COLLEGE OF HEALTH SCIENCES

SCHOOL OF NURSING AND MIDWIFERY

DEPARTMENT OF NURSING

PREVALENCE AND ASSOCIATED FACTORS OF CARDIAC ARRHYTHMIA AMONG CRITICALLY ILL COVID-19 PATIENTS AT EKA KOTEBE COVID-19 CENTER ADDIS ABABA ETHIOPIA 2021, CROSS-SECTIONAL STUDY

BY: KIDEST DEMESSIE (BSC)

A RESEARCH THESIS TO BE SUBMITED TO THE SCHOOL OF GRADUATE STUDENTS, ADDIS ABABA UNIVERSTY COLLEGE OF HEALTH SCIENCE SCHOOL OF NURSING AND MIDWIFERY DEPARTMENT OF NURSING IN PARTIAL FULFILMENT OF THE REQUARMENTS FOR THE A DEGREE OF MASTERS IN CARDIOVASICULAR NURSING

JUNE, 2021

ADDIS ABABA, ETHIOPIA

ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF NURSING AND MIDWIFERY

DEPARTMENT OF NURSING

PREVALENCE AND ASSOCIATED FACTORS OF CARDIAC ARRHYTHMIA AMONG CRITICALLY ILL COVID-19 PATIENTS AT EKA KOTEBE COVID-19 CENTER ADDIS ABABA ETHIOPIA 2021, CROSS-SECTIONAL STUDY

BY: KIDEST DEMESSIE (BSC)

INSTRUCTORS

Mr.'s TEFERA MULUGETA (Asst. prof, PhD fellow),

Dr. HUSSIEN MEKONNEN (PhD)

A RESEARCH THESIS TO BE SUBMITED TO GRADUATE STUDIES, ADDIS ABABA UNIVERSTY COLLEGE OF HEALTH SCIENCE SCHOOL OF NURSING AND MIDWIFERY, DEPARTMENT OF NURSING IN PARTIAL FULFILMENT OF THE REQUARMENTS FOR THE A DEGREE OF MASTERS OFSCIENCE IN CARDIOVASICULAR NURSING

JUNE, 2021

ADDIS ABABA, ETHIOPIA

APPROVAL BY THE BOARD OF EXAMINATION

THIS THESIS BY KIDIST DEMSSIE (BSC NURSE) IS ACCEPTED IN ITS PRESENT FORM BY BOARD OF EXAMINERS AS SATISFYING THESIS REQUIREMENT FOR THE DEGREE OF MASTERS IN CARDIOVASICULAR NURSING.

THESIS EXAMINER:

Dr FEKADU AGA		_____	_____
FULL NAME	RANK	SIGNATURE	DATE

RESEARCH ADVISORS:

FULL NAME			
TEFERA MULUGETA	**Ass.Prof,PhD fellow**	_____	_____
FULL NAME	RANK	SIGNATURE	DATE
Dr HUSSIEN MEKONNEN	**PHD**	_____	_____
FULL NAME	RANK	SIGNATURE	DATE

DEPARTMENT HEAD:

NIGUSE TADELE	MSC, Asst. Professor	_____	_____
FULL NAME	RANK	SIGNATURE	DATE

DECLARATION

By my signature below, I declare and affirm that this thesis is my own work. I have followed all ethical principles of scholarship in the preparation, data collection, data analysis and completion of this thesis. All scholarly matter that is included in the thesis has been given recognition through citation. I affirm that I have cited and referenced all sources used in this document. Every effort has been made to avoid plagiarism in the preparation of this thesis.

This thesis is submitted in partial fulfillment of the requirement for a graduate degree from the Addis Ababa University at College of Health Sciences, School of Nursing and Midwifery Department of nursing. The thesis is deposited in the Addis Ababa University Digital Library and is made available to local, national and international scientific community. I solemnly declare that this thesis has not been submitted to any other institution anywhere for the award of any academic degree, diploma or certificate.

Brief quotations from this thesis may be used without special permission provided that accurate and complete acknowledgement of the source is made. Requests for permission for extended quotations from, or reproduction of, this thesis in whole or in part may be granted by the Head of the Department or all advisers of the theses when in his or her judgment the proposed use of the material is in the interest of scholarship and publication. In all other instances, however, permission must be obtained from the author of the thesis.

PRICIPAL INVESTIGATOR:

KIDEST DEMESSIE SIGNATURE: _____ DATE: _____

RESEARCH ADVISORS:

TEFERA MULUGETA	**Ass. Prof, PhD fellow**	_____	_____
NAME	RANK	SIGNITURE	DATE
Dr HUSSIEN MEKONNEN	**PHD**	_____	
_____			
NAME	RANK	SIGNITURE	DATE

ACKNOWLEDGMENT

First of all, my gratitude goes to Addis Ababa University, college of health science, school of nursing and midwifery for giving this chance and sponsoring me to do this thesis. My acknowledgment also goes to Addis Ababa health bureau, for sponsoring my MSc education. I would also like to forward my deepest appreciation and thanks to my advisors, advisors Tefera Mulugata (Asst. prof, PhD fellow) and Hussien Mekonnen (PHD) for unreserved encouragement, provision of relevant, timely comments and guidance of the overall process of from proposal development to the end of this thesis. My thanks also go to Eka Kotebe COVIOD-19 treatment center management and staffs particularly Intensive care unit case team. It is also my pleasure to thank the data collectors and supervisor. Finally, a big Thank You to my parents for all their sacrifices and love through the years.:

ABBREVIATIONS AND ACRONYMS

ACE2	**A**ngiotensin-**C**onverting **E**nzyme 2
AF	**A**trial **F**ibrillation
AICU	**A**dult **I**ntensive **C**are **U**nit
AZT	**A**zithromycin
COVID-19	**C**oronavirus **D**isease 20**19**
CV	**C**ardiovascular
HCQ	**H**ydroxychloroquine/**C**hloroquine
HDU	**H**igh **D**ependency **U**nit
ICU	**I**ntensive **C**are **U**nit
MERS	**M**iddle **E**ast **R**espiratory **S**yndrome
MSC	Masters of Science
SARS	**S**ever **A**cute **R**espiratory **S**yndrome
SPSS	Statistical Package for the Social science
SVT	**S**puria Ventricular **T**achycardia
TDP	**T**orsades **D**e **P**ointes
VA	**v**entricular **A**rrhythmias
VF	**V**entricular **F**ibrillation
VT	**V**entricular **T**achycardia
WHO	**W**orld **H**ealth **O**rganization

Table of Contents

List of tables

List of figures

ABSTRACT

Background: According to World Health Organization (WHO) June 2 report there were total of 172,173,283 cases and 3,695.990 deaths and, 154, 832,586 recovered with the highest prevalence in the United States America. Cardiovascular and arrhythmic events have been reported in hospitalized COVID-19 patients. COVID-19 has the potential to cause myocardial injury and noted to have heart failure in a study of inpatients from previous studies. There are researches limitation regarding the prevalence and associated factors of the disease in general and particularly among COVID-19 critically ill patients. Understanding the situation in Ethiopia would help to us to improve their status and outcome of clinical service.

Objective: To assess the Prevalence and associated factors of cardiac arrhythmia among critically ill COVID-19 patients in Eka Kotebe COVID-19 center Addis Ababa Ethiopia, 2020.

Method: A Cross-sectional study was applied among 388 sampled medical records of COVID-19 patients at Eka Kotebe hospital. The study periods were from February 25-April 30, 2021. Sample size was calculated by using single and double population proportion formula, A pre-tested and structured record reviews checklist was used to collect data and the data entry and data analysis was done by statistical software like EPI data and SPSS. Bivariable and multivariable binary logistic regression was used to examine the relationship between the dependent and independent variables.

Result: The prevalence of cardiac arrhythmia among critically ill COVID-19 positive patients with 91.5% response rate was found to be 71.4%. Presence of comorbidity (AOR: 11.00 95%CI; 5.57, 21.70), substance use (AOR: 2.77 95%CI 1.54, 4.99), hypokalemia (AOR: 6.85 95%CI; 2.96, 15.86), hyperkalemia (AOR: 9.31 95%CI; 4.75, 18.22) and hypotension (AOR: 2.75 95%CI 1.27, 5.92) are statistically significant associated factors for cardiac arrhythmia.

Conclusion: High prevalence of cardiac arrhythmia was observed in Eka Kotebe critically ill COVID-19positive patients. Presence of underline comorbidity, hypokalemia, hyperkalemia, hypotension and substance (chat, alcohol, cigarettes and others) use were significantly associated with cardiac arrhythmia. Health service organizations have to give attention to monitor vital sign specially blood pressure and to monitor electrolyte balance.

Key Words: COVID-19, comorbidity and Arrhythmia.

1. Introduction

1.1 Background

Coronavirus disease 2019 (COVID-19) is defined as illness caused by a novel coronavirus now called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; formerly called 2019-nCoV), which was first identified amid an outbreak of respiratory illness cases in Wuhan City, Hubei Province China(1). The most typical manifestation of COVID-19 is bilateral interstitial pneumonia, which can be complicated by acute respiratory distress syndrome, multi-organ failure and death in up to 30% of high-risk patients.COVID-19 is known to be a relative of extreme acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) and is caused by the SARS-CoV-2 beta coronavirus, which affects the lower respiratory tract and manifests as human pneumonia(2).

