



**ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCE
SCHOOL OF MEDICINE DEPARTMENT OF ANESTHESIOLOGY
CRITICAL CARE AND PAIN MEDICINE RESEARCH THESIS**

**Mortality and associated factors in covid19 patients admitted to covid19
ICU in ekakotebe general hospital**

November 2020

ADDIS ABABA, ETHIOPIA

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**MORTALITY AND ASSOCIATED FACTORS IN COVID19
PATIENTS ADMITTED TO COVID19 ICU IN EKAKOTEBE
GENERAL HOSPITAL**

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Anesthesiology)

**A Research Thesis To Be Submitted To Addis Ababa University School Of
Medicine, Department Of Anesthesiology, Critical Care and Pain Medicine In
Partial Fulfillment Of The Requirement For Specialty Certificate In Anesthesiology
Critical Care And Pain Medicine.**

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ADDIS ABABA ETHIOPIA

APPROVED BY THE BOARD OF EXAMINATION

The thesis here, entitled “Mortality and associated factors in covid19 patients admitted to covid19 ICU in ekakotebe general hospital,2020” is accepted in its present form by the board of examiners as Partial Fulfillment Of The Requirement For Specialty Certificate In Anesthesiology Critical Care and Pain Medicine.

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Research Project Submission Form

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Acronyms

ABG.....	acid base gas analysis
AKI.....	acute kidney injury
ALI.....	acute liver injury
CKD.....	chronic kidney disease
CLD.....	chronic live disease
CI-	Confidence Interval
Covid	corona virus disease
EKGH.....	ekakotebe generalize hospital
FIO2	fraction of inspired oxygen
HAI.....	hospital acquired infection
HR.....	hazard ration
HR.....	hazard ration
ICU	intensive care unit
IMV	invasive mechanical ventilation
NIMV.....	noninvasive mechanical ventilation
OD.....	odds ratio
OR	odds ratio
PaO2	partial arterial oxygen
PCR	polymerase chain reaction
PEEP.....	positive end expiratory pressure
SPSS	Statistical Package for the Social Sciences

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Abstract

Background the world is facing unprecedented health crisis with the pandemic caused by novel coronavirus SARS COVID19¹. The pathogen is spread by human to human transmission through droplet exposure and contact surface causing minor symptom in majority but critical illness, bilateral pneumonia and ARDS in minority². The burden of escalating the case number of covid19 is presenting a challenge to management of patients in the intensive care unit. The number of patients with covid19 admitted to ICU is escalating in Ethiopia. Identifying the risk factors among patients in the intensive care unit between the survivors and non survivors, and predicting mortality will have significant impact to determine prognosis and direct resource management.

Objective: to identify associated risk factors and mortality of patients with covid19 admitted to ekakotebe intensive care unit.

Method: a 7 month retrospective cohort study was employed at ICU of eka kotebe general hospital. . Review of records of all the patients admitted during the period was carried out. Information on socio-demographic characters, characteristic of patient, comorbidities and lab investigations on admission, and outcomes was collected through trained data collectors and the principal investigator by using prepared questioner. Data compiled and analyzed using computer software and presented using tables, graphs and figure

Result: During the period of the study 163 critical patients were admitted to covid19 ICU with laboratory confirmed covid19. Most patients were male (68.1%; 95% CI, 61.3%-76.1%), with a median age of 60 (95% CI, 58-65; IQR, 50-67) years. One hundred fourteen (69.9%; 95% CI, 63.8%-77.8%) had at least 1 comorbidity. Median time from symptom onset to ICU admission was 7 (95% CI, 6.1-8; IQR, 5-11) days. A total of 73 patients were intubated during the study period, 32 (43.8%) were during admission and the others (41(56.1%)) patients were intubated after mean length of stay of 4.47 (95% CI 3.5-5.5) days at ICU. Median duration on mechanical ventilator was 6 (IQR 3-12 95% CI 5-8, range 1-30) days. The median length hospital stay was 16 (IQR 10-23 range 2-48) days. The median length of ICU stay was 7 (IQR 4-12 95% CI 5-8) days. At the time of censoring, a total of 77 patients (49.1% 95% CI 41.7-56.4) transferred from ICU only 3 patients were still in ICU. And a total of 83(50.9%; CI 43.6-59.5) patients has died in

ICU. Among comorbidities CLD was significantly associated with mortality with (HR: 4 (95%CI 1.28-12). Elevated liver function (HR: 1.83 95 CI (1.08-3.13 p -0.02) and PH<7.35(HR: 1.8(95% CI 1.05-3)), p value-0.03) during admission were also had significantly associated with mortality. The invasive mechanical ventilator was also significantly associated with mortality (HR: 2.27(2.27 (1.12-4), p <0.02).

Conclusion and recommendation: SARS –covid19 has a serious challenge to our health care system in our country Ethiopia and the world. Despite our hospital had lower number of admission during the study period to our ICU, the mortality rate is high³. Patients who require IMV had significant association and absolute high mortality rate. We recommend that a prospective study should be undertaken, with higher number of patients, to strengthen the findings of this study.

1. INTRODUCTION

1.1 Background

Coronavirus disease 2019 (COVID-19) is caused by SARS-CoV-2, a newly emergent coronavirus, that was first recognized in Wuhan, China, in December 2019.⁴ The outbreak of novel coronavirus pneumonia that was first detected in Wuhan in December 2019 resulted in a worldwide pandemic. On February 11, 2020, the World Health Organization (WHO) formally named it coronavirus disease 2019.⁴¹

Current evidence suggests that transmission of SARS-CoV-2 occurs primarily between people through direct, indirect, or close contact with infected people through infected secretions such as saliva and respiratory secretions, or through their respiratory droplets, which are expelled when an infected person coughs, sneezes, talks or sings.⁵

As the covid-19 pandemic accelerates, governments are warning people at high risk to be particularly stringent in observing social distancing measures because if they become ill they are more likely to need critical care including ventilation, and to die.⁶⁷

An important characteristic of an infectious disease, particularly one caused by a novel pathogen like SARS-CoV-2, is its severity, the ultimate measure of which is its ability to cause death. Fatality rates help us understand the severity of a disease, identify at-risk populations, and evaluate quality of healthcare.⁸⁹

Most data on covid-19 are from China, and although most confirmed cases have been classified as mild or moderate, 14% are severe and 5% critical.⁷⁶

Mortality rates of coronavirus disease-2019 (COVID-19) continue to rise across the world. Information regarding the predictors of mortality in patients with COVID-19 remains scarce .predicting mortality is very important: for identifying the risk factors, analysis and solution.¹⁰

