomes.

The study in this part had also sought to establish whether there was an association between Clinical Presentation and disease outcomes of patients with Covid 19 associated acute respiratory distress syndrome at Aga Khan University Hospital ICU. The findings of the study showed that Clinical Presentation (X3) had a very low but a + positive significant an association (r=.170, P<.019) with disease outcomes of patients with Covid 19 associated acute respiratory distress syndrome at Aga Khan University Hospital ICU. This suggests that Clinical Presentation on admission was not only important but also significantly determined the course of treatment was also most likely to determine whether the patient died or not.

4.6 Comparison of outcomes of non-invasive and invasive ventilatory support

The study had sought to establish whether there was a difference between Non-Invasion Method (Non- Mechanical Method) and Invasion Method (Mechanical Ventilation Methods) and the treatment outcomes of the patients with COVID 19 associated acute respiratory distress syndrome at Aga Khan University Hospital ICU.

Table 10 Invasive Ventilation and Non-Invasive ventilation

Methods	Duration in Days					Disease Outcome (Death)		Sig
	Less than 5 Days10(n)	Between 5-10(n)	10-1510(n)	16-2010(n)	Total10 (n)	**Yes**10(n)	**No**10(n)	
Invasive Methods(Mechanical)								
Bi-level	8	8	12	0	28	21	7	0.65
AC/VC	0	8	4	4	16	4	12	
APRV	4	0	12	0	16	16	0	
Total	12	16	28	4	60	41	19	
Non-Invasive Methods(Non-Mechanical								
CPAP	12	0	4	0	16	7	9	
BIPAP	8	0	0	0	8	1	7	
High Flow Oxygen		0	8	0	32	2	30	0.45
Total	**44**	**0**	**12**	**0**	**56**	**10**	**46**	

The findings of the study indicated that a high percentage 85.4% of patients were placed on non-invasive ventilation methods compared to only 58% that were on invasive ventilation. The findings of the study also indicated that 74.3% of the patients that were on invasive Mechanical Ventilation Methods died compared to only 25.6% that were on non-invasive.

4.7 Conclusion

The findings of the study shows that SOFA score on Admission (r=.368, P< .000) and Clinical presentation that include fever, cough, dyspnea and fatigue (r=.170, P<.019) was significant in determining patients outcome. This is consistent with the findings of Mons-Rodriquez et al (2021) who observed that some of the clinical characteristics that increased the probability of developing CARDS and death included presentation with fever and dyspnea. Wang et, al., (2020) similarly observed that patients admitted with severe Covid-19 pneumonia who had a high SOFA Score had poorer outcomes. The findings also established that APACHE score on

admission (r=.014, P> .873) though had a positive association with disease outcomes did not significantly influence the disease outcomes. APACHE score was one of the methods used to predict patients' prognosis. Additionally, the findings indicated that there was no significance association between comorbidities (r=.122, P> .096) and disease outcomes of patients admitted in ICU with COVID 19 pneumonia for treatment at Aga Khan University Hospital.

The findings of the study indicated non-invasive treatment modalities significantly influenced patients' outcomes among patients with Covid 19 associated acute respiratory distress syndrome and that the use of invasive treatment modalities and would not potentially or significantly influence the outcome. The findings of the study also established that there was less mortality reported among the patients that were treated with non-invasive mechanical ventilation compared with the ones on invasive Ventilatory methods.

The results of the null hypothesis testing at 95% Confidence Level indicated that there is a significant association (P< 0.003) between the severity of CARDS and the disease outcomes of patients with Covid 19 associated acute respiratory distress syndrome at Aga Khan University Hospital ICU. The results also established that there is a significant association (P< 0.000) between the method of ventilation and outcome.

CHAPTER FIVE: DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

This chapter contains the summary of findings obtained from the study, conclusions made, recommendations and suggestions for future studies on the find out the management and clinical outcomes of patients with Covid 19 associated acute respiratory distress syndrome. The study focused on the Aga Khan hospitals ICU in Nairobi.