A cardiac arrhythmia simply defined as a variation from the normal heart rate and/or rhythm that is not physiologically justified. An arrhythmia is an irregular heartbeat which sounds like a flutter. In some cases, heart rate may not be altered or in other cases it either becomes sluggish or quick. Generally, arrhythmia can be asymptomatic or mild symptoms such as feeling of light headedness may be apparent. In severe cases tiredness, lightheadedness as well as death might occur(3).As this global pandemic continues to rage, COVID-19-related cardiovascular diseases, particularly arrhythmic manifestations have become apparent.(4)An overall cardiac arrhythmia incidence of 17 percent in patients hospitalized for COVID-19 was suggested by early reports from China. In patients with COVID-19 admitted to the intensive care unit (ICU), a higher arrhythmia rate (44 percent) was observed)(5).Cardiovascular and arrhythmic events have been reported in hospitalized COVID-19 patients. However the signs of arrhythmia and the therapeutic strategies used were not clearly described in these cases (6).

Although the underlying pathophysiology has remained elusive, various single-center studies and surveys around the world have reported a spectrum of electrophysiology issues associated with the disease and its therapies, specifically atrioventricular heart block, atrial fibrillation (AF), and polymorphic ventricular tachycardia (VT). Coexisting hypoxia, electrolyte disarray, and the administration of arrhythmogenic medications (eg, hydroxychloroquine, azithromycin) make it difficult to ascertain the direct and indirect contribution of COVID-19 on cardiac arrhythmias. A

58% increase in out-of-hospital cardiac arrest in the Lombardy region of Italy during the first 40 days of the COVID-19 pandemic raised concerns regarding the risk of arrhythmia associated with SARS-CoV-2 infection. In the United States, a large single-center study of 700 patients demonstrated that admission COVID-19 patients to the intensive care unit were independently associated with a 10-fold increase in arrhythmia risk.

Based on the literature, there is reason to suspect a high prevalence of cardiac arrhythmia in covid-19 patient, but the only limited finding is done especially in our country. Such a gap of cardiac arrhythmia should be addressed scientifically by supplementing concrete evidence about the burden of cardiac arrhythmia and factors associated withfor policymakers and concerned stakeholders which would be helpful for sound decision making. Also, a Lack of information about cardiac in covid-19 patients may be a factor that contributes to poor or neglected attention for cardiac disease for covid-19 patients. Appropriate cardiac disease health interventions and care should be a priority for this population.

1.2. Statement of the problem

COVID-19 was initially reported to the WHO on December 31, 2019. On January 30, 2020, the WHO declared the COVID-19 outbreak a global health emergency. On March 11, 2020, the WHO declared COVID-19 a global pandemic(7). According to WHO report which is updated on June 2, 2021 there were total cases of 172,173,283;3,695.990 death,and154, 832,586 were recovered with the highest prevalence in the united states of America; and In African countries with a total of 4,909,386 cases, 131,632 deaths, 4,426,070 recoveries (with South Africa's highest cases since1,675,013 total cases, 56,711 deaths and 1,565,684 recovered) (8).

In Ethiopia, the first case of COVID-19 was reported in 2020 March 16 by the Ethiopian Ministry of Health and introduced by two foreigners(9). This number is higher also in Ethiopia i.e. 272,036cases , 4,178 deaths, 242,442 recovered on June 2, 2021 WHO on African report (10).

The rapid spread of the novel coronavirus (COVID-19) has caught much of the world off-guard. (11)COVID-19 can have a major impact on heart function and induce cardiac injury. Cardiac injury is associated with increased severity of the illness and fatal results. In the pathophysiology of cardiac complications, a number of pro-inflammatory mediators play a key role in COVID-19.

Previous research has identified that common complications in COVID-19 are ARDS (20%), arrhythmias (17%), shock (9 %), and acute heart injury (7 %). A better understanding of the cardiovascular effects of SARS-CoV-2 infection is therefore essential for mitigating poor prognosis in patients with COVID-19 (12).

A study conducted in China reported 7 percent overall incidence rate of ventricular tachycardia (VT) and ventricular fibrillation (VF) during hospitalization(13). In addition, reports from Italy and New York City have described a concomitant increase in out-of-hospital cardiac arrests that are associated with the cumulative incidence of COVID-19(14).Cardiac arrhythmias, including life-threatening VAs, may be the consequence of direct effects of COVID-19 infection, but also of the deleterious effects of systemic illness(15).

Most of the literature shows myocardial injury especially cardiac arrhythmia was observed in critically ill COVID-19 patients. Know that cardiac injury is an important predictor of death. The initial findings suggested that patients admitted to the intensive care unit (ICU) had an arrhythmia burden of 44.4% however, the exact nature of these arrhythmias was not characterized(16).But arrhythmia could be considered one of the main complications of COVID-19, and proactive monitoring and management of arrhythmia is needed(8).

COVID-19 has the potential to cause myocardial injury, with at least 17% found to have an elevated troponin and 23% noted to have heart failure in a study of 191 inpatients from Wuhan, China. And fulminant myocarditis with cardiogenic shock have also been reported, with associated atrial and ventricular arrhythmias(17).These challenges are somewhat different to traditional arrhythmia management, depending on the clinical situation. There are patients with arrhythmias caused by COVID-19(18).A study has shown that cardiac arrhythmias may occur in up to 44% of patients with severe COVID-19, and has been associated with an increased risk of death. Cause of death analysis in COVID-19 patients revealed that approximately 40% of deaths were due to myocardial damage and/or heart failure (42).

The Covid-19 infection increases the susceptibility of patients to life-threatening cardiac arrhythmias. This is not only due to the pathophysiology of the virus in cardiac myocyctes but also the combination with cardiac comorbidities and pro-arrhythmic drug interactions. Appropriate precaution and measures must be executed in order to prevent adverse patient outcome. However, the manifestations of arrhythmia and the treatment strategies used in these

patients were not well described. Efforts have been made a better understand the cardiac arrhythmic symptoms and treatment methods in hospitalized COVID-19 patients. The better understanding of cardiac arrhythmic symptoms, its prevalence and factors associated assists in provision of care. Consequently, this research assessed the magnitude of arrhythmias, and its factors associated with cardiac arrhythmias in critically ill COVID-19 patients. So far now in our country no published data that indicates cardiovascular disease incidence following COVID 19 infection specifically cardiac arrhythmia and associated factors. So, this study will fill the information gap related to the prevalence and associated factor of cardiac arrhythmia among critically ill COVID-19 patients.

1.3. Significance of the study

The study used to identify the associated factors in cardiac arrhythmia among critically ill patients with COVID-19 and its prevalence. This study would be helpful in providing basic information for educators. Health care service provider (Nurses and Doctors), who work at COVID-19 treatment center as a baseline in their counseling/health education session of cardiac arrhythmia and researcher's. Health care providers could also be assisted in initiating early screening, diagnosis and management of arrhythmias in patients with COVID-19 based on the finding. It will serve as an input resource and data for the health administration on the current status of cardiac arrhythmia among COVID-19 patients. The health professional and other non-governmental organizations will use the finding for their irreplaceable support and intervention in the hospital for COVID-19 patients. The researcher will use it as a background on the current status of cardiac arrhythmia prevalence and will help them to do and investigate more with different techniques. At large it will help as input for policymaker, service planners, and strategy designers on the current status of cardiac arrhythmia specifically in COVID-19 patients, Addis Ababa, Ethiopia.

2. LITERATURE REVIEW

2.1. Overview of COVID-19andCardiac Arrhythmia

The review of the WHO data reveals some perplexing facts (19).Impairment of coagulation system by SARS-CoV-2 the first experiences in the Wuhan province in China and then in other parts of the world allowed to estimate the putative incidence of thromboembolic complications ranging from around 15% to 85% in hospitalized COVID-19 patients. Of note, thromboembolic risk is influenced by race and ethnicity, and is significantly lower in Chinese compared to Caucasian individuals(20). A systematic review done on the incidence and treatment of arrhythmias secondary to coronavirus infection in human the cumulative incidence of arrhythmia across studies of hospitalized patients was 6.9%. Drug-induced long QT syndrome secondary to anti-malarial and anti-microbial therapy was a significant contributor to arrhythmia formation, with an incidence of 14.15% (21).

2.2. Prevalence of arrhythmia in COVID-19 patients

Recent studies have shown that myocardial injury is prevalent primarily in critically ill COVID-19-infected patients through various mechanisms, primarily due to direct cardiomyocyte damage(22). Cardiovascular diseases (CVDs) have become a major predictor of the severity of COVID-19 and Infection with COVID-19 can also precipitate known arrhythmias that may increase the risk of morbidity and mortality(23)(18). In addition, more frequent malignant arrhythmias developed in patients with elevated troponin including ventricular tachycardia/ventricular fibrillation, compared to those without elevated troponin(24). In addition, during the recovery phase of acute pulmonary disease, there have been anecdotal reports and experiences of patients developing cardiopulmonary arrest with pulseless electrical activity or ventricular fibrillation(25).

A study conducted in China in patients with COVID-19, cardiac arrhythmia was similar in 2003 to patients with SARS. Sinus tachycardia was the most common type of arrhythmia in patients with COVID-19, particularly in severe and critical cases. Persistent tachycardia was not consistent with oxygen saturation and body temperature (26).

A study conducted in Wuhan, China 7 percent of patients report palpitations as a presenting symptom. 16.7% of hospitalized patients and 44.4 % of ICU patients with COVID-19 had cardiac arrhythmias. (22)

A study conducted University of Pennsylvania; Philadelphia, Pennsylvania identified 53 arrhythmia-related events including 9 cardiac arrests, 25 incident AFcases, 9 clinically significant Brady arrhythmia's, and 10 NSVTs. With the exception of the cardiac arrest cases, none of the 3 arrhythmia types were independently associated with acute mortality (5).