A systematic review of published articles from January 1 to a April 30 on risk factors associated with mortality of covid19 revealed that patients with hypertension, coronary artery disease and diabetes had higher mortality of covid19. those who died compared with those who alive they

had elevated troponin, alanine transferase enzyme ,c reactive protein, creatinin, interleukin 6 and d dimer and low albumin level.¹¹

To conclude patients with baseline cardio metabolic disease and evidence of increased acute inflammation and end organ damage (cardiac, renal, liver , and hematologic) on admission were associated with increased risk of mortality due to COVID 19 infection.⁷¹¹¹²

1.2 Statement of the problem

Current status of covid19 is increasing all over the world, and the number of case and mortality has increased in Ethiopia too. Since march 13 (the first confirmed case in Ethiopia) the total confirmed cases is accelerating fast to reach 87,169 and The number of deaths also reaches to 1325 as of October 15,2020.¹³

Investigating the factors associated with mortality of critical patients, admitted to ICU will help to evaluate the prognosis and find optimal management. Early studies done in china Several factors that led to the progression of COVID-19 pneumonia were identified, including age, history of smoking, maximum body temperature at admission, respiratory failure, albumin, and C-reactive protein.¹⁴.

There is no study or survey in Ethiopia. This study will be done on mortality and associated risk factors with covid19 patients at ICU.

1.3 Significance of the study

Knowing the mortality and associated risk factors of covid19 patients at ICU will help to predict mortality and to advance the management.

The aim of this stud is to identify the risk factors, predict mortality and to develop guideline for further management.

2. LITERATURE REVIEW

The first human coronaviruses weren't discovered until the mid-1960s and take their name from the distinctive spikes with rounded tips that decorate their surface, which reminded virologists of the appearance of the sun's atmosphere.²⁶

The first human cases of COVID-19, the disease caused by the novel coronavirus causing COVID-19, subsequently named SARS-CoV-2 were first reported by officials in Wuhan City, China, in December 2019.¹⁵ Current evidence suggests that transmission of SARS-CoV-2 occurs primarily between people through direct, indirect, or close contact with infected people through infected secretions such as saliva and respiratory secretions, or through their respiratory droplets, which are expelled when an infected person coughs, sneezes, talks or sings⁵.

Up to October 15, 2020, more than 37,704,153 cases of severe acute respiratory syndrome coronavirus-2 (SARSCoV-2) infection had been reported from 210 countries and territories; more than 1,079,029 people had died¹⁵.

One of the most critical clinical and public health questions during the emergence of a completely novel pathogen, especially one that could cause a global pandemic, pertains to the spectrum of illness presentation or severity profile.¹⁶⁹ For the patient and clinician, this affects triage and diagnostic decision-making, especially in settings without ready access to laboratory testing or when surge capacity has been exceeded. It also influences therapeutic choices and prognostic expectations. For managers of health services, it is important for rapid forward planning in terms of procurement of supplies, readiness of human resources to staff beds at different intensities of care and generally ensuring the sustainability of the health system through the peak and duration of the epidemic⁹.

Prognostic factors are known as good indicators to predict disease progression and severity level⁹. Currently, it is well established that the case fatality rate for SARS-CoV-2 infection increases with age and number of comorbidities¹⁰. Other factors, such as the decline of the immune function¹⁷, proinflammatory profile¹⁸ and alterations in the Angiotensin I Converting Enzyme 2 (ACE2) are also being described by relevant clinical reports as predictors for COVID-19 progression¹⁹.

Studies are ongoing on in different world to understand the factors associated with mortality of adult patient admitted to ICU. There are few studies which analyze the difference among the survivors and non survivors admitted to ICU.

According to American journal of medicine study done on Clinical Characteristics, Associated Factors, and predicting COVID-19 Mortality published on April 2020.it was retrospective cohort study and the result showed that Risk factors associated with COVID-19 mortality was associated with older age (OR=2.15, 95% CI=1.35, 3.43), male sex (OR=1.97, 95% CI=1.29, 2.99), history of diabetes (OR=2.34, 95% CI=1.45, 3.76), lymphopenia (OR=1.59, 95% CI=1.03, 2.46), and increased procalcitonin (OR=3.91, 95% CI=2.22, 6.91, per SD increase) on admission, but this study doesn't explain wither they died at ICU or not.²⁰

Similarly study had done at Wuhan china with risk factors associate with mortality of patients with covid19 which retrospective, multicenter cohort study April 202. In the study they include 197 patients, among them 137 were discharged and 54 died in hospital. 91 (48%) patients had a comorbidity, with hypertension being the most common (58 [30%] patients), followed by diabetes (36 [19%] patients) and coronary heart disease (15 [8%] patients). Multivariable regression showed increasing odds of in-hospital death associated with older age (odds ratio 1.10, 95% CI 1.03–1.17, per year increase; $p=0.0043$), higher Sequential Organ Failure Assessment (SOFA) score (5.65, 2.61–12.23; $p<0.0001$), and d-dimer greater than 1 $\mu\text{g/mL}$ (18.42, 2.64–128.55; $p=0.0033$) on admission .but unlike the above study ,lymphopenia ,comorbidities and sex was not associated as a risk factor. And the sample of interest(died) is small.²¹.

Systematic review and meta- analysis done by journal of medical virology in May 2020 .which includes 14 studies to evaluate the risk factors associated with mortality in COVID- 19. The presence of comorbidities such as hypertension (odds ratio [OR], 2.5; 95% confidence interval [CI], 2.1- 3.1; $P < .00001$), coronary heart disease (OR, 3.8; 95% CI, 2.1- 6.9; $P < .00001$), and diabetes (OR, 2.0; 95% CI, 1.7- 2.3; $P < .00001$) were associated with significantly higher risk of death amongst patients with COVID- 19.And those who died, compared with those who survived, differed on multiple biomarkers on admission including elevated levels of cardiac troponin (+44.2 ng/L, 95% CI, 19.0- 69.4; $P = .0006$); C- reactive protein (+66.3 $\mu\text{g/mL}$, 95% CI, 46.7- 85.9; $P < .00001$); interleukin- 6 (+4.6 ng/mL, 95% CI, 3.6- 5.6; $P < .00001$);

D- dimer (+4.6 µg/mL, 95% CI, 2.8- 6.4; $P < .00001$); creatinine (+15.3 µmol/L, 95% CI, 6.2- 24.3; $P = .001$); and alanine transaminase (+5.7 U/L, 95% CI, 2.6- 8.8; $P = .0003$); as well as decreased levels of albumin (−3.7 g/L, 95% CI, −5.3 to −2.1; $P < .00001$).but this study doesn't include sub-Saharan countries.¹¹.