5.2 Discussion of findings

5.2.1 Socio-Demographic Characteristics

The results indicated that all the demographic factors of age, gender, marital status and employment had a significant association with disease outcomes among the CARDS Patients. Patients that were more advanced in age were reported to have higher mortality rate than those aged less than 50 years. This supports the findings of Prado *et al.* (2020) who noted that patients that were more aged had a high mortality rate compared to those that were younger. Additionally, Grasselli *et al.*, (2020) also established that older patient were more likely to die of CARDS compared to the younger ones with the same condition. Similarly report from World health Organization (2020) reported old age as one of the risk factors that lead to severe disease. This is supported by Baldani (2020) who reported that older people have higher rates of comorbidities and may experience more severe Inflammatory responses therefore they are at a higher risk of death.

The results also indicated more men than women developed CARDS. Grasselli et al, (2020) made similar observations reporting more males than females were admitted into ICU with CARDS. Yang et al., as well in his study reported severe disease in males than females. Wire (2020) reported that across different parts of the world morbidity and Mortality associated with CARDS was more in males than female and associated Factors being higher expression of angiotensin-converting enzyme-2 in male than female,sex based immunological differences driven by sex hormone and X chromosome. The other factor could be gender behavior related to lifestyle with more men smoking than women. Behavior could be other factor where studies

reported men not adhering adequately to preventive measures such as frequent handwashing, and stay at home orders.

5.2.2 Clinical Characteristics of Patients with CARDs admitted to the ICU

The results also indicated that most of the patients who developed CARDS were advanced in age, had preexisting comorbid diseases either diabetes or hypertension. The most prevalent finding in the Confirmed CARDS was Diabetes Mellitus and hypertension which would influence the severity of the disease especially among male patients. This is consistent with the findings by Hao *et al.,* (2020) and Baradaran et al., (2020) that being male, having diabetes mellitus, cloudy chest x-rays findings, derangement of some laboratory results were risk factors for progression to CARDS.

The results also established a significant relationship between high levels of ferritin and low levels of lymphocyte count and the disease outcome of the patients with Covid 19.Most patients had high levels of D-Dimers The results also established that the patients with CARDS were associated with complication such as disorientation, agitation, restlessness, acute kidney failure among others. The results are consistent with the findings by Atkins *et al. (*2020) who established a significant association with renal diseases and Asthma that are risk factors for COVID -19 patient hospitalization. This therefore highlights the need for further analysis on the risk factors for CARDS male Patients. The study also established significance relationship between X-ray findings and disease progression

This was consistent with findings by Revzin *et al.,* (2020) who reported that patients with ground glass opacities (GGOs) in 2 lung zones are more likely to require hospitalization while those with GGOs in three Lung zones required hospitalization, intubation and mechanical ventilation.

Additionally, there was significance relationship between Kidney failure and death outcome among male patients with CARDS. This supported findings by Atkins *et al. (*2020) who established that kidney disease and asthma were risk factors for COVID -19 hospitalization in men and not women. The results also indicated that half of the patients with Covid 19 associated acute respiratory distress syndrome had spent between 1-10 days in ICU. This indicated that CARDS Patients was associated with long hospital stay compared to other conditions.

5.2.3 Management of Patients with CARDs and their outcomes

While invasive and non-invasive methods remain the effective methods in the treatment of CARDS, the results indicated that 93.8% the patients that were on High flow oxygen nasal cannula were discharged the results also indicated that 68.3% of the patients that were on invasive methods died compared to 33.3% that were on non-invasive methods. The results indicated that the highest death outcomes were with the Invasive mechanical ventilation treatment methods of CARDS. The results are not consistent with the findings by Zuccon *et al.* (2021) that non-invasive methods were related to better diseases outcomes among CARDS Patients.

5.2.4 Correlation between severity of Diseases at admission and treatment outcomes

SOFA score on admission significantly influenced outcomes on the patients CARDS while APACHE score did not. The findings are inconsistent with the findings by While Zou *et al.,* (2020) that indicated that patients with an APACHE Score of greater than or equal to 17 were at more risk and the mortalities was higher for those admitted in ICU. This therefore calls for more interrogation on the extent to which APACHE Score influenced patients of COVID 19 pneumonia treatment outcome.

5.2.5 Comparison of outcomes of non-invasive and invasive ventilatory support

While non-invasive methods were found to have an influence on the outcomes of patient with CARDS, invasive methods did not. The results are consistent with Zuccon *et al.* (2021) that established a significant relationship between non-invasive mechanical ventilation and better diseases outcomes among for CARDS.