A retrospective analysis of patients hospitalized with COVID-19 infection worldwide with and without incident cardiac arrhythmias shows from 4526 patients across 4 continents and 12 countries 18% of whom had an arrhythmia COVID-19 positive patients who developed cardiac arrhythmia 51% survived to hospital discharge(27).

A survey conducted by Gopinathannair.R and his associates reported that In COVID-19 patients, a variety of supraventricular and ventricular arrhythmias were reported, (21%) atrial fibrillation cases, (5.4%) reported atrial flutter,(3.5%) reported sustained atrial tachycardia, and (5.7%) supraventricular paroxysmal tachycardia(4).

2.3. Factors associated with arrhythmias in patient with COVID-19

The combination of severe infection, hypoxia, sepsis, and/or hemodynamic instability predisposes patients with COVID-19 to myocardial injury and potentially dangerous arrhythmias. In this brief narrative review, the authors highlight the incidence, risk factors, and pathophysiology of development of arrhythmias in patients with COVID-19, and provide a pragmatic approach for risk mitigation and management of these arrhythmias(28).Patient with hypokalemia, hypomagnesaemia, bradycardia and class IA and class III anti-arrythmics are at higher risk for QT prolongation with known risk factors. Electrolytes should be continually monitored, maintaining a potassium level of >= 4mEq/L and a magnesium level of >=2mEq/L to avoid amassing risk factors.(29)

2.3.1. Socio-demographic factors

The following symptoms were proportionally more prevalent in females compared with males: ($P < 0.001$). Males more frequently suffered from cough and fever ($P < 0.001$). There was no significant difference in the duration of the disease regarding sex(30). Also, age and incident AF (OR 1.05 [95% CI 1.02 – 1.09]); and prevalent heart failure and brady arrhythmias (OR 9.75 [95% CI 1.95 – 48.65]) were independently associated(14).

Race also has been proposed as another determinant for increased mortality in patients affected by COVID-19, with African-Americans at a higher risk. Although this is likely due to a combination of multiple cultural and socioeconomic factors, an underlying genetic susceptibility to SARS-CoV-2 infection(31,32)

2.3.2. Behavioral factors

In 2019, around a fourth (24.9%) of the global population (both sexes combined) aged 15 years and older were current users of some form of tobacco, and more than 8 million people died from tobacco use including both tobacco smoking and smokeless tobacco use in 2017. Active smoking has been reported to increase the risk of viral respiratory diseases. Smokers have an increased risk for community-acquired pneumonia. About 20% of COVID-19 patients develop pulmonary infiltrates and some of these will develop very severe disease, hypoxia, and progression to ARDS. The angiotensin-converting enzyme (ACE-2) protein, which is expressed on the surface of lung type-2 pneumocystis, is an entry receptor for SARS-CoV-2. 4 ACE-2 gene expression and is higher in smokers than in non-smokers, which may explain the increased risk of severe COVID-19 in this population. Effects of current smoking (9.4%, vs. 5.6% among former smokers or nonsmokers(33).

A retrospective observational study done in Turkey older age, chronic obstructive pulmonary disease (COPD) and CAD were significantly associated with ICU admission. Current smoking and former smoking were risk factors for ICU admission. Older age, COPD, CAD and congestive heart failure (CHF), were significantly associated with mortality. Current smoking and former smoking were also risk factors for mortality(34). A meta-analysis of 647 studies showed that current smokers (pooled OR 2.17, 95% CI 1.70– 2.76, n = 13 studies; pooled HR 1.52, 95% CI 1.13–2.04, n = 7 studies) and ex-smokers (pooled OR 1.49, 95% CI 1.26–1.75, n =

8 studies; pooled HR 1.18, 95% CI 0.91–1.52, n = 6 studies) were more likely to develop CAP compared to never smokers(35).

2.3.3. Clinical factors

Comorbidities were associated with the severity of COVID-19. The fatality rate also increased in patients with comorbidities (36). Comorbidities including chronic cardiac disease, non-asthmatic chronic pulmonary disease, chronic kidney disease, liver disease, and obesity were associated with higher in-hospital mortality(37). There are conflicting results in studies for the prevalence of comorbidities and the factors affecting COVID-19 severity and mortality. The interpretation of the effects of smoking on COVID-19 is difficult, because one of the factors affecting smoking status is gender, and cardiovascular diseases are more common in smokers (34).

A meta-analysis of 637 cases of MERS identified the prevalence of cardio vascular disease was 30%, the prevalence of hypertension and diabetes were 50% and 50% respectively (48).

Another meta-analysis among 1527 patients in Wuhan, China indicate the prevalence of hypertension, cardiac and cerebrovascular disease, and diabetes to be 17.1%, 16.4%, and 9.7% respectively among patients with COVID-19(34).

Another study conducted in China on the title of cardiovascular manifestation among COVID-19 patients reveled that hypotension during treatment (AOR=3.46, 95%CI 2.086-17.146), P= 0.043), Mild pericardial effusion (AOR= 3.430, 95% (1.803-15.180), P=0.047), and sever cardiac injury (AOR=2.421, 95%CI (1.812, 20.112), P=0.044) (36).

Sympathetic activity: Factors associated with increased sympathetic activity, such as anemia, pain, agitation, ventilator desynchrony, hypoxia, hypercarbia, acidosis, and hypovolemia are suggested in some studies, all of which can be potent triggers in these patients for the development of supraventricular arrhythmias. There is increasing evidence that the coagulation system is impaired in critically ill patients with COVID-19 with a high incidence of hyper coagulable disorders(38). Boston university although patients with pre-existing coronary artery disease have worse outcomes and increased risk of death, a direct relationship between coagulation impairment from COVID-19 and propagation of arrhythmias due to exacerbation of pre-existing coronary artery disease has not been described(28).

Myocardial damage: In patients with COVID-19, myocardial damage could be a major cause of enhanced arrhythmic risk. In 5.9 percent of patients, specifically, malignant ventricular arrhythmias, that is, ventricular tachycardia/fibrillation, were detected(39). The overall incidence of arrhythmias was 7.5 percent, 43 percent of which occurred in patients admitted to the ICU. Cardiac injury has been reported in up to 30% of COVID-19 patients. However, cardiac injury was mainly defined by troponin elevation without description of associated structural abnormalities and its time course has never been studied(40). Some studies suggest that the cardiac damage secondary to SARS-CoV-2 may be linked to ACE2, present in the cell membrane of CV, lung, and kidney tissues. The physiological role of ACE2 is to perform the conversion of angiotensin II in a molecule of angiotensin 1–7, causing vasodilation and decrease of hydric retention, through Mass receptor, acting as counter-regulator of the blood pressure elevation(41).

Hypoxemia: About 5% evolve to the third phase, or severe pneumonia, with worsening of the respiratory condition, hypoxemia, and fever(32). The high incidence of arrhythmias in COVID-19 is thought to be multifactorial; Hypoxmia is one of its factors. The vast majority of patients presenting with a systemic illness consistent with COVID-19 will not have symptoms or sign of arrhythmia or conduction system disease. However, patients in whom arrhythmia may be seen include patients with myocardial injury, shock and hypoxia (32).

Proinflammatory mediators: A variety of proinflammatory mediators that may play important roles in the pathophysiology of cardiac and arrhythmic complications are associated with SARS-CoV-2 infection. In 19 percent of hospitalized patients with COVID-19, cardiac injury was observed in a single center study and was associated with a higher risk of hospital mortality. It is therefore plausible that these patients are at an even greater risk of developing cardiac arrhythmias(38). Mild evidence may be attributed to hypoxia and inflammatory damage incurred by the virus (42). Epidemiological evidence suggests that COVID19 infection is associated with myocardial injury and arrhythmic complications (12).

Disturbances of fluids, electrolytes and acid-base balance: Hypokalemia results in cellular hyper polarity, increases resting potential, and hastens depolarization in cardiac cells and lung cells. Severe hypokalemia of less than 3mmol/L plasma K+ can trigger ventricular arrhythmia (43).

Hypokalemia: It is prevailing in patients with COVID-19 and occurs in up to 61% of hospitalized patients(44). This is assumed to be due to increased urinary and/or gastrointestinal loss of potassium. SARS-CoV-2 binds ACE2 and enhances the degradation of ACE2, and thus decreases the countering effects of ACE2 on the renin-Ang II system the final effect is to increase reabsorption of sodium and water, and thereafter increase blood pressure and excretion of potassium. Besides, patients with COVID-19 often have gastrointestinal symptoms such as diarrhea and vomiting, lowering potassium resources in the human body Subsequently, hypokalemia results in cellular hyper polarity, increases resting membrane potential and hastens depolarization in cardiac cells that predispose to AF(19).

Hypotension: According to different finding show that COVID-19 patients who were critically sick are prone to present with persistent refractory shock in the course of COVID-19 infection, and has a sigh of poor prognosis. Hypotension was an independent risk factor for critical status and a poor prognosis; therefore, blood pressure should be closely monitored during the hospitalization period and further attention should be paid to that developing hypotension. Cardiac arrythmia in patients with COVID-19 was similar to patients with SARS in 2003(26).

Drug therapy: An important risk factor for the development of arrhythmias hydroxychloroquine/chloroquine (HCQ) + azithromycin (AZM)in COVID-19 patients is polypharmacy and associated drug interactions(4). Indeed, multiple commonly used medications contribute to a pro-arrhythmic state in a patient population already at risk. Furthermore, impaired drug clearance due to critical illness and associated organ dysfunction promotes drug accumulation, thereby accentuating these interactions. There is increasing recognition of the potential role of pharmacologic treatments in increasing the susceptibility to QT-related life-threatening VAs, particularly TdP (28).