With similar topic other study was done at Germany. The study includes 1904 patients with a median age of 73 years, 48.5% (924/1904) of whom were female. The mortality rate was 17% (317/1835; 95% confidence interval (95%CI) 16–19), the rate of admission to the intensive care unit (ICU) was 21% (399/1860; 95%CI 20–23), and the rate of invasive mechanical ventilation was 14% (250/1850: 95%CI 12–15).and they found the most prominent risk factors for death were male sex (hazard ratio (HR) 1.45; 95%CI 1.15–1.83), pre-existing lung disease (HR 1.61; 95%CI 1.20–2.16), and increased patient age (HR 4.11 (95%CI 2.57–6.58) for age >79 years versus <60 years). Among patients admitted to the ICU, the mortality rate was 29% (109/374; 95%CI 25–34) and higher in ventilated (33% [77/235; 95%CI 27–39]) than in non-ventilated ICU patients (23%, 32/139; 95%CI 16–30; $p < 0.05$).²²in this study the median age is high which will be contrary to our country. And they didn't found the cardiovascular and laboratory biomarkers significant association with mortality.²³

Study done on Risk Factors Associated with Mortality among Patients With COVID-19 in Intensive Care Units in Lombardy, Italy, retrospective, observational cohort study included 3988 patients. Of the 3988 patients included in this cohort study, the median age was 63 (interquartile range [IQR] 56-69) years; 3188 (79.9%; 95% CI, 78.7%-81.1%) were men, and 1998 of 3300 (60.5%; 95% CI, 58.9%-62.2%) had at least 1 comorbidity. At ICU admission, 2929 patients (87.3%; 95% CI, 86.1%-88.4%) required invasive mechanical ventilation (IMV),which is contrary to Germany study which is 14%.⁽²². Hospital and ICU mortality rates were 12 (95% CI, 11-12) and 27 (95% CI, 26-29) per 1000 patients-days, respectively.

Similarly the independent risk factors associated with mortality included older age (hazard ratio [HR], 1.75; 95% CI, 1.60-1.92), male sex (HR, 1.57; 95% CI, 1.31-1.88), high fraction of inspired oxygen (FiO₂) (HR, 1.14; 95% CI, 1.10-1.19), high positive end-expiratory pressure (HR, 1.04; 95% CI, 1.01-1.06) or low PaO₂:FiO₂ ratio (HR, 0.80; 95% CI, 0.74-0.87) on ICU admission, and history of chronic obstructive pulmonary disease (HR, 1.68; 95% CI, 1.28-2.19), hypercholesterolemia (HR, 1.25; 95% CI, 1.02-1.52), and type 2 diabetes (HR, 1.18; 95% CI,

1.01-1.39). No medication was independently associated with mortality (angiotensin-converting enzyme inhibitors HR, 1.17; 95% CI, 0.97-1.42; angiotensin receptor blockers HR, 1.05; 95% CI, 0.85-1.29).²⁴.

but the study Survival and predictors of deaths of patients hospitalized due to COVID-19 from a retrospective and multicenter cohort study in Brazil had high rate of ICU admission 41%(18939/46285) and the mortality was high (50.8%).patients with diabetic diabetes HR 1.17 (95% CI 1.11–1.24), neurological disease HR 1.34 (95% CI 1.22–1.46), kidney disease HR 1.11 (95% CI 1.02–1.21), heart disease HR 1.14 (95% CI 1.08–1.20), black or mixed race of HR 1.50 were associated with mortality at ICU. ²⁵But there was no association between sex HR 1 (95% CI 1.01–1.1), and patients with asthma HR 0.71 (95% CI 0.61–0.81) found to be protective. Similarly age >68 years HR 2.77 (95% CI 2.66–2.88) and, invasive ventilator support HR 2.94 (95% CI 2.81–3.07) were associated with mortality²⁶.

Study done at Egypt on outcome of patients admitted to ICU, of 32 patients admitted to ICU with case control study they found that There was a statistically significant difference in the duration of symptoms before hospitalization, mechanical ventilation and ICU and total hospital stay between the expired group and survivors ($P < 0.01$). Current smoking and smoking severity were statistically significantly ($P < 0.01$) higher in the expired group compared to survivors. Also, there was a statistically ($P < 0.05$) significant positive correlation between mortality and smoking severity ($r = 0.640$). There were statistically highly significant ($P < 0.01$) differences in the mean values of APACHE II score (21.11 ± 3.70 vs 24.21 ± 3.82), SOFA score (5.83 ± 2.64 vs 8.85 ± 2.17) and CPIS (7.55 ± 1.14 vs 8.64 ± 1.39) between the expired group and survivors respectively. There was also statistically significant positive correlation between mortality and old age ($r = 0.633$), obesity ($r = 0.712$), diabetes mellitus ($r = 0.685$), renal failure ($r = 0.705$), chronic heart diseases ($r = 0.591$), COPD ($r = 0.523$), malignancy ($r = 0.692$), kidney transplantation ($r = 0.644$) and liver cirrhosis ($r = 0.525$) ($P < 0.05$).but there was no association between male and female. but this study has small sample size and doesn't include survival analysis ²⁷.

3. OBJECTIVES

3.1 General objective

To study Mortality and associated factors in covid19 patients admitted to covid19 ICU in eka kotebe general hospital, 2020.

3.2 specific objectives

- 1 to describe the risk factors associated the mortality of covid19 patients
- 2 to determine the mortality of critical covid19 infected patients at ICU
- 3 to describe admission pattern

4 METHODOLOGIES

4.1 study area

The study was conducted in ekakotebe general hospital which is located in the center of Addis Abeba, Ethiopia. The hospital started its service since 2017 but currently the hospital is working as center of covid19 isolation and management center after emergence of covid19 pandemic. The hospital has 1000 beds and 18 beds for critical patients. It provided treatment for 2554 covid19 patients until October 15.

4.2 Study design

Retrospective cohort study was employed.

4.3 Populations

4.3.1 Source population

All patients admitted to adult ICU of Eka kotebe general hospital.

4.3.2 Study population

All adult patients who are admitted to ICU of eka kotebe general hospital from march 15 to October 15 with confirmed covid19 PCR test.

4.4 Inclusion and exclusion criteria

4.4.1 Inclusion criteria

All adult patients admitted to ICU of eka kotebe general hospital

4.4.2 Exclusion criteria

Patients referred to other hospital for different reasons.

4.4 Sampling technique

All patients admitted to ICU of ekakotebe general hospital in study period were included (convenient method of sampling).

4.5 variables

4.5.1 Dependent variable

Patient outcome

4.5.2 Independent variable

Age

Sex

Comorbidities

Duration of symptom before hospitalization

Type of symptoms

Length of ICU stay

ACE inhibitors

Mechanical ventilation

Length of MV

Smoking history

Laboratory investigations upon admission

Respiratory parameter upon admission

4.6. Data collection procedure

Data was collected by review of patient's records in the ICU with a prepared questioner. The principal investigator and three other medical residents were participated during data collection after proper training and close supervision was done by the principal investigator and each filled check list was rechecked for completeness.