5.3 Conclusion

The findings of the study established a significant relation between demographic factors of Gender and Age of patients had a high significant influence to the disease out comes of the patients admitted in ICU with CARDS at Aga Khan University Hospital, the most patients were advanced in age with many of them being male. The findings of the study shows that SOFA score on Admission (r=.368, P< .000) and Clinical presentation that include fever, cough , dyspnea and fatigue (r=.170, P<.019) was significant in determining whether the patients

admitted in ICU with COVID 19 pneumonia for treatment at Aga Khan University Hospital died or survived .The finding also established that APACHE score on admission (r=.014, P> .873) though had a positive association with disease outcomes it did not significantly influence the disease outcomes of patients with Covid 19 associated acute respiratory distress syndrome at Aga Khan University Hospital ICU. Additionally, the findings indicated that there was no significance association (r=.122, P> .096) with disease outcomes of patients with CARDS at Aga Khan University Hospital ICU.

The findings of the study indicated modalities of ventilation significantly influenced outcomes among patients with CARDS. The findings of the study also established that there was less mortality reported among the patients that were treated with non-invasive mechanical ventilation. Results from hypothesis testing also indicated that there is a significant association between the severities of CARDS and that there is a significant association (P< 0.000) between the method of ventilation and outcome.

5.4 Recommendations

5.4.1 Socio-Demographic Characteristics

There is need for effective evaluation of the patients with CARDs demographic information that include age, gender, marital status and employment given that such information have a great impact on the disease outcomes among such patients. Additional, there is need for special care for the patients that are more advanced in age as there are more likely to die compared to much younger CARDs patients.

5.4.2 Clinical Characteristics of Patients with CARDs admitted to the ICU

When treating CARDs patients, there is need to consider whether the patients have other chronic conditions such as kidney disease , Asthma , diabetes and hypertension as these are not only risk factors for COVID -19 patient but may also affect the treatment outcome if they are not properly addressed. There is also need to evaluate the CARDs patients for their levels of ferritin and lymphocyte count as these also influence their treatment outcome.

5.4.3 Management of Patients with CARDs and their outcomes

While invasive and non-invasive methods remain the effective methods in the treatment of CARDS, there is need for the facility to consider the best method of treatment that can reduce the percentage of possible deaths given that the highest death outcomes were with the Invasive mechanical ventilation treatment methods of CARDS

5.4.4 Correlation between severity of Diseases at admission and treatment outcomes

There is need for effective APACHE score assessment before treatment for patients with CARDS in order to identify the best course of treatment. There is also need of a review on the APACHE score and the SOFA score on Admission for COVID 19 other than the use the normal acceptable done for other conditions. While there is no current specific tool for evaluating COVID 19 infections, and the medical staff continues to use the existing tools as heighted by Attaway *et al. (*2021) , there is need for more research on better tools for better diagnosis of the disease patients with Covid 19 associated acute respiratory distress syndrome for better treatment outcome.

5.4.5 Comparison of outcomes of non-invasive and invasive ventilatory support

Lastly, there is also need of establishing critically when non-inversion treatment modalities and inversion methods should be used as proper selection as both of the methods have a significant influence on the patients' outcomes. Last but not least, there is need for properly establishing the cause of death due to a particular line of treatment in order to improve on the treatment outcome.

5.5 Suggestions for Further Studies

There is need for further studies on the cost associated with the use of various ventilatory approaches so that the patients do not go through unnecessary cost that would be avoided by the doctors.