2.4. Conceptual framework

After reviewing different literatures (10,12,14, 15,23 25-30) about factors associated with Cardiac arrhythmia and COVID 19 the following conceptual frame work is adapted and showing the interaction between socio-demographic, sympathetic activity triggers, Disturbances of fluids, electrolytes and acid-base balance, Behavioral factors (smoking, comorbidity, myocardial damage) and associated factor of cardiac arrhythmia among critically ill covid-19 patients

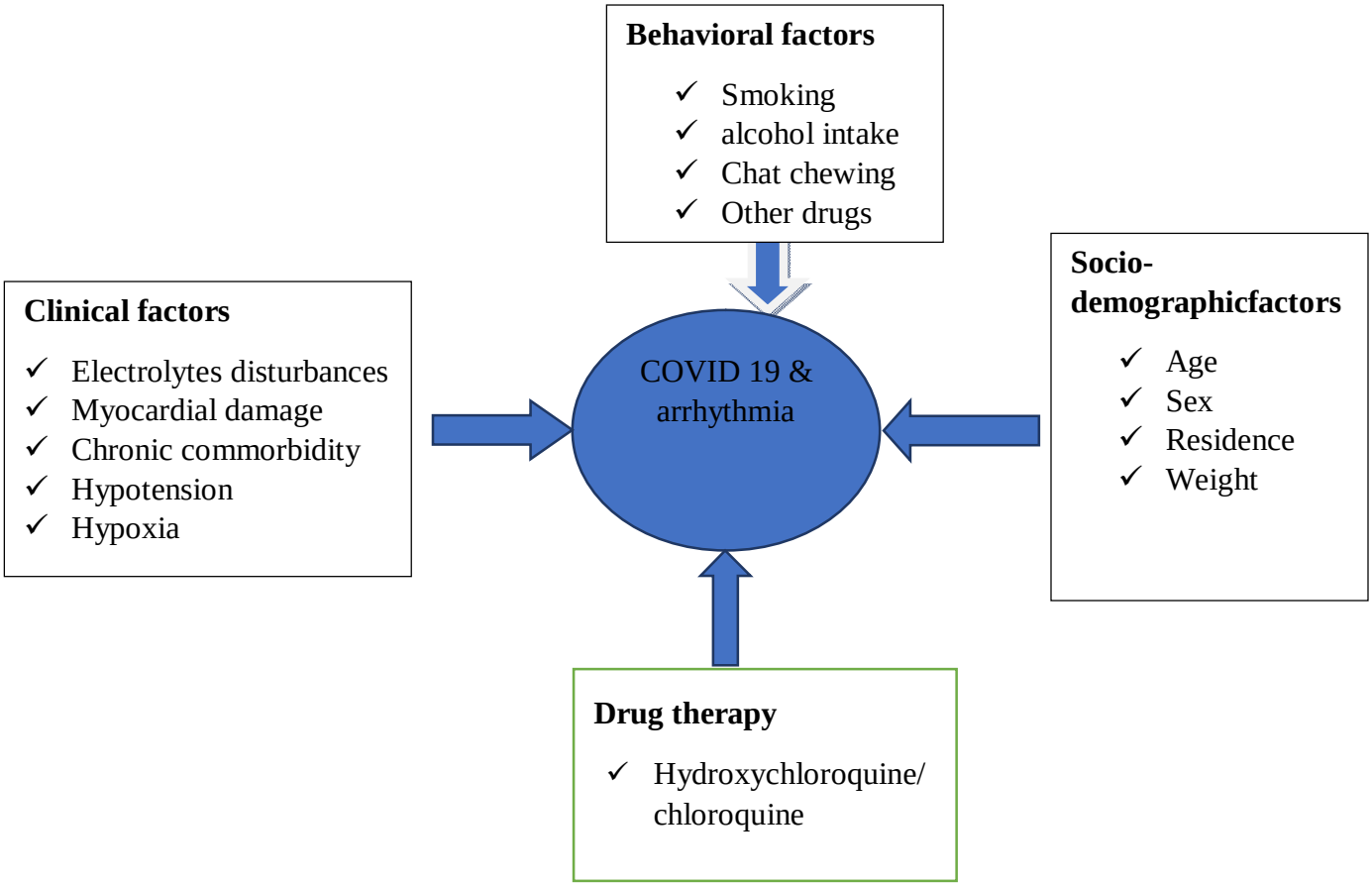

Figure 1: Conceptual framework for associated factor of cardiac arrhythmia among critically ill covid-19 patients.

3. OBJECTIVES

3.1. General objectives

To assess the Prevalence and associated factor of Cardiac arrhythmia among critically ill COVID-19 patients in COVID -19 center Eka Kotebe, Addis Ababa, Ethiopia, 2021.

3.2. Specific Objectives

To assess the prevalence of cardiac arrhythmias in critical ill COVID-19 patients in COVID-19 center, Eka Kotebe, Addis Ababa, 2021.

To identify factors associated with cardiac arrhythmias in critical ill COVID-19 patients COVID-19 center, Eka Kotebe, Addis Ababa, 2021.

4. Materials and Methods

4.1. Study area and study period

The study conducted at Eka kotebe General Hospital, COVID-19 center, from research and training directorate office, located in Yeka Sub city Woreda 12, Addis Ababa, Ethiopia. The hospital was built as part of an expansion to Amanuel Mental Specialized Hospital and launched its service three years ago, in 2009 E.C. Half of the hospitals service is dedicated to the treatment and care of patients with the mental illness while the rest of the services include surgery, Gynecology and obstetrics, internal medicine, pediatrics ophthalmology and dentistry. Since March13th, 2020 Eka Kotebe was converted in to COVID-19 treatment center and become the first hospital in the country to be fully dedicated to this cause. Moreover, the hospitals capacity for inpatient service has been maximized to 600 beds including 20 functioning ICU beds and 2 dialyses machine. It is a COVID 19 treatments center and also high load of COVID 19 patients in Ethiopia. Until the data collection period there were 1500 patients treated as COVID-19 in the hospital. The study was conducted from January 01-March 30, 2021.

4.2. Study Design

Institution based cross-sectional study conducted at Eka Kotebe COVID-19 center Addis Ababa.

4.3. Source population

All confirmed COVID-19 patients discharged do you to recovery, transfer, LAMA or death at Eka Kotebe hospital.

4.4. Study population

The study populations were all COVID -19 patients discharged due to recovery, transfer, LAMA or death from AICU, HDU and sever ward during the study period at Eka kotebe hospital.

4.5. Inclusion and Exclusion criteria

4.5.1. Inclusion criteria

Those confirmed COVID-19 patients' having medical records.

All adult patient's

4.5.2. Exclusion criteria

Patients who had incomplete medical record and history of arrhythmia.

4.6. Sample size

The sample size was calculated by using single population proportion formula. Since there were no studies done on the subject, and as it is new dynamic study prevalence was considered to be 50% to calculate the sample size.

Where: - n= required sample size

$Z\alpha /2$= 1.96 (Z=score corresponds to 95% confidence level)

P= prevalence (50% is preferred to obtain the largest possible sample size)

d2= margin of error (0.05)

n= 388

The final sample size was 388.

By doing population correction formula

S=n/(1 + (n/N))

S= Sample size of corrected formula

n= the calculated sample size by single population formula

N= current study of source population

S= 388/1+ 388/1500 = 388/ 1.26

S= 308, and to get higher sample size for a better data quality we add 25% of the calculated sample size so it become 385

And if we add 10% non-response rate the final sample size become 424.

4.7. Operational definition

ARRHYTEMIA: For any of a heterogeneous group of conditions in which there is abnormal electrical activity in the heart below 60bpm bready cardiac and above 100bpm tachycardia, cardiac arrhythmia is a generic term. Some arrhythmias can only cause irritating symptoms such as heart beating awareness very quickly; others can cause life-threatening conditions such as a stroke or cardiac arrest. Any arrhythmia documented during hospitalization by looking patient's medical records (45).

Electrolyte Disorders: An imbalance of calcium, chloride, magnesium, potassium, or sodium with in the blood from laboratory result.(43)

Hypokalemia: When serum potassium levels are lower 3.5mmol/L hypokalemia is present. It is a fairly common electrolyte disorder with different causes, particularly in hospitalized patients, and sometimes requires urgent medical care(46).

Hypoxia: In biology and medicine, the state of the body in which oxygen starves tissues. The disorder is called anoxia in its extreme form, where oxygen is entirely absent or in Partial saturation oxygen (Spo2) below 90%(47).

Myocardial damage: A myocardial infarction (MI), commonly known as a heart attack, occurs when blood flow decreases or stops to a part of the heart, causing damage to the heart muscle. Chest pain or irritation that may flow through the shoulder, arm, back, neck or jaw is the most common symptom on imaging ECG shows ST elevation. Any documented diagnosed during hospitalization by looking patient's medical records (48).

Incomplete medical record: Medical record that missed at least one socio- demographic variable.

Normal body weight: Body mass index of the patient between 18.5 – 24.9 Kg/m2.(49)

Under weight: The Body mass index of patients below 18.5 Kg/m2.(49)

Over weight: The Body mass index of patients above 25.0 Kg/m2.(49)

Diabetic mellitus: Patients records in medical record diagnosed with diabetic mellitus.

Hypotension: A patients diagnosed as hypotension in the medical record.

Chronic kidney disease: A disease who diagnosed as chronic kidney disease that is treated with in the hospital and recorded in the medical records.

Anemia: When a patient had records of hemoglobin level less than 11g/dl.(50)

Substance use: A recorded history of substance use in patient history format with in the medical recorded.