4.7 Data analysis procedure

First the data was checked for completeness and consistency. Then it was entered in to the computer using epi-data version 4.1 software then exported to SPSS version 26 software for analysis. Descriptive statistics, bi-variable and multi variable cox regression hazard model were done to determine factors associated with mortality of patients admitted to Ekakotebe general hospital covid19 ICU.

4.8 Data quality assurance

During the data collection supervision was under taken by the principal investigator throughout and regular follow up was made. Cross check for completeness and consistency of data on daily basis. Once the data had been collected and checked for completeness, and accuracy, it was sorted, categorized and summarized.

4.9 Operational definition

Outcome -patient status after critical care in the ICU which include survived, or died

Survived –patient discharged alive by physician fulfilling discharge criteria from ICU

Died- a patient who sustained irreversible cessation of circulatory and respiratory function after ICU admission

Referred- patients sent to other hospital for special intervention after admission to ICU

Coexisting Conditions (comorbidity)– A known diagnosed underlying illness the patient have like hypertension, diabetic, ischemic heart disease or others as per chart review.

Home medication_ medications that the patient was taking at home within 1 week prior to admission. Does not include those started at an outside hospital if the patient was transferred

Adult –A person with age greater than >18

Elevated liver enzyme -ALT/AST>40U/L up on admission

Elevated renal function test- creatinin >1.4mg/dl

Lymphopenia –absolute lymphocyte count less than 1000 upon admission

4.9 Dissemination plan

The study result will be presented to Addis Ababa University, School of Medicine, Department of Anesthesiology and documents will be disseminated to all responsible bodies in the study area, for the hospital where the study is conducted, FMOH and Addis Ababa university school of Medicine.

4.10 Ethical considerations

Prior to the study ethical approval was obtained from the **Institutional Review Board of eka kotebe general hospital**. Cooperation letter obtained from management of the hospital before data collection. All data obtained in the course of the study was kept confidentially and used solely for the purpose of the study. Due to the retrospective character of the study, patient's consent was not necessary according to local requirements. The study was conducted after ethically reviewed and approved by Ethical Review board of Addis Ababa University, department of anesthesiology and critical care and pain medicine and permission obtained from eka kotebe general Hospital. The reliability of the study findings was guaranteed by implementing quality control measures throughout the whole processes of data collection

5. Result

5.1 Socio -demography characteristics

A total of two thousand five hundred fifty four patients admitted to our hospital and hundred seventeen patients admitted to ICU during the study period; 7 patients excluded from the study (3 patients transferred to other hospital and 4 patients have lost their charts).rate of admission to ICU was 6.6%.

Therefore *one hundred sixty three* patients were analyzed and out of this one hundred eleven were male (68.1%; 95% CI, 61.3%-76.1%]), with a median age of 60 (95% CI, 58-65; IQR, 50-67) years. And fifty two patients were female (31.9%; 95% CI, 23.9%-38.7%]), with a median age of 55 (95% CI, 60-66; IQR, 41-67) years. (figure 1 and figure2)

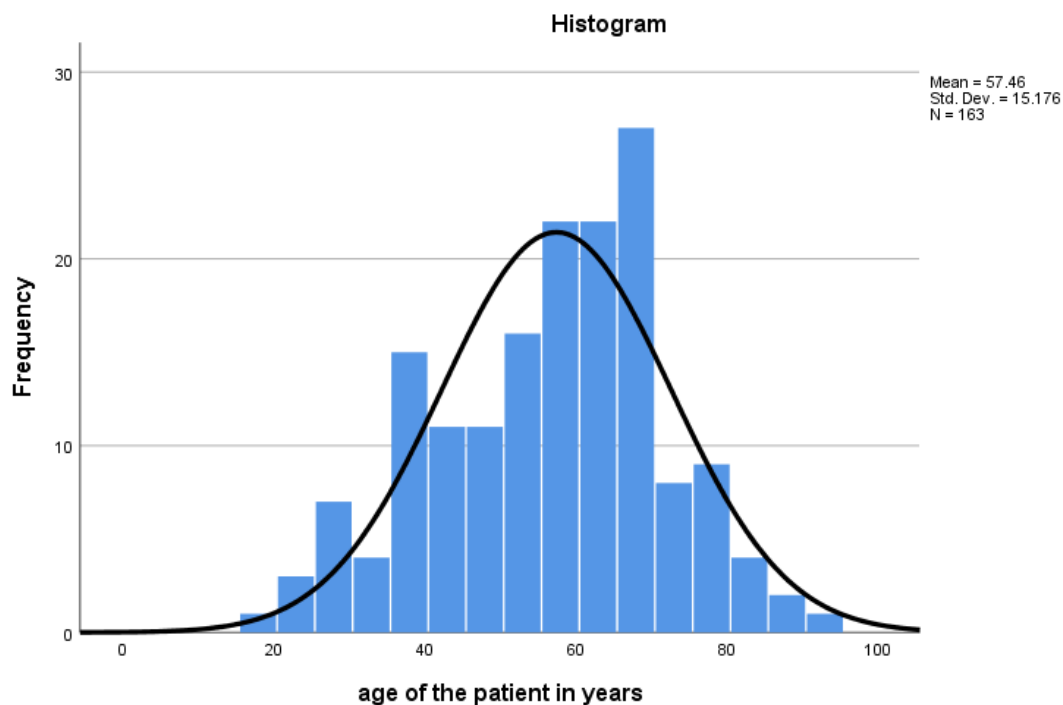


Figure 1: Age distribution of patients admitted to ekakotebe general hospital, covid19 ICU 2020

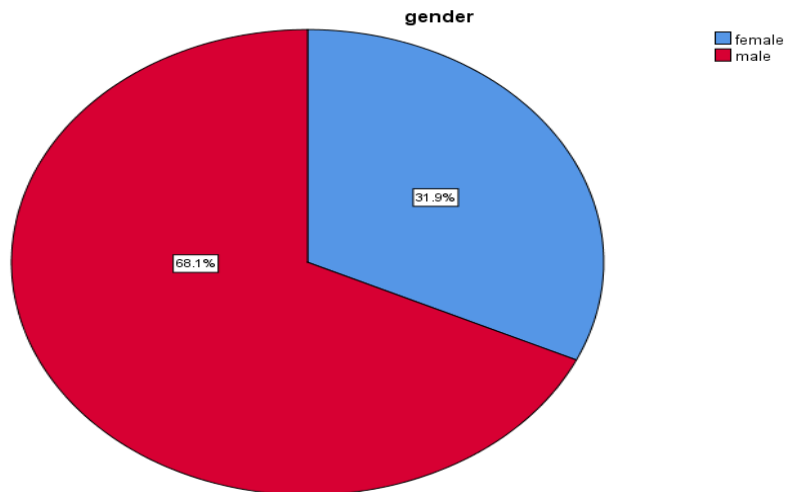


Figure 2: Gender frequency of patients admitted to ekakotebe general hospital covid19 ICU 2020

5.2 Outcome of patients

From 163 admitted patients total of eighty three (50.9%; CI 43.6-59.5) have died. From this patients nineteen (23%) were female and sixty four (77%) were male patients.