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APPENDIX 1: DATA COLLECTION TOOL

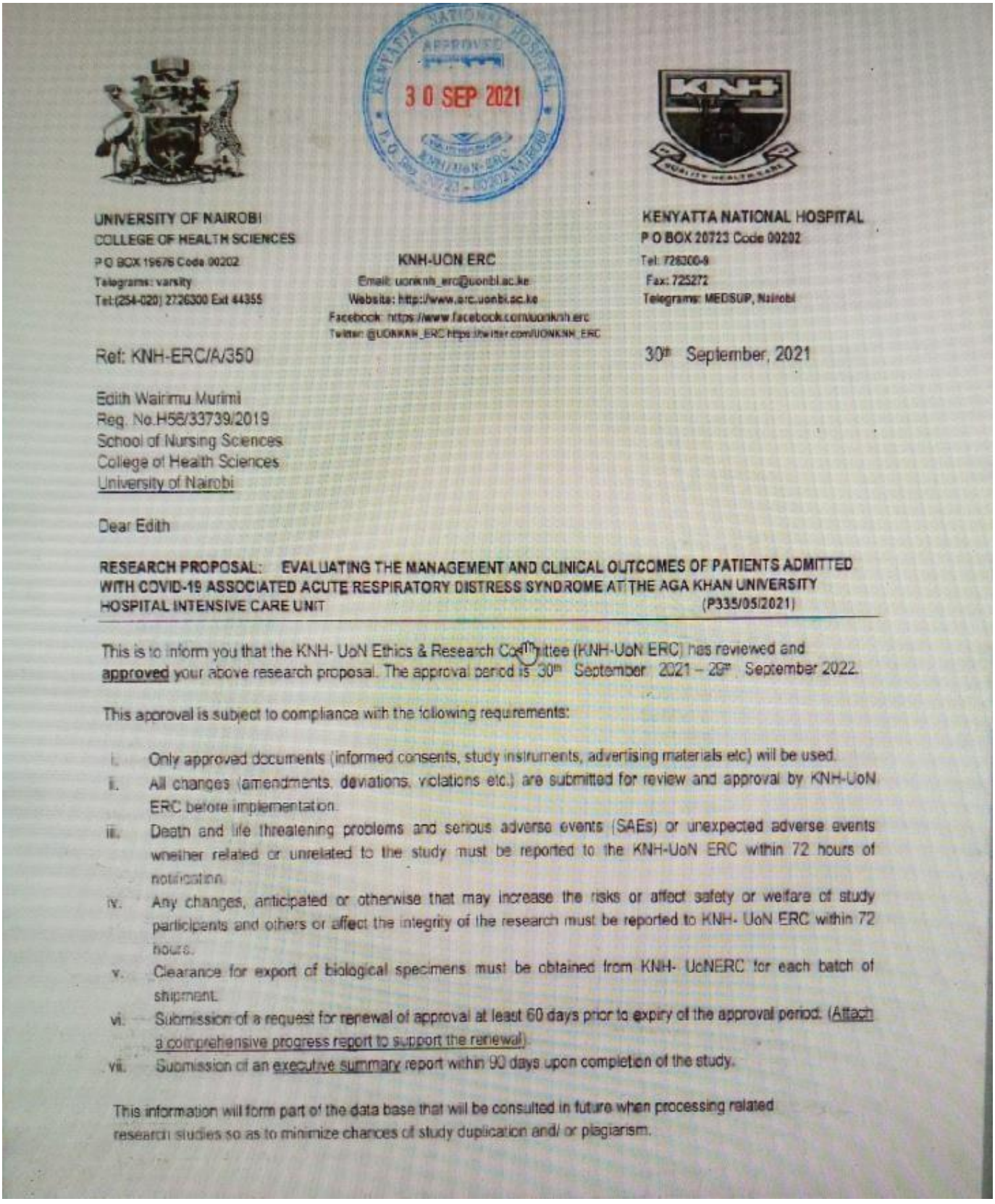
DATA ABSTRACTION TOOL

DATA ABSTRACTION TOOL Study No.
a. Sociodemographic data
Age
18-29
30-39
40-49
50-59
60-69
70-79
80+
Gender M ☐ F ☐
Marital status Married☐ Single☐ Divorced☐ Separated ☐
Employment status Employed ☐ Self-employed☐ Unemployed☐
b. Clinical characteristics
Comorbidities:
Known Hypertension Yes ☐ No ☐
Known Diabetes Yes ☐ No☐
Known COPD Yes☐ No☐
Known Asthmatic Yes☐ No☐
c. No of days in ICU
1-10
11-20
21-30
31-40
41-50
+51
d. APACHE score on admission
Severity /APACHE score Score Survival Death
1-10
10-17
17-25
>25
e. SOFA Score on admission
Severity Score Survival Death