4.8. Variables of the study

4.8.1. Dependent variables

Arrhythmia (Any arrhythmia documented during hospitalization by looking patient's medical records)

4.8.2. Independent variables

Socio demographic factors: Age, sex, residence and weight

Clinical factors: Hypoxia, electrolyte imbalance, acid base imbalance, Diabetic mellitus, hypotension, hypoxia and anemia

Behavioral factors: Smoking, alcohol intake, chat chewing and other substances

4.9. Sampling technique

First, we selected Eka kotebe hospital by purposive sampling techniques and then a list of patient's cards that treated as confirmed COVID-19 patients was taken by lottery methods to get individuals information during data collection period from their medical records.

4.10. Data collection tool and procedure

Data abstraction sheet was used to assess prevalence and associated factors of cardiac arrhythmia. The data abstraction sheet was prepared in English by reviewing relevant literature to the problem under study and by considering the information available in the Eka Kotebe COVID-19 treatment center medical register book to include all possible variables that address the objective of the study. Data abstraction sheet have three parts (socio-demographic, clinical and behavioral factors). The tool was prepared based on patient medical registration format used

in the hospital. Since it is not possible to get in or out of the treatment center, the information was documented electronically by using telegram. The principal investigator also involved in overlooking the overall data collection process to make sure that for data completeness and give support as needed.

4.11. Data quality control

To assure the data quality the checklist were pre-tested two week before the data collection period among 5% of the study subjects in Field hospital which governed by under St.Peter Specialized Hospital in order to make sure collected all necessary information and in need of some adjustment. The developed checklist was evaluated by experienced researchers. After one day training were given for data collector by the principal investigator on the purpose of the study, the data collection tool (checklist), data collection methods, and ethical concerns during data collection were started by two clinical nurses who were working in the study site and had experience for data collection. One MSc holder nurse was employed as a supervisor. The supervisor monitored the data collection process of the data collectors and if any problem happens, they tried to solve or contact the principal investigator. Principal investigator and supervisors made spot-checking and reviewing the complete checklist by the data collectors ensures completeness and consistency of the information. Consistency was examined through random selection of cards by the principal investigator.

4.12. Data analysis

Cleanness of the collected data was checked. Data were entered into Epi-data version 4.6.0.2 and export to and analyzed by using SPSS version 25.0. After carefully undertaking data entry, the data analysis was used by calculating univariant analysis such as the mean, standard deviation, frequency, percentage and by creating tabular displays of the data using a table. A simple logistic regression analysis was used to examine a direct relationship between a single outcome variable and independent variables. Multivariable logistic regression modeling was conducted to identify the independent predictors of cardiac arrhythmia. Those variables with $p<0.01$ in the bivariate logistic regression analysis were entered into a multivariable logistic regression model and statistical significance was considered at $P<0.05$ declared as significant associations. Model fitness was tested by Hosmer and lemshow goodness of fit test. Adjusted odds ratio with 95%CI and p-value of less than 0.05 was used to determine the final model.

4.13. Ethical considerations

Ethical clearance was obtained from research and ethical review committee of Addis Ababa University, College of health sciences, School of Nursing and Midwifery. A formal letter of cooperation from the University was submitted to the hospital administrative body for data collection. Permission obtained from all concerned body in the hospital. Next to these, searching and obtaining of the selected samples' medical record was processed with the assigned person. Care taken from disclosing patient's records and confidentiality were maintained by omitting their name and personal identification from the data collection format. Finally, all collected data were coded and locked in a separate room before entered into the computer and were locked by password after entered to the computer. Since data took from medical records, there is no harm to the subject.

4.14. Dissemination of the result

The result will be submitted to Addis Ababa University research and community service directorate office, College Health Sciences, School of Nursing and Midwifery. Also, the result will be disseminated to the school library and to Eka Kotebe hospital. Further effort will be made to present it on workshop and conference and to publish in peer-reviewed.

5. RESULTS

5.1. Description of socio-demographic, clinical and individual characteristics of respondents

5.1.1. Description of socio-demographic characteristics

The total study sample was 388 with 91.5% response rate. Among that more than half 223(57.5%) were males. The mean and median age was 55 and 58 years respectively (SD=14.470), majority of (70%) study participants was above 40years, ninety two (23.7%) and 182 (46.9%) were in the age group 45-59 and above 60years respectively. Regarding weight of patients more than half (64.6%) were under normal weight. Half (51.5%) of patients are referred from governmental hospital the remaining 28.4% and 20.1% are referred from private hospital and health center respectively.

Table 1: Description of socio-demographic characteristics of critically ill COVID-19 positive patients at Eka Kotebe COVID-19 treatment center, Addis Ababa, Ethiopia.

Variable	Category	Frequency	Percent (%)
Sex	Male	223	57.5%
	Female	165	42.5%
Residency	A/A	337	86.9%
	Outside A/A	51	13.1%
Age	15-24	15	3.9%
	25-34	40	10.3%
	35-44	59	15.2%
	45-59	92	23.7%
	60+	182	46.9%
BMI	Under-weight	18	4.6%
	Normal-weight	250	64.4%
	Over-weight	120	30.9%

5.1.2. Behavioral characteristics

Among 388 study participants above half 214(55.2%) had history of substance use, fifty nine (27.6%) and 55 (25.7%) of them had history of chat chewing only and smoking only respectively.

Table 2: Description of behavioral characteristics of critically ill COVID-19 positive patients at Eka kotebe COVID-19 center Addis Ababa, Ethiopia.

Variables	Category	Frequency	Percent (%)
Substance use	Yes	214	55.2%
	No	174	44.8%
History of smoking only	Yes	55	14.2%
	No	333	85.8%
History of chat chewing only	Yes	59	15.2%
	No	329	84.8%
History of alcohol intake only	Yes	13	3.4%
	No	375	96.6%
History of smoking and chat chewing	Yes	37	9.5%
	No	351	90.5%
History of smoking and alcohol intake	Yes	7	1.8%
	No	381	98.2%
History of smoking, chat chewing and alcohol intake	Yes	31	8%
	No	357	92%
Other (cocaine, heroin)	Yes	11	2.8%
	No	377	97.2%

5.1.3. Clinical factors

As it showed in table 3, at least one or more comorbid disease were presented in 236(86.6%) of the study participants, more than one third (35.6%) of them had chronic heart disease. Sixty five (16.8%) and 90 (23.2%) of the study participants electrolyte result shows hypokalemia and

anemia respectively. Eighty nine (22.9%) of the study participants had hypoxic at the time of arrhythmia diagnosis

Table 3: Description of clinical characteristics of critically ill COVID-19 positive patients at EkaKotebe COVID-19 center Addis Ababa, Ethiopia 2021.

Variables	Category	Frequency	Percent (%)
Chronic comorbidity	Yes	336	86.6%
	No	52	13.4%
Types of comorbidity	CHD/HNT	84	25%
	CVD	22	6.5%
	Metabolic disorder/DM/Dyslipidemia	38	11.3%
	HIV	25	7.4%
	Cancer	20	6.0%
	COPD	27	8.0%
	Major organ failure	49	14.6%
	Other	71	21.1%
Potassium level	Hypokalemia	65	16.8%
	Hyperkalemia	172	45.6%
	Normal level	146	37.6%
02 saturation	Hypoxia	89	22.9%
	Normal level	299	77.1%
Acid-base imbalance	Acidosis	320	82.5%
	Alkalosis	24	6.2%
	Normal range	44	11.3%
Hypotension	Yes	153	39.4%
	No	235	60.6%
Anemia	Yes	90	23.2%
	No	298	76.8%

5.2. Prevalence of cardiac arrhythmia among critically ill COVID-19 patients

The prevalence of cardiac arrhythmia among critically ill COVID-19 positive patients was found to be 71.4% (Figure 2).

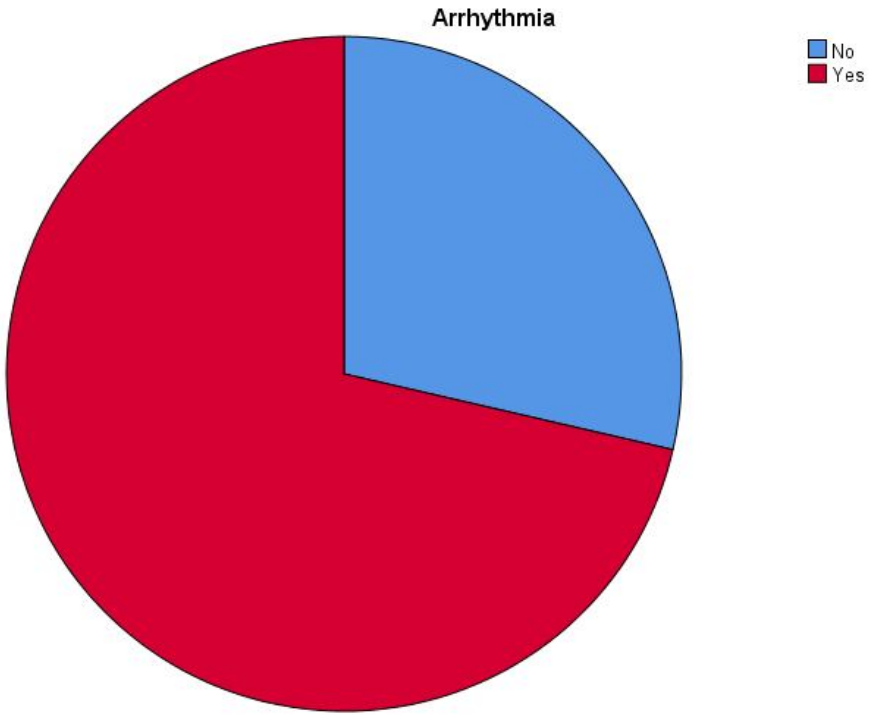

Figure 2: The prevalence of cardiac arrhythmia among critically ill COVID-19 positive patients at Eka Kotebe in Addis Ababa, Ethiopia, 2021

5.3. Treatment outcome

Among the total 71.4% patients who develop cardiac arrhythmia majority of (62.1%) are died and only 3.2% of them are discharged to their home. From 28.6% patients who had not developed cardiac arrhythmia 18.9% of them are died and the remaining 37.8%, 27.0% and 16.2% are transfer, referred and discharged respectively.