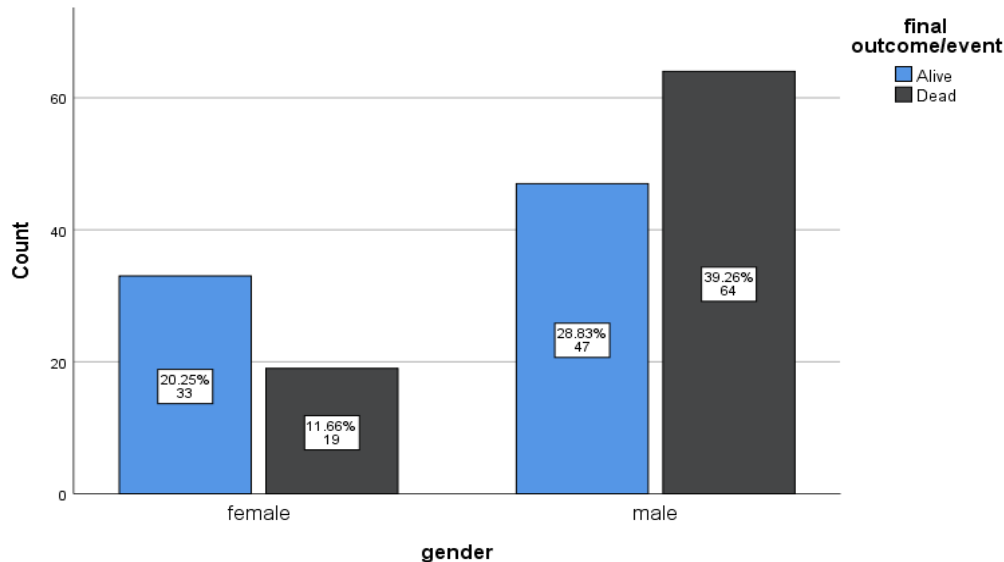


Figure 3: Outcome of patients by gender of patients admitted to ekakotebe general hospital covid19 ICU 2020

5.3 Comorbidities

One hundred fourteen (69.9 %;) had at least 1 comorbidity. Hypertension was the most common comorbidity (68 [41.7%]), followed by diabetic (54 [31.9]) and heart disease (30 [18.4%]).

Table 1: frequency of patients admitted to ekakotebe general hospital covid19 ICU 2020

Comorbidity	Number(percent)
Hypertension	68(41.7%)
DM	52(31.9%)
Cardiac	30(18.4%)
RVI/TB	15(9.2%)
Psychiatry disorders	13(8%)
Asthma/COPD	11(6.7%)
malignancy	11(6.7)
CKD	8(4.9%)
CLD	11(6.1%)
Stroke	6(3.7%)
Smoking	9(5.5%)

5.4 Symptoms before admission

Cough was the most common symptom of patients admitted to ICU of one hundred twenty five (76.7%) followed by shortness of breath of one hundred twenty four (76.1%) and easy fatigability of eighty five (52.1%) patients. and Median time from symptom onset to ICU admission was seven (95% CI, 6.1-8; IQR, 5-11) days

Table 2: frequency of symptoms of patients before admission to ekakotebe general hospital covid19 ICU 2020

Symptom	Number(percent)
Cough	125(76.7%)
Shortness of breath	124(76.1%)
Easy fatigability	85(52.1%)
Fever	67(41.1%)
Chest pain	36(22.1%)
Abdominal symptom/loss of appetite	36(22.1%)
Myalgia/arthralgia	34(20.9%)
Headache	33(20.2%)
Hemoptysis	25(18.3%)
Anosmia	20(12.3%)
sore throat	13(8%)

5.5 Angiotensin converting enzyme inhibitors

There were only twelve patients who were on ACE inhibitor and 8 of them have died. (Figure 4)

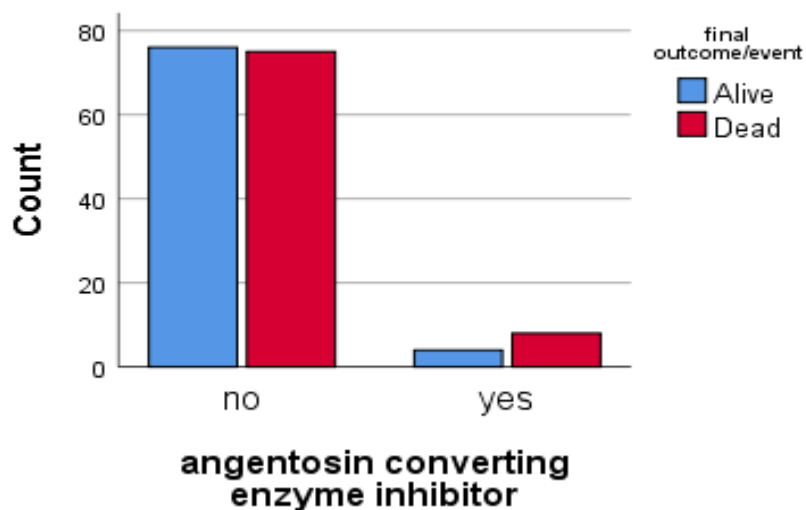


Figure 4 : frequency and outcome of patients who was on ACE inhibitors admitted to ekakotebe general hospital covid19 ICU 2020

5.6 Respiratory support upon admission to ICU

Up on admission to ICU 56.3% were on oxygen support (intranasal or facemask oxygen), 23.9% were on CPAP and 19.6% were on IMV. Forty three (26.4%) patients were intubated after mean length of stay of 4.47 (CI 3.5-5.5) days at ICU