1-5
6-10
11-15
16-20
21-24
f. Clinical presentation
Fever ☐
Dyspnea ☐
Cough ☐
Fatigue ☐
g. Radiological
Normal X-ray (as reported) Yes ☐ No☐
If abnormal X-ray
Bilateral glass like opacities Yes☐ No☐
Other abnormal x-ray reports (Indicate as per report)
h. Laboratory investigations
D-dimers levels low ☐ <220 ng/mL Normal ☐ >220,<500 ng/mL High ☐ >500 ng/mL
Positive PCR test Yes ☐ No ☐
Ferritin levels Low☐<30 µg/l Normal ☐ 24-336 µg/l High ☐ >336 µg/l
Lymphocyte count Low ☐ <18% of WBC's Normal ☐ 18-45% of total WBC's High☐ >45% of WBC's
i. Complications (tick)
o Kidney failure as reported by the clinician
o Neurological deficits (new as reported by the clinician)
o Amnesia- asking patients memory-related questions; current and past events
o Disorientation- asking questions related to date time and place
j. Treatment modalities
a. High flow oxygen via nasal cannula Yes☐ No☐
b. Noninvasive mechanical ventilation (NIV) CPAP Yes☐ No☐

BIPAP Yes☐ No☐	
c. Duration in of treatment in days 0-10 ☐ 11-20 ☐ 21-30 ☐ 31-40 ☐ 41-50 ☐ +51 ☐	
c. Invasive mechanical ventilation	
Mode	
FiO2	
PS (cm H2O)	
TV	
PEEP (cmH2O)	
Duration of mechanical ventilation in days	
k. Outcomes	
DEATH	Yes ☐ No ☐
DISCHARGED	Yes ☐ No ☐

APPENDIX 2: KNH ERC RESEARCH APPROVAL



KENYATTA NATIONAL HOSPITAL
APPROVED
30 SEP 2021
KNH/UoN-ERC

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/350

30th September, 2021

Edith Wairimu Murimi
Reg. No.H58/33739/2019
School of Nursing Sciences
College of Health Sciences
University of Nairobi

Dear Edith

RESEARCH PROPOSAL: EVALUATING THE MANAGEMENT AND CLINICAL OUTCOMES OF PATIENTS ADMITTED WITH COVID-19 ASSOCIATED ACUTE RESPIRATORY DISTRESS SYNDROME AT THE AGA KHAN UNIVERSITY HOSPITAL INTENSIVE CARE UNIT (P335/05/2021)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH-UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 30th September 2021 – 29th September 2022.

This aporoval is subject to compliance with the following requirements:

i. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
ii. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
iii. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affect 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 KNH- UoNERC for each batch of shipment.
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.

This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC webste **http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M.L CHINDIA
SECRETARY, KNH- UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chair, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Director, School of Nursing Sciences, UoN
Supervisors: Dr. Dorcas Maina, School of Nursing Sciences, UoN
Dr. Eunice Omondi, School of Nursing Sciences, UoN

APPENDIX 3: AGA KHAN UNIVERSITY IERC APPROVAL

THE AGA KHAN UNIVERSITY

Faculty of Health Sciences
Medical College

Ref: 2021/IERC-160 (v2)
December 7, 2021

Dr. Dorcas Maina - Supervisor,
Ms. Edith Wairimu Murimi
Masters Student - University of Nairobi & Staff Aga Khan University, Nairobi,

Dear Dr. Dorcas Maina/ Ms. Edith Wairimu Murimi and team,

Re: **EVALUATING THE MANAGEMENT AND CLINIAL OUTCOMES OF PATIENTS ADMITTED WITH COVID 19 ASSOCIATED ACUTE RESPIRATORY DISTRESS SYNDROME AT THE AGA KHAN UNIVERSITY HOSPITAL INTENSIVE CARE UNIT**

The Aga Khan University, Nairobi Institutional Ethics Review Committee (IERC), is in receipt of your protocol resubmitted to the Research Office (RO) on December 03, 2021. The IERC reviewed and approved this project *{as per attached official stamped protocol and attachments - version Ref: Ref: 2021/IERC-160 (v2) and KNH-UON ERC approval letter Ref: KNH-ERC/A/350.* You are authorized to conduct this study from **December 07, 2021**. This approval is valid until **December 06, 2022** and is subject to compliance with the following requirements;