Table 4: Description of treatment outcome of critically ill COVID-19 positive patients develops cardiac arrhythmia and their counter parts at Eka Kotebe, Addis Ababa, Ethiopia.

Outcome	**Arrhythmia**			
	Yes		**No**	
	Frequency	Percentage	Frequency	Percent (%)
Discharge	9	3.2%	18	16.2%
Transfer	64	23.1%	42	37.8%
Death	172	62.1%	21	18.9%
Refer	32	11.6%	30	27.0%

5.4. Factors associated with cardiac arrhythmia among critically ill COVID-19 patients

Bivariate logistic regression analysis was done to see the association of each independent variable with cardiac arrhythmia. Variables with a P-value of less than 0.01 on bivariate logistic regression which are age, sex, substance use, anemia, presence of comorbidities, potassium level, oxygen saturation and hypotension were entered to multivariable analysis. In the final model the strength of association was measured by OR with 95% confidence interval and variables associated with cardiac arrhythmia with P-value <0.05 considered as significantly associated.

Table 5: Bi-variable logistic regression of cardiac arrhythmia among critically ill COVID-19 positive peoples in Eka Kotebe treatment center Addis Ababa, Ethiopia, 2021 G.C.

Variables	Categories	Cardiac arrhythmias		COR	P-value
		Yes	No	(95%CI)	
Sex	Male	168(60.6%)	55(49.5%)	1.57(1.00, 2.44)	0.046
	Female	109(39.4%)	56(50.5%)	1	
Residency	A/A	239(86.3%)	98(88.3%)	1	0.453
	Outside A/A	38(13.7%)	13(11.7%)	1.19(0.61, 2.35)	
Age	15-24	7(2.5%)	8(7.2%)	1	
	25-34	27(9.7%)	13(11.7%)	2.37(0.71, 7.96) *	0.162
	35-44	40(14.4%)	19(17.1%)	2.41(0.76, 7.61) *	0.135
	45-59	65(23.5%)	27(24.3%)	2.75(0.91, 8.34) *	0.074
	60+	138(49.8%)	44(39.6%)	3.58(1.23, 10.45) *	0.019
Substance use	Yes	165(59.6%)	49(44.1%)	1.86(1.19, 2.91) *	0.006
	No	112(40.4%)	62(55.9%)	1	
BMI	Under-weight	13(4.7%)	5(4.5%)	1.14(0.39, 3.29)	0.741
	Over-weight	90(32.5%)	30(27.0%)	1.31(0.80, 2.15	0.233
	Normal-weight	174(62.8%)	76(68.5%)	1	
Comorbidity	Yes	264(95.3%)	72(64.9%)	11.00(5.6, 21.70)*	0.000
	No	13(4.7%)	39(35.1%)	1	
Potassium level	Hypokalemia	54(19.5%)	11(9.9%)	6.29(3.04, 13.00) *	0.000
	Hyperkalemia	159(57.4%)	18(16.2%)	11.32(6.29,	0.000

				20.35) *	
	Normal level	64(23.1%)	82(73.9%)	1	
02 saturation	Hypoxia	81(29.2%)	8(7.2%)	5.32(2.47, 11.43) *	0.000
	Normal level	196(70.8%)	103(92.8%)	1	
Hypotension	Yes	136(49.1%)	17(15.3%)	5.33(3.02, 9.41) *	0.000
	No	141(50.9%)	94(84.7%)	1	
Acid-base imbalance	Acidosis	227(81.9%)	93(83.8%)	0.81(0.26, 2.46)	0.576
	Alkalosis	17(6.1%)	7(6.3%)	0.81(0.39, 1.68)	0.710
	Normal range	33(11.9%)	11(9.9%)	1	
Anemia	Yes	75(27.1%)	15(13.5%)	2.38(1.29, 4.35) *	0.005
	No	202(72.9%)	96(86.5%)	1	

Key 1= Reference

***** Significant by COR at p-value ≤0.01

In the multivariable analysis model the strength of association was measured by OR with 95% confidence interval and variables associated with cardiac arrhythmia with P-value <0.05 such as presence of comorbidity, substance use, hypokalemia, hyperkalemia and hypotension were significantly associated.

Our study finding shows that patients who had chronic comorbidity were ten time more possibility to develop cardiac arrhythmia than their counterparts those who have no chronic comorbidity (AOR: 10.31; 95%CI 4.64, 22.90)

Patients who have hypokalemic and hyperkalemia were six times and nine times higher chance to develop cardiac arrhythmia then patients who had normal potassium level (AOR: 6.85 95%CI; 2.95, 15.86) and(AOR; 9.31; 95%CI: 4.75, 18.23) respectively.

Patients who had hypotensive were four times higher chance to develop cardiac arrhythmia than their counterparts those who had normal oxygen saturation (AOR: 2.66; 95%CI: 0.97, 7.31)

Our study finding also shows patients who had substance use story had three times higher chance to develop cardiac arrhythmia than who had no substance use history (AOR: 2.77; 95%CI: 1.54, 4.99)**.**

Table 6: Bi-variable and multivariable logistic regression of cardiac arrhythmia among critically ill COVID-19 positive peoples Addis Ababa, Ethiopia, 2021 G.C.

Variables	**Categories**	**Cardiac arrhythmias**		**COR**	**AOR**	**P-**
		Yes	No	**(95%CI)**	**(95%CI)**	**value**
Substance use	Yes	165(59.6%)	49(44.1%)	1.86(1.19, 2.91) *****	**2.77(1.54, 4.99) ****	0.001
	No	112(40.4%)	62(55.9%)	1	1	
Comorbidity	Yes	274(98.9%)	62(55.9%)	11.00(5.6, 21.70)*	**10.31(4.64, 22.90) ****	0.000
	No	3(1.1%)	49(44.1%)	1	1	
Potassium level	Hypokalemia	54(19.5%)	11(9.9%)	6.29(3.04, 13.00) *****	**6.85(2.95, 15.86) ****	0.000
	Hyperkalemia	159(57.4%)	18(16.2%)	11.32(6.29, 20.35) *****	**9.31(4.75, 18.23) ****	0.000
	Normal level	64(23.1%)	82(73.9%)	1	1	
Oxygen saturation	Hypoxia	81(29.2%)	8(7.2%)	5.32(2.47, 11.43) *****	2.66(0.97, 7.31)	0.058
	Normal level	196(70.8%)	103(92.8%)	1	1	
Hypotension	Yes	136(49.1%)	17(15.3%)	5.33(3.02, 9.41) *****	**2.75(1.27, 5.92) ****	0.010
	No	141(50.9%)	94(84.7%)	1	1	
Anemia	Yes	75(27.1%)	15(13.5%)	2.38(1.29, 4.35) *****	1.59(0.72, 3.52)	0.250
	No	202(72.9%)	96(86.5%)	1	1	

Key 1= Reference

***** Statistically significant by COR at p-value <0.01

******Statistically significant by AOR at p-value <0.05

6. DISCUSSION

This study aimed to assess the prevalence and associated factors of cardiac arrhythmia among critically ill COVID-19 positive patients from 01, 2021 to March 30, 2021in Eka Kotebe treatment center, Addis Ababa, Ethiopia. In this study, the prevalence of cardiac arrhythmia among critically ill COVID-19 positive patients in Eka Kotebe was 71.4%our study finding was much higher than the studies done in Wuhan, China, 44.4 % of ICU patients with COVID-19 had cardiac arrhythmias, other study also shows the overall incidence of arrhythmias was 7.5 percent, 43 percent of which occurred in patients admitted to the ICU(5). Other worldwide retrospective analysis also shows from 4526 patients across 4 continents and 12 countries 18% of whom had an arrhythmia(27). This might be due to difference in study sample size and study time between the studies.

Among the total 71.4% patients who develop cardiac arrhythmia majority of (62.1%) are died and only 3.2% of them are discharged to their home. The number of discharge in our finding was much less than a retrospective analysis of patients hospitalized with COVID-19 infection worldwide with and without incident cardiac arrhythmias, the study shows from total COVID-19 positive patients who developed cardiac arrhythmia 51% survived to hospital discharge(27). This might be due to different in treatment; developed countries might use advanced technology for critically ill patients.

The finding indicates that patients who had underlying comorbidity were ten times higher chance to develop cardiac arrhythmia than who have no underlying disease. Our funding was consistent with the a narrative review done in critically ill COVID-19 patients, the study shows underlying comorbidity predisposes patients with COVID-19 to myocardial injury and potentially dangerous arrhythmias (28). Comorbidities were associated with the severity of COVID-19. The fatality rate also increased in patients with comorbidities (36). Comorbidities including chronic cardiac disease, non-asthmatic chronic pulmonary disease, chronic kidney disease, liver disease, and obesity were associated with higher in-hospital morbidity(37). A worldwide retrospective review shows cardiac comorbidities were common in patients with arrhythmia: 69% had hypertension, 42% diabetes, 30% had heart failure, and 24% had coronary artery disease. Most had no prior history of arrhythmia(27).