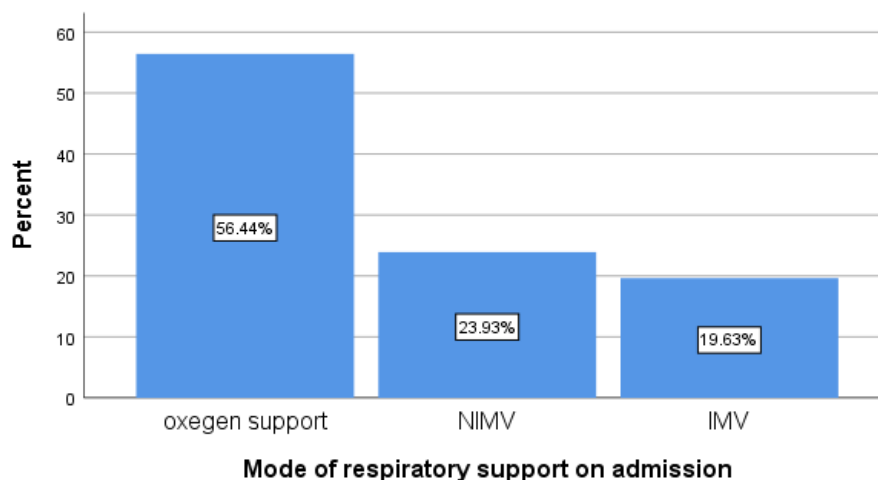


Figure 5: mode of respiratory support of patients upon admission to ekakotebe general hospital covid19 ICU 2020

5.7 Respiratory and laboratory parameters

The mean FIO₂ required upon admission was 75 % (95% CI 70-80) for died and 42% for the alive patients. The mean of PaO₂ /FIO₂ 155(95% CI 140-170).The mean of PaO₂/FIO₂ for alive was 196(95% CI 176-212) and the mean for died was 120(95% CI 104-138).

Table 3 : Means of respiratory and laboratory investigations of patients upon admission to ekakotebe general hospital covid19 ICU

Charachterstics	Total mean(SD)	N missed value
FIO ₂	58 (SD-25)	7
PAO ₂ /FIO ₂	155 (SD-85)	13
PEEP	9.5 (SD-4)	4
Wbc	12100 (SD-10038)	3
Platlet	1003 count (SD-7516)	4
Lymphocyte	1054 count (SD-892)	3
hematocrite	39mg/dl (SD-7.5)	7
AST	68 IU/L (SD-94)	4
ALT	77 iu/l (SD-130)	5
ALP	110 (SD-69)	13
Bilirubin	1.71 (SD-4.2)	138
Creatinin	1.47 (SD-1.48)	6
Urea	30.7 (SD-27)	20
Sodium	138.9 (SD-10)	3
potassium	6.4 (SD-16)	4
Chlorine	100 (SD-14)	49
Calcium	8 (SD-0.9)	49
magnisum	2.36 (SD-0.5)	125
PT	18 (SD-5)	60
PTT	32.9 (SD-13)	61
INR	1.4 (SD-0.5)	58

5.8 Acid base values

On ABG analysis eighty five (54.5%) patients had normal PH, sixty five (41.6%) had PH <7.35 and six (3.85%) had PH >7.45 up on admission.

Table 4: PH value of patients up on admission to ekakotebe general hospital covid19 ICU 2020

ABG PH value	Number (%)
PH- 7.35-7.45	85(54.5%)
<7.35	65(41.6%)
>7.35	6(3.85%)

5.9 Observation time and main outcomes patients admitted to Ekakotebe general hospital covid19 ICU

Cumulative observation time was 2772 patient-days from ICU admission to end of follow-up for the 163 patients (median observation time, 16 [range, 2-48] days; IQR, 10-22 days). After a median follow-up of 12 (IQR, 7-18; range, 2-40) days, there were 83 deaths (overall mortality, 50.9% CI 42.4%-60%) and. Rate of death was 3% patient days at hospital.

A total of 73 patients were put on mechanical ventilator and the Median duration on mechanical ventilator was 6(IQR3-12 95% CI 5-8, range 1-30) days. Only 7 of them survived during the study period. But 66 (92%) of the patients who were put on MV died at ICU.

Median length hospital stay was 16 (IQR 10-23 range 2-48) days. Median length of ICU stay was 7 (IQR 4-12 95% CI 5-8) days. Median duration on mechanical ventilator was 6 (IQR 3-12 95% CI 5-8, range 1-30) days. At the time of censoring, a total of 80 patients (49.1% 95% CI 41.7-56.4) didn't have the event (death). 77(96%) patients discharged home and 3(4%) patients are still at ICU.

A total of 16 patients (9.9% 95% CI 6.2-14.7) received hemodialysis and none of them survived. A total 17 (23%) patients of those who require IMV had iatrogenic pneumothorax.

5.10 Regression analysis result

Bivariate cox regression analysis of the dependent variable and each of the independent variables was done to assess the statically association and select independent variables statically significant association with dependent variable to include in the multivariate logistic cox regression analysis model. Variables that had association with the outcome variable with p value of <0.05 and variables that were expected to have association with the outcome variable from the literature were selected for the final model.

At bivarable analysis with cox regression hazard model; males were significantly associated with mortality(HR1.795; 95%CI(1.07-0.09), and patients with age above 60 years was also associated with higher hazard of mortality (HR 1.54; CI 0.934-2.55) but there was no statically significant association(p-0.09).

Patients who had symptom of hemoptysis and anosmia were significant associated with mortality at bivarable analysis.(p-<0.05)

Among comorbidities chronic liver disease and malignancy were associated with mortality at bivariable analysis ($p < 0.05$).

And there was no other illness or medication (ACE inhibitor) associated with mortality.

Patients who require higher FIO₂ (>60%), low PaO₂/fio₂ (<100), and high PEEP (>10) during admission had increased mortality ($p < 0.05$). Low lymphocyte count, elevated AST/ALT and creatinin/(>1.4mg/dl) and low PH(<7.35) had increase mortality($P < 0.05$).

Patients who were put on NIMV or IMV during admission were associated with increased hazard of mortality ($p \text{ value} < 0.05$).a

Table 5: bivariate cox regression hazard model of risk factors associated with mortality of patients admitted to ekakotebe general hospital covid19 ICU

Characheterstics	number	number of death	hazard ratio(95%CI)	p value
Age				
<60 years	52	20(38.4%)	1.34 (0.86-2)	0.193
>60 years	113	63(55.7%)	1.55(0.93-2.55)	0.09
Sex				
Women	52	19(36.5%)	1	
Male	111	64(57.6%)	1.80(1.07-2.99)	0.025*
Comorbidities				
None	49	20(40.8%)	0.77(0.46-1.27)	0.31
Hypertension	68	38(55.8%)	1.15(0.746-1.77)	0.52
Diabetic	52	27(52%)	0.99(5.74-1.441)	0.69
IHD	14	7(50%)	0.83(0.38-1.03)	0.63
CKD	8	5(62%)	0.89(0.36-2.2)	0.75
CLD	11	11(100%)	2.445(0.983-6)	0.05*
Asthma/COPD	11	7(63%)	1.83(0.84-4)	0.13