1. The conduct of the study shall be governed at all times by all applicable national and international laws, rules and regulations. IERC guidelines and Aga Khan University Hospital policies shall also apply, and you should notify the committee of any changes that may affect your research project (amendments, deviations and violations)
2. Researchers desiring to initiate research activities during COVID-19 pandemic must comply with the COVID-19 SOPs for Research as well as submit to the Research Office a Request Form to Initiate, Reinstate or Continue Research During COVID-19 Pandemic.
3. **Prior** to human subjects enrolment you must obtain a research license from the National Commission for Science, Technology and Innovation (NACOSTI), *where applicable*, site approvals from the targeted external site(s) and file the copies with the RO.
4. *As applicable*, **prior** to export of biological specimens/data, ensure a Material Transfer Agreement (MTA)/Data Transfer Agreement (DTA), is in place as well as seek shipment authority/permit from the relevant government ministry. Copies of these approvals, should be submitted to the RO for records purpose.
5. All Serious Adverse Events and the interventions undertaken must be reported to the IERC as soon as they occur but not later than 48 hours. The SAE shall also be reported through the AKUHN quality monitoring mechanism(s) at Client Relations Department of the Chief of Staff's Office.
6. All consent forms must be filed in the study binder and where applicable, patient hospital record.
7. Further, 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; as well as submit the completed Self-Assessment Tool -Monitoring Ethical Compliance in Research. You must advise the IERC when this study is complete or discontinued and a final report submitted to the Research Office for record purposes.
8. The hospital management should be notified of manuscripts emanating from this work.

If you have any questions, please contact Research Office at AKUKenya.ResearchOffice@aku.edu or 020-366 2148/1136.

With best wishes,

Dr. Christopher Opio,
Chair - Institutional Ethics Review Committee (IERC)

APPENDIX 4: NACOSTI APPROVAL

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Ref No: 949395

Date of Issue: 24/October/2021

RESEARCH LICENSE

This is to Certify that Ms.. Edith wairimu Murimi of University of Nairobi, has been licensed to conduct research in Nairobi on the topic: Evaluating management and clinical outcomes of patients admitted with Corvid 19 associated acute Respiratory Distress Syndrome at the AgaKhan University Hospital Intensive Care Unit for the period ending : 24/October/2022.

License No: NACOSTI/P/21/13581

949395

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Verification QR Code

NOTE: This is a computer generated License. To verify the authenticity of this document, Scan the QR Code using QR scanner application.

THE SCIENCE, TECHNOLOGY AND INNOVATION ACT, 2013

The Grant of Research Licenses is Guided by the Science, Technology and Innovation (Research Licensing) Regulations, 2014

CONDITIONS

1. The License is valid for the proposed research, location and specified period
2. The License any rights thereunder are non-transferable
3. The Licensee shall inform the relevant County Director of Education, County Commissioner and County Governor before commencement of the research
4. Excavation, filming and collection of specimens are subject to further necessary clearence from relevant Government Agencies
5. The License does not give authority to tranfer research materials
6. NACOSTI may monitor and evaluate the licensed research project
7. The Licensee shall submit one hard copy and upload a soft copy of their final report (thesis) within one year of completion of the research
8. NACOSTI reserves the right to modify the conditions of the License including cancellation without prior notice

National Commission for Science, Technology and Innovation
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E-mail: dg@nacosti.go.ke / registry@nacosti.go.ke
Website: www.nacosti.go.ke

APPENDIX 5: STUDY PLAN

ACTIVITY	February 2021-april 2021	May-2021	June 2021	September 2021	October 2021	November 2021
Proposal development and school approval						
Ethics approval						
Resubmission of proposal						
Data collection						
Data analysis,						
Presentation Report Submissions Thesis Defense						
Final report writing and submission						

APPENDIX 6: STUDY BUDGET

Stationary	Cost
5 reams of printing papers@600	2400
Printing of proposal paper 3 copies@300	1500
Printing of data abstraction tool 134 copies@50sh	6700
Statistician	45000
Printing of thesis and binding 3 copies@600	1800
Unforeseen contingencies	10,000
Total	67,400