This might be due to immunity differences between peoples living with a chronic disease and their counterparts, peoples who are living with chronic disease like hypertension, cardio vascular disease, cancer, metabolic disorder and others have immunocompromised and they develop cardiac arrhythmia when they are infected with SARS-CoV- 2 than peoples who are free from chronic diseases.

Patients whose electrolyte results showed hypokalemia were seven higher chances to develop cardiac arrhythmia than patients who had normal potassium level. This is assumed to be due to increased urinary and/or gastrointestinal loss of potassium. SARS-CoV-2 binds ACE2 and enhances the degradation of ACE2, and thus decreases the countering effects of ACE2 on the renin-AngII system the final effect is to increase reabsorption of sodium and water, and thereafter increase blood pressure and excretion of potassium. Besides, patients with COVID-19 often have gastrointestinal symptoms such as diarrhea and vomiting, lowering potassium resources in the human body subsequently, hypokalemia results in cellular hyper polarity, increases resting membrane potential and hasten depolarization in cardiac cells that predispose to AF This might be due to hypokalemia results in cellular hyper polarity, increases resting potential, and hastens depolarization in cardiac cells and lung cells. Severe hypokalemia of less than 3 mmol/L plasma K+ can trigger ventricular arrhythmia (44,51)

Patients whose electrolyte results showed hyperkalemia were nine times higher chance to develop cardiac arrhythmia than patients who had normal potassium level.

The odds of patients who had hypotensive were three times higher chance to develop cardiac arrhythmia than their counterparts those whose blood pressure were under normal range. This is in line with reports of the study conducted in China on the title of cardiovascular manifestation among COVID-19 patients revealed that hypotensive patients have three times higher chance to develop cardiac arrhythmia than their counterparts (AOR=3.462)(46). Other study also shows cardiac arrhythmia in patients with COVID-19 was similar to patients with SARS in 2003(26). Other worldwide retrospective review also shows almost half of the patients with VT were hypotensive with systolic blood pressure of <90 mm Hg at the time of their arrhythmia(27).

Our study finding also shows patients who had substance use story had three times higher chance to develop cardiac arrhythmia than who had no substance use history. Active smoking has been reported to increase the risk of viral respiratory diseases. Smokers have an increased risk for community-acquired pneumonia. The angiotensin-converting enzyme (ACE-2) protein, which is expressed on the surface of lung type-2 pneumocystis, is an entry receptor for SARS-CoV-2. (33). A retrospective observational study done in Turkey shows in addition to (older age, COPD, CAD and CHF) current smoking and former smoking were significantly associated with mortality (34). Other studies also show about 20% of COVID-19 patients develops pulmonary infiltrates and some of these will develop very severe disease, hypoxia, and progression to ARDS (47).

Factors that are significantly associated in another study like age and acid base imbalance are not statistically significant in our study(51)(27).

7. Strength and limitation of the study

7.1. Strength

The study used us first-hand information about prevalence and associated factors of cardiac arrhythmia among critically ill COVID-19 positive patients

This study tried to review the medical record of arrhythmia diagnosed with COVID-19 positive patients

7.2. Limitation

Cross-sectional nature of the study may not allow showing temporal relationship

Due to the unavailability of data the study lacks important factors associated with cardiac arrhythmia like the habit physical exercise, troponin level and drug therapy.

8. Conclusion

A high prevalence of cardiac arrhythmia was observed in Eka Kotebe critically ill COVID-19 positive patients. Majority of patients who developed cardiac arrhythmia treatment outcome was death. Presence of underline comorbidity, hypokalemia, hyperkalemia, hypotension and substance (chat, alcohol, cigarettes and others) use were significantly associated with cardiac arrhythmia.

9. Recommendation

According to the findings from this study, the following recommendations have been suggested to different stakeholders;

9.1. For Ministry of health

Ministry of health

Have to prepare a strategy to give special attention for COVID-19 positive patients who have underline comorbidity and addicted with different substance.

The government has to prepare a strategy to increase laboratory and imaging performance and to do testing for troponin, ACE2 and ECHO.

9.2. For health service organization

Health service organizations

Have to give attention to monitor vital sign specially blood pressure and to monitor electrolyte balance.

Give health education to clients about the high prevalence and risk factors of cardiac arrhythmia.

9.3. For health professionals

Health professionals

Have to know about high prevalence of cardiac arrhythmia among COVID-19 positive patients.

Try to detect cardiac arrhythmia early and to act immediately because once it happens prognosis was poor.

9.3. For researchers

Researchers who are interested to conduct study about cardiac arrhythmia among critically ill COVID-19 patients should be better to do a prospective follow-up study to include important variables we missed in our study.

References

1. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054–62.

2. Sohrabi C, Alsafi Z, O'Neill N, Khan M, Kerwan A, Al-Jabir A, et al. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). Int J Surg. 2020;76(February):71–6.

3. Antzelevitch C, Burashnikov A. Overview of Basic Mechanisms of Cardiac Arrhythmia. Card Electrophysiol Clin. 2011;3(1):23–45.

4. Gopinathannair R, Merchant FM, Lakkireddy DR, Etheridge SP, Feigofsky S, Han JK, et al. COVID-19 and cardiac arrhythmias: a global perspective on arrhythmia characteristics and management strategies. J Interv Card Electrophysiol. 2020;59(2):329–36.

5. Bhatla A, Mayer MM, Adusumalli S, Hyman MC, Oh E, Tierney A, et al. COVID-19 and cardiac arrhythmias. 2020;17(9):1439–44.

6. Gopinathannair R, Merchant FM, Lakkireddy DR, Etheridge SP, Feigofsky S, Han JK, et al. COVID-19 and cardiac arrhythmias: a global perspective on arrhythmia characteristics and management strategies. J Interv Card Electrophysiol. 2020;329–36.

7. Petrakis D, Margină D, Tsarouhas K, Tekos F, Stan M, Nikitovic D, et al. Obesity ‐ a risk factor for increased COVID‐19 prevalence, severity and lethality (Review). Mol Med Rep. 2020;22(1):9–19.

8. Tadesse DB, Gebremeskel GG, Asefa GG, Abay M, Demoz GT. The burden, admission, and outcome of COVID-19 in Africa: protocol for a systematic review and meta-analysis. Emerg Microbes Infect. 2020;9(1):1372–8.

9. Shigute Z, Mebratie AD, Alemu G, Bedi A. Containing the spread of COVID-19 in Ethiopia. J Glob Health. 2020;10(1):1–4.

10. Zikargae MH. Covid-19 in ethiopia: Assessment of how the ethiopian government has executed administrative actions and managed risk communications and community

engagement. Risk Manag Healthc Policy. 2020;13:2803–10.

11. Tai W, He L, Zhang X, Pu J, Voronin D. Characterization of the receptor-binding domain (RBD) of 2019 novel coronavirus : implication for development of RBD protein as a viral attachment inhibitor and vaccine. Cell Mol Immunol. 2020;(March).

12. Wang Y, Wang Z, Tse G, Zhang L, Wan EY, Guo Y, et al. Cardiac arrhythmias in patients with COVID-19. J Arrhythmia. 2020;36(5):827–36.

13. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular Implications of Fatal Outcomes of Patients with Coronavirus Disease 2019 (COVID-19). JAMA Cardiol. 2020;5(7):811–8.

14. Bhatla A, Mayer MM, Adusumalli S, Hyman MC, Oh E, Tierney A, et al. COVID-19 and cardiac arrhythmias. Hear Rhythm. 2020;17(9):1439–44.

15. Manolis AS, Manolis AA, Manolis TA, Apostolopoulos EJ, Papatheou D, Melita H. COVID-19 infection and cardiac arrhythmias. Trends Cardiovasc Med. 2020;11(xxxx):1–10.

16. Si D, Du B, Ni L, Yang B, Sun H, Jiang N, et al. Death, discharge and arrhythmias among patients with COVID-19 and cardiac injury. Cmaj. 2020;192(28):E791–8.

17. Lakkireddy DR, Chung MK, Deering TF, Gopinathannair R, Albert CM, Epstein LM, et al. Guidance for rebooting electrophysiology through the COVID-19 pandemic from the Heart Rhythm Society and the American Heart Association Electrocardiography and Arrhythmias Committee of the Council on Clinical Cardiology: Endorsed by the American College o. Hear Rhythm. 2020;17(9):e242–54.

18. Chin A, Moses J, Thornton A. AND COVID-19 Arrhythmias and COVID-19 infection CHALLENGES TO ARRHYTHMIA. :362–9.

19. Gawałko M, Kapłon-Cieślicka A, Hohl M, Dobrev D, Linz D. COVID-19 associated atrial fibrillation: Incidence, putative mechanisms and potential clinical implications. IJC Hear Vasc. 2020;30:1–8.

20. Al-Tawfiq JA, Leonardi R, Fasoli G, Rigamonti D. Prevalence and fatality rates of

COVID-19: What are the reasons for the wide variations worldwide? Travel Med Infect Dis. 2020;35(March):101711.

21. Incidence and treatment of arrhythmias secondary to coronavirus infection in humans: a systematic review. :0–3.

22. Babapoor-farrokhran S, Rasekhi RT, Gill D, Babapoor S. Arrhythmia in COVID-19. 2020;1430–5.

23. Chakafana G, Mutithu D, Hoevelmann J, Ntusi N, Sliwa K. Interplay of COVID-19 and cardiovascular diseases in Africa: an observational snapshot. Clin Res Cardiol. 2020;2(0123456789).