Stroke	6	5(83%)	1.351(0.54-3.30)	0.51
Malignancy	11	5(45.4%)	1.12(0.45-2.77)	0.05*
RVI/TB	15	8(53%)	1.44(0.67-2.50)	0.35
Smoking	9	6(66%)	1.16(0.55-2.67)	0.72
ACE inhibitors	12	8 (66%)	1.10(0.529-2.29)	0.79
Duration of symptom (>7 day/<7day)	70	37(52%)	1 (0.64-1.50)	0.98
Length of ICU stay				
< 7day	91	34(37%)	1	
>7day	72	49(68%)	1.22(0.78-1.90)	0.38
Respiratory Parameter				
FIO2 <60	104	36(34.6%)	1	
FIO2>60	55	47 (85%)	3.29 (2.1-5.06)	<0.001*
PaO2/FIO2 ratio				
>100	102	32(31%)	1	
<100	61	51 (83%)	3.782(2.4-5.9)	<0.001*
PEEP				
< 10 cmh2o	61	39(45%)	1	
>10 cmh2o	27	25 (30%)	1.672(1.01-2)	0.045*
Respiratory support During admission				
Oxygen support	92	30 (32%)	1	
NIMV	39	24(61%)	1.995(1.16-3.4)	0.012*
IMV	32	29(90%)	4.04(2.4-6.7)	<0.0001*
Blood gas analysis				
PH normal	85	32(37.60%)	1	
PH<7.35	65	47(72.3%)	2.785(1.759-4.4)	<0001*
PH>7.35	6	3 (50%)	1.562(0.47-5.0)	0.46
Lymphocyte count				
LYM>1000	65	17 (26%)	1	
LYM<1000	95	65 (68.4%)	3.334(1.95-5.1)	<0.0001*

Liver function test					
Normal	86	33(38.0%)	1		
elevated	73	49(67%)	2.269(1.45-3.53)	<0.0001*	
renal function test					
normal	115	45(40.5%)	1		
elevated	43	36 (83%)	2.569(1.655-3.98)	<0.0001*	
quick sofa score					
zero	36	9(25%)	1		
one	106	57(53.7%)	2.085(1.38-5.6)	0.004*	
2 or more	19	15 (80%)	4.05(1.76-9.3)	0.001 *	
Fever	67	38(56.7%)	1.465(0.95-2.25)	0.84	
Cough	125	61(48.8)	0.89(0.49-1.31)	0.39	
Shortness of breath	124	64(51.6%)	1.103(0.66-1.83)	0.70	
Easy fatigability	85	49(57.6%)	1.115(0.74-1.8)	0.5	
Sore throat	14	4(28.5%)	0.537(0.192-1.468)	0.22	
Myalgia/arthralgia	34	16(47%)	1.007(0.58-1.74)	0.98	
Anosmia	20	15(75%)	2.22(1.3-4.05)	0.04*	
Hemoptysis	25	18(72%)	1.75(1.03-2.96)	0.03*	
Chest pain	36	18(50%)	1.005(0.59-1.695)	0.98	
Headache	33	19(57%)	1.009(0.65-1.83)	0.71	
Abdominal symptoms	22	12(54.5%)	1.12(0.6-2.05)	0.73	
1=reference *= P-value < 0.05					

Multivariable analysis

At multivariate analysis with cox regression hazard model sex and age were not significantly associated with mortality (HR: 1.16 (CI: 1.16(0.6-2)).among comorbidities CLD was significantly associated with mortality with (HR: 4 (95%CI 1.28-12).

Among laboratory findings Elevated liver function (HR: 1.83 95 CI (1.08-3.13 p -0.02) and PH<7.35 were significantly associated with mortality (HR: 1.8(95% CI 1.05-3)), p value- 0.03.(table

Patients who put on invasive mechanical ventilator were significantly associated with mortality (HR: 2.27(2.27 (1.12-4) ,p <0.02).(table 8)

There were no any symptom significant associated with mortality.

Table 6 : Multivariable cox regression hazard model analysis of risk factors associated with mortality of patients admitted to ekakotebe general hospital covid19 ICU 2020

Characheterstics	hazard ratio (95% CI)	p value
Anosmia	1.55 (0.89-2.9)	0.18
Hemoptysis	1.1(0.6-2)	0.75
Stroke	1.29(0.4-4)	0.66
Malignancy	2.332(0.66-8.1)	0.18
PaO2/fio2 (<100/>100)	1.512(0.72-3)	0.26
Lymphocyte count<100	1.79(0.9-3)	0.08
Increased LFT	1.83(1.08-3.13)	0.02*
Increased RFT	0.96(0.5-1.7)	0.89
Age above 50	1.63(0.8-1.7)	0.12
Fio2<60	1.69(0.8-3)	0.13
Sex(M/F)	1.16(0.6-2)	0.62
PH<7.35	1.80(1.05-3)	0.03*
CLD	4.0(1.28-12)	0.01*
IMV	2.27(1.12-4)	0.02 *

6. DISCUSSION

We provide analysis to 163 patients and though low rate of admission²⁸²⁵ : mortality of our study was 50.4% of those admitted to ICU which is similar to study done at Brazil²⁶, but higher than studies done at European countries²⁹³⁰²⁴²⁹. Mortality of patients with critically ill patients with covid19 varied among published literatures³¹¹⁹. This variability may explained by ICU organization, availability of advanced equipment like ECMO, dialysis machine²². And at sub analysis group 73 patients who require mechanical ventilation had mortality rate of 92% which is similar to earlier study done at Wuhan china⁹.

In contrary to study done in Italy ,brazil and Germany: Age and sex were not independent risk factor for mortality in our study, though males have higher mortality at bivariable analysis²⁹³²²⁴. This may be due to small sample size or and may be smaller median age of our population distribution.

Among comorbidities, hypertension was the most frequent followed by diabetic and cardiac illness, despite this there was no significant association with mortality. Conversely patients with chronic liver disease, although affecting small percentage of patients were independently associated with mortality which is contrary to study done in Brazil, Italy and Spain, where by hypertension, diabetic and cardiac illness found to have significant association with mortality.²⁴⁴³²³³. But our study is similar with early study done in Wuhan china with small sample size of 197 patients and they didn't found any comorbidity that had significant association with mortality⁴. Therefore this may be due to our study has small sample size.

Data on the effect of drugs acting on the renin-angiotensin system are of particular interest because ACE2 is the primary receptor for SARS-CoV-2 entry into the host cells³¹. in our patients who took long term medication of ACE inhibitors ,though small sample size there were no significant association of mortality ,similar to studies done in Italy²⁴.

Similarly patients with elevated liver enzyme (ALT/AST>40IU/L HR: 1.8 (1.08-3.1) p-0.02), and PH<7.23 (HR:1.8(1.05-3) p-0.03) were found to have significant association with mortality which is similar with study of the Systematic review and meta- analysis done by journal of medical virology²⁵. This will explain the fact that the increment of pro-inflammatory factors predicts the mortality of covid19 patients³³²⁵.

Patients who require invasive mechanical ventilation was independently associated with mortality at covid19 ICU but High fio2 (>60), low PaO2 (100) and high PEEP (>10) were not independently significantly associated with mortality which is contrary to other studies done in Italy and USA^{24 32}. This may be due to high mortality rate of patients who require intubation.

7. STRENGTH AND LIMITATION

7.1 Strength

Lack of literature available in Ethiopia and other developing countries makes this study a stepping stone to various small and large scale studies in this area.

7.2 Limitations

Our study has several limitations

It is retrospective study data mainly collected by chart review and IHMS data recorded of the hospital.

It has small sample number of patients, which we believe it may have effect on result of analysis especially for age and comorbidities which were having significant association on other researches

And our study couldn't asses' important variable like body mass index and respiratory system compliance which may have significant association on mortality.

Lack of complete laboratory investigations and lose patients chart.

8. CONCLUSION AND RECOMMENDATION

8.1 Conclusion

SARS –covid19 has a serious challenge to our health care system in our country Ethiopia and the world¹⁹. Despite our hospital has lower rate of admission to our ICU, the mortality rate is high in our ICU³. Despite our limitation our study data highlights the important factors associated with mortality patients with covid19 admitted to our ICU.

Though supportive care management is the main stay of critically ill covid19 positive patients³⁴, we may need to advance our ICU organization and skilled personnel to decrease the mortality rate. Critical patients who require invasive mechanical ventilation had high mortality rate and absolute mortality.

8.2 Recommendation

We recommend that a prospective study should be undertaken, with higher number of patients, to strengthen the findings of this study.

We also recommend that proper recording and chart keeping might be important for this study.

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10 ANNEX

10.1 subject information sheet

Addis Ababa University School of Medicine Department of Anesthesia, Critical Care and Pain Medicine Information Sheet

Study title – mortality and associated risk factors covid19 patients admitted to covid19 ICU at EkaKotebe general hospital Addis Abeba, Ethiopia 2020.

Purpose-- The study will be, helpful to evaluate mortality and associated risk factors with of covid19 patients admitted to covid19 ICU at Eka Kotebe general hospital Addis Abeba, Ethiopia. Information collected during this study could be used by the [MOH], organizations supporting the services, and researchers, for planning service improvement or for conducting further studies of health services. More over the main aim of this study is to write a thesis as a partial requirement for the fulfillment of the requirement for the Specialty certificate in Anesthesiology.

Confidentiality: The information provided from the chart will be confidential .There will be no information that will identify the respondent's personal information and your organization. The questioner will be coded to exclude showing names.

Contact address

If there are any questions or enquires any time about the study, please contact and speak to the principal investigator. Dr Tessema baraki /0914856652, Tessemabaraki1@gmail.com.

1.2 Questioner

1 Age _____in years 2 Sex M ☐ F ☐

2 Patient symptoms before admission

1 fever ☐ 2 cough ☐ 3 dyspnea ☐ 4 sore throat ☐ 5 myalgia ☐ 6 anosmia ☐

7 chest pain ☐ 8 headache ☐ 9 hemoptysis ☐ 10 runny nose

8 nausea vomiting ☐ 9 abdominal pain ☐ 10 diarrhea ☐

3 How long does the patient have symptom before admission to ICU? _____days

4 what was the worst vital sign on the first 24 hour upon admission to ICU?

1 PR ____ RR ____ T0 ____ BP ____ GCS ____ qSOFA score ____
APACHEII ____

5 What comorbidities does the patient have?

1 none ☐ 2 hypertension ☐ 3 diabetic ☐ 4 IHD ☐ 5 other cardiac illness ☐

6 CKD ☐ 7 CLD ☐ 8 Asthma ☐ 9 COPD ☐ 10 stroke ☐ 11 RVI ☐

12 Malignancy ☐ specify please _____ 13 others _____

6 Was the patient taking any of this medication? If yes, please write for how long he/she taking.

1 aspirin ____ 2 ACEI ____ 3 statin ____ 4 blocker ____ 5 ART ____ 6 CA channel blockers ____

7 others. _____

7 did the patient smoke cigarette? 1 yes ☐ 2 no ☐ , if yes _____-pack/day _____years

8 what was the mode of respiratory support upon admission to ICU?

1 oxygen support 2 NIMV 3 IMV

9 If the patient was on Mechanical ventilator support, what was his oxygenation status during admission? 1 FIO2 ____ 2 PEEP ____ 3 PaO2/FIO2 Or PSO2/FIO2 4 PH ____

5 PCO2- ____ 6 lactate ____ (please write ABG analysis for all patients)

10 Was the patient put IMV during his stay at ICU, up on admission that was not? 1 yes ☐ 2 no ☐

10.1 if yes to no 10, how many days did the patient stay at ICU before intubation ? _____ days.

11 how many days did the patient stay on IMV? _____ days

12 Was the patient put on prone position during his stay at ICU? 1 yes 2 no (duration _____)

13 patient laboratory investigations upon admission

1 wbc ____ 2 hematocrit ____ 3 PLT ____ 4 Neutrophil count ____ 5 lymphocyt ____

7 ALT ____ 8 AST ____ 9 ALP ____ 10 Bilirubin ____ 11 Cr ____ 12 BUN ____

13 Na+ ____ 14 K+ ____ 15 CL- ____ 16 Ca+ ____ 17 Mg+ ____

18 PT ____ 19 PTT ____ 20 INR ____ 21 Albumin ____ 22 cholesterol ____

23 Troponin ____ 24 other IX ____ specify please.

14 X RAY finding 1 normal ☐ 2 bilateral infiltrate ☐ 3 unilateral infiltration ☐ 4 other, specify please

15 did the patient require vasopressor up on admission? 1 yes ☐ 2 no ☐

16.1 if yes 1 single pressor _____ 2 double pressor _____ [Write the type and dose}

17 was the patient require new or revision of antibiotics for new infection during his stay at ICU?
1 Yes ☐ 2 no ☐

18 did the patient had any complication during his stay at ICU?

1 re intubation ☐ 2 pneumothorax ☐ 3 septic shock 4 AKI ☐ 7 PE/DVT _____
5 E- imbalance ☐ _____ specify. 6 bed sore ☐ 8 others please specify _____

19 did the patient require dialysis 1 yes ☐ 2 no ☐

20 how many days did the patient stay at ICU? _____days

21 what was the outcome of the patient? 1 died ☐ 2 discharged to ward ☐

22 what happened to the patient discharged to ward? 1 discharged to home ☐ 2 readmitted to ICU ☐ 3 died at ward ☐ 4 still he/she is at hospital ☐

23 how many days did the patient stay at the hospital since admission to ICU? _____days