24. Li X, Pan X, Li Y, An N, Xing Y, Yang F, et al. Cardiac injury associated with severe disease or ICU admission and death in hospitalized patients with COVID-19: A meta-analysis and systematic review. Crit Care. 2020;24(1):1–16.

25. Liu J, Virani SS, Alam M, Denktas AE, Hamzeh I, Khalid U. Coronavirus disease-19 and cardiovascular disease: A risk factor or a risk marker? Rev Med Virol. 2020;(May):1–9.

26. Chen Q, Xu L, Dai Y, Ling Y, Mao J, Qian J, et al. Cardiovascular manifestations in severe and critical patients with COVID-19. Clin Cardiol. 2020;43(7):796–802.

27. Arrhythmia C, Garan H, Yeo I, York N, Hospital P, Jain S, et al. Worldwide Survey of COVID-19 – Associated Arrhythmias. 2021;(February).

28. Karamchandani K, Quintili A, Landis T, Bose S. Cardiac Arrhythmias in Critically Ill Patients With COVID-19: A Brief Review. J Cardiothorac Vasc Anesth. 2020;000:1–8.

29. Who W. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. 2020;2019(March).

30. Lechien JR, Chiesa-Estomba CM, Place S, Van Laethem Y, Cabaraux P, Mat Q, et al. Clinical and epidemiological characteristics of 1420 European patients with mild-to-moderate coronavirus disease 2019. J Intern Med. 2020;288(3):335–44.

31. Yancy CW. COVID-19 and African Americans. JAMA - J Am Med Assoc. 2020;323(19):1891–2.

32. Azevedo RB, Botelho BG, Hollanda JVG de, Ferreira LVL, Junqueira de Andrade LZ, Oei SSML, et al. Covid-19 and the cardiovascular system: a comprehensive review. J Hum Hypertens. 2020;

33. Mehra MR, Desai SS, Kuy S, Henry TD, Patel AN. Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19. N Engl J Med. 2020;382(25):e102.

34. Caliskan T. Smoking and comorbidities are associated with COVID-19 severity and mortality in 565 patients treated in Turkey : a retrospective observational study. 2020;66(12):1679–84.

35. Baskaran V, Murray RL, Hunter A, Lim WS, McKeever TM. Effect of tobacco smoking on the risk of developing community acquired pneumonia: A systematic review and meta-analysis. PLoS One. 2019;14(7):1–18.

36. Besteiro B, Coutinho D, Gomes F, Almeida M, Almeida J. Review of the Prognosis Factors of COVID-19 Infection. Adv Infect Dis. 2021;11(02):196–215.

37. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: Prospective observational cohort study. BMJ. 2020;369(March):1–12.

38. Kochi AN, Tagliari AP, Forleo GB, Fassini GM, Tondo C. Cardiac and arrhythmic complications in patients with COVID-19. J Cardiovasc Electrophysiol. 2020;31(5):1003–8.

39. Lazzerini PE, Boutjdir M, Capecchi PL. COVID-19, Arrhythmic Risk, and Inflammation: Mind the Gap! Circulation. 2020;7–9.

40. Doyen D, Dupland P, Morand L, Fourrier E, Saccheri C, Buscot M, et al. Characteristics of cardiac injury in critically ill patients with COVID-19. Chest. 2020;

41. Keihanian F, Bigdelu L. Cardiovascular considerations in COVID-19: A comprehensive review. Ther Clin Risk Manag. 2020;16:1089–97.

42. He J, Wu B, Chen Y, Tang J, Liu Q, Zhou S, et al. Case Report Characteristic

Electrocardiographic Manifestations in Patients With COVID-19. 2020;36:1–4.

43. Kardalas E, Kardalas E, Paschou SA, Anagnostis P, Muscogiuri G, Siasos G. Hypokalemia : a clinical update. 2018;(2):135–46.

44. chen dong, Li X, song qifa, Hu C, Su F, Dai J. Hypokalemia and Clinical Implications in Patients with Coronavirus Disease 2019 (COVID-19). 2020;

45. Humphreys M, Warlow C, McGowan J. Arrhythmias and their Management. Nurs Card Patient. 2013;(August 2013):132–55.

46. Connections E, Ahead P. Page 1 of 32. 2018;(1):1–32.

47. Gilany K, Vafakhah M. Hypoxia : a Review Hypoxia : a Review. 2014;(June).

48. Eggers KM. Defining acute myocardial infarction. Hear Metab. 2015;(67):34–8.

49. Nuttall FQ. Body Mass Index. 2015;50(3).

50. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. :1–6.

51. Temgoua MN, Chanseaume S, Hilic E, Karamoko K, Tochie JN, Beyina G, et al. Paroxysmal atrial fibrillation associated with a moderate form of COVID-19 in a middle-aged man with low cardiovascular risk factor: More still needs to be done in this topic. Clin Case Reports. 2021;9(4):1986–90.

Annex: data collection checklist

	MRN			
code	Questions	Alternative responses		Skip
101	Age	……Years		
102	Sex	1. Male 2. Female		
103	Phone no			
104	V/S during admission	1. BP……. 2. Pulse…… 3. RR……. 4. To…….. 5. Spo2…… 6. RBS		
105	What is the weight of the patients?	……Kg		
106	What is the height of the patients?	……Meter		
107	Where is the residence of the patients	1.Urban (from Addis Ababa) 2.Rural (out of Addis Ababa)		
108	Which is the patient's ethnic group?	1.Amhara 2.Oromo 3.Tigre 4. Others (specify)…….		
109	Does the patent have Health Insurance?	1.Yes 2. No		
110	Where is the patient referred from? Other facility or not	1.Not referred from other facility 2.Referred from health center 3.Referred from hospital 4. Referred from privet facilities?		
111	When the patients arrive /Date of admission	……(dd/mm/yr.)		
112	What is the date and the time of arrhythmias? /Date and time of Arrhythmia is diagnosed	……(dd/mm/yr.)		
113	When the patients discharge from	……(dd/mm/yr.)		

	hospital? /Date and time of discharge/			
114	For how many days the patients stay in the hospital before Arrhythmia /total duration of stay before arrhythmia	…… (in number)		
115	For how many days the patients stay in the hospital after Arrhythmia Date of discharge and time Date of out from Arrhythmia and time	…… (in number) ……(dd/mm/yr.) ……(dd/mm/yr.)		
116	What is the cause for arrhythmia	1.Gastric fluid loss 2.Electrolit imbalance 3.Acide base balance 4.Sevarity of disease 5.Hypoxia 6.Others (specify)……		
117	Did the patients have privies comorbidity?	1.Hyprtenion 2.diabetic maltase 3. Dyslipidemia 4.Cardiac 5.HIV 6.Cancer 7. COPD 7. Major organ failure 8 Others (specify)……		
118	Did the patients ever used any of the following substances	Smoking 1. Yes… 2. No… 3. If yes amount (in packet per day) …… Katc 1. Yes…. 2. No…… 3. If yes how frequent Daily…. weekly …. Alcohol 1. yes…. 2. No…… 3. If yes how frequent Daily …. weekly…. 5. Other substances (specify)……		

119	Patents VS during discharge, transfer, refer or death	1. BP….. 2. Pulse….. 3. RR…… 4. To…… 5. Spo2……		
Laboratory investigation at the diagnosis of arrhythmia				
201	CBC	1. WBC……. 2. Hgb ……. 3. ESR……. 4. Lymphocyte…… 5. Platelet……		
202	LFT	1. AST……. 2. ALT…… 3. ALP….		
203	RFT	1. Creatine 2. BUN		
204	Electrolyte	1. Potassium…. 2. Sodium…… 3. Calcium…… 4. Mg 5. Cl		
205	Coagulation profile	1. INR…. 2. PT 3. PTT		
206	Lipid profile	1. LDL. 2. HDL 3. Triglyceride 4. Total cholesterol		
207	Cardiac biomarker	1. CKMB 2. Troponin		
208	Abg	1. PH 2. Pco2 3. Pco3		
209	Image	1. Echo 2. ECG 3. CXR		
210	Patients outcome	1. Discharge ….. 2. Transfer…… 3. Refer….. 4. Death……		
211	Type of medication taken	Antibiotic 1. Vancomycin 2. Meropenem 3. Cefepime 4. Ceftriaxone		

		5. Others Antiviral 1. Remedisever 2. Azithromycin 3. Tocso 4. Others Steroid 1. Dexamethasone 2. Hydrocortisone 3. Predensalon 4. Others Antifungal 1. Fluconazole 2. Cotrimoxazole 3. Caspi fungi 4. Others Vasopressors 1. Dopamine 2. Dobutamine 3. Adrenaline 4. Noradrenaline 5. Others Sedation 1. Ketamine 2. Diazepam 3. Propofol 4. Midazolam 5. Others Antipain 1. Tramadol 2. Morphine 3. Fentanyl 4. Others		

Declaration

I the undersigned declare that the work entitled "Prevalence and associated factor of cardiac arrhythmia among critically ill covid-19 patients at Eka-kotebe covid-19 center Addis Ababa Ethiopia, 2021." presented in this proposal is original. It has not presented to any other places. Where the work of other person has been used, reference has been provided. It is in this regard that I declare this work as original mine.

Investigator Signature Date

Kidest Demessie (Bsc) _____ _____

Advisor

Tefera Mulugeta (Bsc, MSc, Assistant Professor) _____ _____

Co-advisor

Tadesse Bedada**(**Bsc, MSc) _____ _____

Dr. Hussen Mekkonen**(**Bsc, MPH, PhD,Assistant Professor) _____ _____